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Ulusal Travma ve Acil Cerrahi Dergisi

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Our journal is indexed in several prestigious databases, with the indexing history detailed below:

As of 2001, the journal has been indexed in Index Medicus / Medline and Scopus. Starting from 2005, it is included in Excerpta Medica and EMBASE. From 2007 onwards, it has been listed in the Science Citation Index Expanded (SCI-E) and the Journal Citation Reports / Science Edition. Since 2014, the journal is indexed in EBSCOhost and ProQuest. As of 2023, it has been added to PubMed Central.

The journal's impact factor in SCI-E indexed journals is 1.1 according to the 2023 Journal Citation Reports (JCR). In PubMed, the journal is cited as 'Ulus Travma Acil Cerrahi Derg'.

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Unless specifically indicated otherwise at the time of submission, rejected manuscripts will not be returned to the authors, including accompanying materials.

Priority of publications is given to original studies; therefore, selection criteria are more refined for reviews and case reports.

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The cover letter must contain a brief statement that the manuscript has been read and approved by all authors, that it has not been submitted to, or is not under consideration for publication in, another journal. It should contain the names and signatures of all authors. The cover letter is uploaded at the 10th step of the "Submit New Manuscript" section, called "Upload Your Files".

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EXPERIMENTAL STUDY

Comparison of intra-abdominal adhesions formation following implantation of synthetic, biosynthetic, and biologic meshes in a rat model

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ABSTRACT

BACKGROUND: Intra-abdominal adhesions remain a significant challenge in incisional hernia repair, often resulting in complications such as bowel obstruction and chronic pain. Although various prosthetic meshes have been developed, their comparative adhesion profiles have not been fully elucidated. This experimental study aimed to compare the severity of intra-abdominal adhesions and the associated histopathological responses induced by synthetic, biosynthetic, biological, and chemically treated meshes in a standardized rat model.

METHODS: Fifty Wistar albino rats were randomly assigned to five groups (n=10 each): control, polypropylene mesh (Prolene®), polypropylene mesh impregnated with tissue adhesive (Tisseel®), dual mesh (Gore® DualMesh®), and biological mesh (Permacol®). A standardized 2×2 cm full-thickness abdominal wall defect was created in each animal, followed by intraperitoneal mesh implantation. On post-operative day 30, macroscopic adhesions were assessed using the Modified Diamond Scale. Histopathological evaluation included grading of fibrosis, inflammation, vascular proliferation, and giant cell reaction. Statistical analysis was performed using the Kruskal–Wallis test and post hoc multiple comparison analyses.

RESULTS: The Prolene mesh group demonstrated the highest adhesion severity (mean Modified Diamond score: 2.80±1.23), which was significantly greater than that observed in the biological mesh (p=0.010), dual mesh (p=0.002), and tissue adhesive-impregnated Prolene groups (p=0.033). Fibrosis and inflammation were also most pronounced in the Prolene and dual mesh groups, whereas the biological mesh group exhibited milder responses (fibrosis p=0.028; inflammation p=0.033 compared to Prolene). Vascular proliferation and giant cell counts were significantly lower in the biological mesh group (p=0.004 and p<0.001, respectively).

CONCLUSION: Biological and dual meshes, as well as tissue adhesive-treated meshes, were associated with significantly reduced adhesion formation and milder histopathological responses compared to untreated polypropylene mesh. Although no material completely prevented adhesion formation, low-porosity meshes and anti-adhesive strategies appear promising for reducing adhesion-related morbidity in intraperitoneal hernia repair. Further studies are warranted to confirm these findings and optimize mesh selection.

Keywords: Biologic mesh; dual mesh; ıntra-abdominal adhesions; polypropylene mesh; rat model.

INTRODUCTION

Ventral, incisional, and inguinal hernias are common conditions encountered in general surgical practice, affecting millions of individuals worldwide. Incisional hernias develop following surgical procedures, with an incidence reported to be approximately 12.8%, and nearly one-third of affected patients undergo surgical repair.[1]

Over time, a wide range of synthetic and non-synthetic mesh materials have been developed for the repair of anterior ab-

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dominal wall defects. When autologous tissue is insufficient, large defects are commonly managed using prosthetic materials. Among these, polypropylene mesh, introduced in 1962, remains one of the most widely used options, along with polyester, polytetrafluoroethylene (PTFE), and polyglactin (Vicryl®). Despite extensive clinical experience, there is no universally accepted ideal mesh material, as each option presents inherent advantages and limitations.

Meshes placed within the peritoneal cavity elicit a foreign body reaction, leading to adhesion formation in adjacent tissues. Following peritoneal injury, inflammatory exudate is converted into a fibrin matrix, resulting in fibrous bands that connect neighboring structures.[2,3] Intra-abdominal adhesions represent a significant source of post-operative morbidity, including chronic pain and mechanical bowel obstruction.[4] Consequently, numerous experimental and clinical studies have aimed to mitigate adhesion formation associated with mesh use in incisional hernia repair.

Therefore, a comprehensive evaluation of multiple mesh types under identical experimental conditions remains limited in the current literature.

The aim of this study was not only to compare intra-abdominal adhesion formation among different mesh types but also to provide a comprehensive head-to-head evaluation of polypropylene mesh (Prolene®), tissue adhesive-impregnated polypropylene mesh (Tisseel®), dual mesh (Gore® DualMesh®), and biologic mesh (Permacol®) under standardized experimental conditions.

MATERIALS AND METHODS

Animals and Experimental Design

This study was approved by the Ankara University Local Ethics Committee for Animal Experiments (decision number: 2013-16-125, date: 25.09.2013).

The experimental procedures were conducted between November 2013 and April 2014.

In this study, 50 Wistar albino rats weighing 200–250 g, obtained from the same laboratory, were used. The animals were housed at room temperature in standard cages in groups of five. Standard laboratory chow and tap water were provided ad libitum before and after the procedures. The rats were randomly divided into five groups of 10 animals each: Group I (control), Group II (polypropylene mesh, Prolene®), Group III (polypropylene mesh impregnated with tissue adhesive, Tisseel®), Group IV (dual mesh, Gore® DualMesh®), and Group V (biological mesh, Permacol®).

Surgical Procedure

All procedures were performed under sterile conditions. Anesthesia was induced intramuscularly using ketamine (40 mg/kg) and xylazine (5 mg/kg). Spontaneous respiration was maintained throughout the procedure. A single pre-operative intramuscular dose of ceftazidime pentahydrate (20 mg/kg) was administered for antibiotic prophylaxis.

The anterior abdominal wall was shaved and cleansed with 10% povidone-iodine (Fig. 1). A 3 cm midline incision was made, extending above and below the umbilicus, and skin flaps were prepared by separating the subcutaneous tissue from the fascia bilaterally (Fig. 2,3). A standardized 2×2 cm full-thickness abdominal wall defect, including muscle, fascia, and peritoneum, was created using a 2 cm transverse incision (1 cm to the left and right of the midline) and 2 cm longitudinal pararectal incisions. The abdominal wall segment was excised to directly expose the intra-abdominal contents.

Sterilized mesh materials measuring 3×2.5 cm were placed intraperitoneally using the inlay technique. Each mesh was fixed to the abdominal wall fascia approximately 0.5 cm behind the wound edges using 6/0 polypropylene sutures (Prolene®, Ethicon, USA) at the upper corners and along the medial and lateral borders. The skin was closed continuously with 3/0 silk sutures (Fig. 1).

On post-operative day 30, the animals were euthanized with high-dose ether anesthesia. A U-shaped relaparotomy incision was made from the lateral abdominal walls, extending from below the costal margins to the pelvis, to avoid disruption of the implantation site (Fig. 2).

Evaluation of Adhesions

Adhesions were assessed macroscopically using the Modified Diamond Scale, which grades adhesion extent, vascularity, and tenacity. The scoring criteria are summarized in Table 1. Histopathological assessment included grading of fibrosis, inflammation, vascular proliferation, and foreign body giant cell reaction, according to the criteria presented in Table 2.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 11.5 (SPSS Inc., Chicago, IL, USA). For continuous variables, descriptive statistics were presented as mean±standard deviation (SD) (median [minimum–maximum]). Comparisons between independent groups were performed using the Kruskal–Wallis test. When statistically significant differences were identified, post hoc



Figure 1. An experimental animal prepared for surgery.

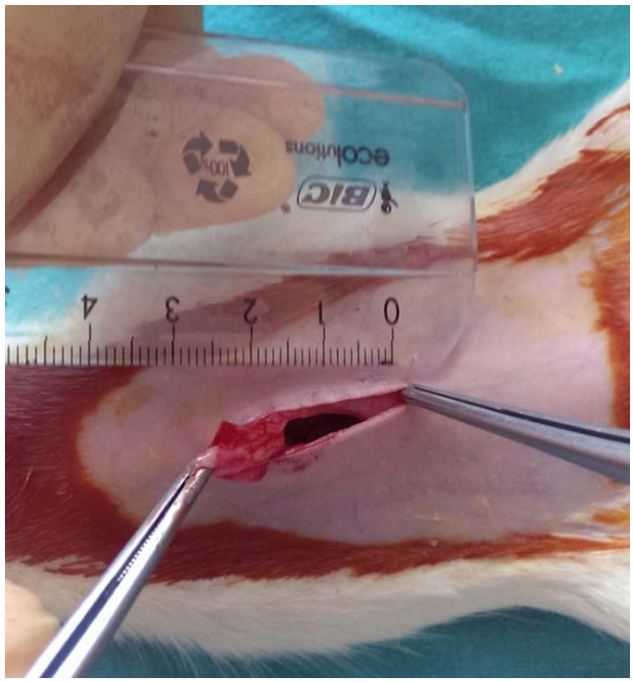


Figure 2. A 3 cm midline laparotomy was performed on the subjects.

multiple comparison tests were applied to determine the specific group differences.

RESULTS

Macroscopic Adhesion Assessment

The Modified Diamond Scale scores differed significantly among the groups (p=0.002). The Prolene mesh group demonstrated the highest adhesion severity (mean±SD: 2.80±1.23; median [1–4]), which was significantly greater than that observed in the control (p<0.001), tissue adhesive-impregnated Prolene (p=0.033), dual mesh (p=0.002), and biological mesh groups (p=0.010). The tissue adhesive-impregnated Prolene group exhibited lower adhesion scores compared to Prolene alone but remained higher than the control group (p=0.026). Overall, adhesions requiring sharp dissection were most frequently observed in the Prolene group, whereas the biological and dual mesh groups exhibited less extensive adhesions.

Fibrosis

Fibrosis scores also showed significant variation among the groups (p<0.001). The Prolene and tissue adhesive-impregnated Prolene groups exhibited the highest fibrosis levels (both 2.60±0.52), significantly exceeding those of the control (p<0.001) and dual mesh groups (p<0.001). The biological mesh group demonstrated moderate fibrosis (2.00±0.67), which was significantly lower than that observed in the Prolene group (p=0.028) but higher than the control group (p=0.006). The dual mesh group showed significantly lower fibrosis compared to both the Prolene (p<0.001) and tissue adhesive-impregnated Prolene groups (p<0.001) (Fig. 3).

Inflammation

Inflammation differed significantly among the groups (p<0.001). The dual mesh group demonstrated the highest inflammation scores (2.20±0.42), significantly exceeding all other groups (dual vs. control: p<0.001; dual vs. biological mesh: p=0.001; dual vs. tissue adhesive-impregnated Prolene: p=0.001). The Prolene group also exhibited moderate inflam-

Table 1. Adhesion scores

Score	Extent (percentage of silastic surface covered by adhesions (%)	Type	Tenacity
0	None	None	None
1	25<	Filmly, no vessels (trans-parent)	Adhesions essentially fell apart
2	25–50	Filmly, no vessels (transpar-ent)	Adhesions lysed with traction
3	50–75	Dense, vascular, small vessels	Adhesions required sharp dissection
4	75>	Dense, vascular, and big ves-sels	

Table 2. Histopatological observation scores

Score	Fibrosis	Inflamation	Vascular proliferation	Giant cell
0	None	None	None	None
1	Mild intensity	giant cells in all areas intestinal lymphocyte and plasma cells	Mild intensity	A small number
2	Moderate intensity	at each site (giant cells eosinophil neutrophil)	Moderate intensity	Medium number
3	Intense	many inflammatory cells and micro-abscesses at each site	İntense	Large number

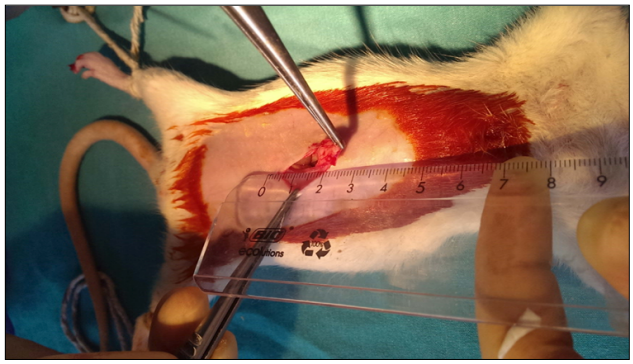


Figure 3. A 2×2 cm anterior abdominal wall defect was prepared.

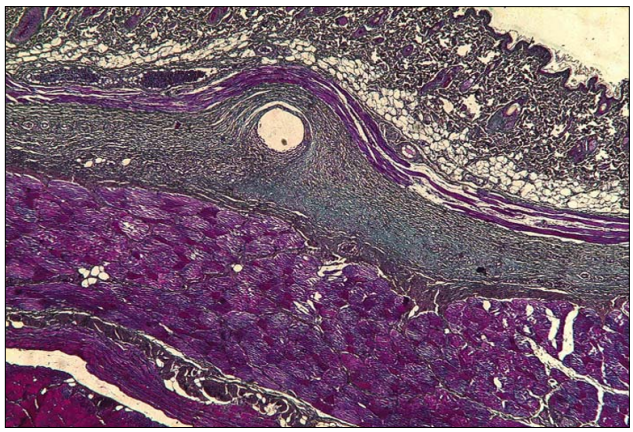


Figure 4. Biological mesh. Mild fibrosis was observed (Masson Trichrome, ×40).

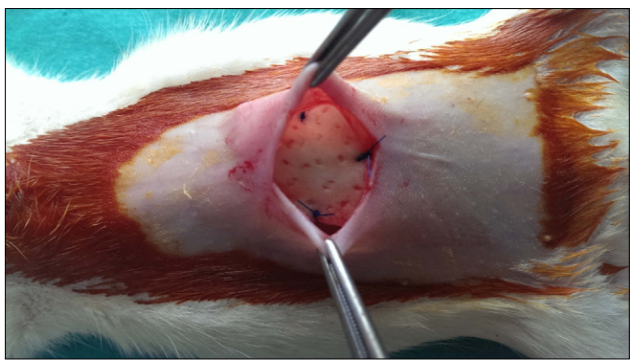


Figure 5. Mesh fixed to the abdominal wall.

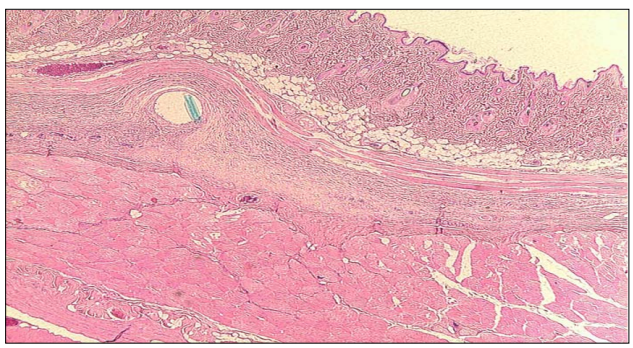


Figure 6. Biological mesh. No significant multinucleated giant cells were observed in the abdominal wall (Hematoxylin and Eosin, ×40).

mation (1.90±0.57), which was significantly higher than that observed in the control ($p<0.001$) and biological mesh groups ($p=0.033$) (Fig. 5). The biological mesh group demonstrated mild inflammation, similar to that observed in the tissue adhesive-impregnated Prolene group (both 1.40±0.52) (Fig. 4).

Vascular Proliferation

Vascular proliferation scores differed significantly among the groups ($p<0.001$). The dual mesh group exhibited the highest vascular proliferation (2.10±0.57), which was significantly greater than that observed in the Prolene ($p=0.011$), tissue adhesive-impregnated Prolene ($p=0.001$), and biological mesh groups ($p<0.001$). The biological mesh group demonstrated minimal vascular proliferation (0.50±0.71), which was significantly lower than that observed in the Prolene group ($p=0.004$) (Fig. 5).

Foreign Body Giant Cell Reaction

Giant cell counts also differed significantly among the groups ($p<0.001$). The dual mesh group elicited the most prominent giant cell response (2.80±0.42), significantly exceeding all other groups ($p<0.001$). The Prolene and tissue adhesive-impregnated Prolene groups demonstrated moderate reactions (1.80±0.63 and 1.50±0.53, respectively), whereas the biological mesh group exhibited minimal giant cell presence (0.30±0.48) (Fig. 6). Comparisons between the biological mesh and Prolene groups ($p<0.001$), as well as between the dual mesh and Prolene groups ($p<0.001$), were statistically significant (Fig. 6). A detailed comparison of all findings is presented in Table 3.

DISCUSSION

Abdominal wall defects may occur following trauma, infection, incisional hernia, or resection of large abdominal wall tumors. Such defects are managed either by primary closure or by the use of prosthetic materials. Despite their clinical utility, adhesions frequently develop following elective intra-abdominal procedures or the placement of prosthetic meshes. These adhesions may result in serious complications, including intestinal obstruction, chronic abdominal pain, enterocutaneous fistula formation, technically challenging reoperations, and infertility in women.[5]

The primary objective in the repair of abdominal wall defects is to restore tensile strength through fibrous tissue regeneration. During fascial healing, proliferating myofibroblasts produce collagen, which subsequently forms scar tissue. However, as remodeling progresses, only approximately 20% of the original tensile strength of the fascia is restored. Because this scar tissue lacks the mechanical properties of native fascia, it is insufficient to withstand normal intra-abdominal pressures. Therefore, reinforcement with synthetic grafts has become standard practice. Various materials, including silver, steel, tantalum, cellulose, polyvinyl, nylon, silastic, and carbon fibers, have been investigated; however, most were abandoned over time due to technical challenges and associated complications.

Intra-abdominal adhesions are among the most concerning complications for surgeons. Adhesions are abnormal fibrous connections between serosal surfaces that normally remain separate and typically form following peritoneal injury. Predisposing factors include advanced age, malnutrition or obesity, pulmonary disease, and repeated surgical interventions at the

Table 3. Comparison of groups by degree of adhesion

Parameter	Group	Descriptive Statistics*	p	Compreation	p
Modified diamond scale	Control (1)	0.30±0.48 (0 [0–1])	0.002	1–2	<0.001
	Prolen (2)	2.80±1.23 (3 [1–4])		1–3	0.026
	Tissue adhesive-impregnated prolene (3)	1.40±1.27 (1 [0–4])			
				2–3	0.033
	Dual (4)	0.90±1.29 (0.5 [0–4])		2–4	0.002
	Biological mesh (5)	1.30±1.49 (1 [0–4])		2–5	0.010
Fibrosis	Control (1)	1.10±0.74 (1 [0–2])	<0.001	1–2	<0.001
	Prolen (2)	2.60±0.52 (3 [2–3])		1–3	<0.001
	Tissue adhesive-impregnated prolene (3)	2.60±0.52 (3 [2–3])		1–5	0.006
	Dual (4)	1.50±0.53 (1.5 [1–2])		2–4	<0.001
				2–5	0.028
	Biological mesh (5)	2.00±0.67 (2 [1–3])		3–4	<0.001
				3–5	0.028
Inflamation	Control (1)	0.60±0.52 (1 [0–1])	<0.001	1–2	<0.001
	Prolen (2)	1.90±0.57 (2 [1–3])		1–3	0.005
	Tissue adhesive-impregnated prolene (3)	1.40±0.52 (1 [1–2])		1–4	<0.001
	Dual (4)	2.20±0.42 (2 [2–3])		1–5	0.005
				2–3	0.033
	Biological mesh (5)	1.40±0.52 (1 [1–2])		2–5	0.033
				3–4	0.001
				4–5	0.001
Vascular	Control (1)	0.50±0.53 (0.5 [0–1])	<0.001	1–2	0.004
	Prolen (2)	1.30±0.48 (1 [1–2])		1–3	0.027
	Tissue adhesive-impregnated prolene (3)	1.10±0.57 (1 [0–2])		1–4	<0.001
	Dual (4)	2.10±0.57 (2 [1–3])		2–4	0.011
				2–5	0.004
	Biological mesh (5)	0.50±0.71 (0 [0–2])		3–4	0.001
				3–5	0.028
				4–5	<0.001
Giant cell	Control (1)	0.00±0.00 (0 [0–0])	<0.001	1–2	<0.001
	Prolen (2)	1.80±0.63 (2 [1–3])		1–3	<0.001
	Tissue adhesive-impregnated prolene (3)	1.50±0.53 (1.5 [1–2])		1–4	<0.001
	Dual (4)	2.80±0.42 (3 [2–3])		2–4	<0.001
				2–5	<0.001
	Biological mesh (5)	0.30±0.48 (0 [0–1])		3–4	<0.001
				3–5	<0.001
				4–5	<0.001

same site.[6] Ischemia is a major contributor to adhesion formation. Experimental studies have demonstrated that adhesions are less likely to develop in the absence of ischemia. Conversely, when ischemia affects intact mesothelial surfaces, adhesion formation becomes more likely. Local fibrinolytic activity increases in non-ischemic tissues and decreases in ischemic areas, thereby promoting adhesion development.

Although numerous studies have compared different mesh types, to our knowledge, no previous study has simultaneously evaluated biological mesh alongside synthetic, biosynthetic, and tissue adhesive-impregnated meshes within a single experimental model. In experimental rat models, several anti-adhesion strategies have been investigated, demonstrating varying degrees of efficacy in reducing adhesion formation following peritoneal injury, including crystalloids such as methylene blue and Ringer's lactate, as well as barrier agents such as Seprafilm and Interceed.[7-9] Matthews et al.[10] compared intraperitoneally placed Prolene and PTFE meshes in rabbits, assessing adhesion rates by microlaparoscopy at 1, 3, 9, and 16 weeks. They reported a higher incidence of adhesions with Prolene (55%) compared to PTFE (30%) meshes.

Peritoneal injury initiates the cascade leading to adhesion formation, with the extent of tissue damage determining the severity of the inflammatory response and subsequent adhesion development. Accordingly, meticulous surgical technique – minimizing tissue trauma, maintaining hemostasis, avoiding thermal injury, and preventing contamination – has been shown to reduce post-operative adhesions.[11] In addition, Minardi et al.[12] suggested that hernia repair outcomes may be improved by enhancing early vascularization through the incorporation of elastin into collagen-based meshes. In the present study, macroscopic assessment using the Modified Diamond Scale revealed significantly fewer severe adhesions in the biological mesh group compared to the Prolene mesh group ($p=0.001$). Adhesions requiring sharp dissection were predominant in the Prolene group, whereas most adhesions in the biological mesh group could be separated by traction. A significant reduction in adhesion severity was also observed in the tissue adhesive-impregnated Prolene mesh group compared to untreated Prolene ($p=0.033$). Experimental studies have also explored the use of fibrin sealants for mesh fixation, reporting adequate mechanical stability and favorable tissue response without increased adverse effects.[13]

Meshes with lower porosity, such as dual mesh and biological mesh, tend to form encapsulated barriers associated with reduced adhesion formation. In these materials, fibrin deposition is limited to discrete areas, resulting in a milder inflammatory response. Overall, all mesh types were associated with some degree of adhesion formation; however, adhesions were less extensive in low-porosity meshes and in those treated with tissue adhesives. Furthermore, histopathological analysis in the present study demonstrated significantly lower levels of inflammation, fibrosis, and foreign body giant cell reaction in the biological mesh group compared to the other groups.

Recent experimental studies have focused on evaluating composite and barrier-coated meshes to minimize adhesion formation following intraperitoneal implantation.[14] Several clinical and experimental studies have reported increased adhesion-related complications following intraperitoneal placement of uncoated polypropylene meshes, whereas composite barrier-coated and biologic meshes have been associated with reduced adhesion severity and improved biocompatibility.[4,15]

More recent animal studies support these findings, demonstrating that the use of barrier-coated or biological meshes reduces foreign body reaction, fibrosis, and vascular proliferation, and suggesting their preferential use in intraperitoneal applications.[16] In line with these data, the present study confirms that biological and dual meshes, as well as tissue adhesive-treated polypropylene meshes, elicit significantly milder macroscopic and histopathological responses compared to conventional polypropylene meshes, thereby supporting current approaches aimed at optimizing mesh selection and surface modification strategies in abdominal wall reconstruction.

More recent evidence has emphasized the importance of mesh composition and biomechanical properties. Deeken and Lake demonstrated that the structural and mechanical characteristics of mesh materials significantly influence tissue integration and host response.[17]

In addition, available evidence highlights the importance of careful mesh selection, particularly when considering biologic and biosynthetic materials in abdominal wall reconstruction.[18]

Furthermore, biosynthetic and biologic meshes have been shown to provide favorable outcomes in selected high-risk settings, supporting their role in reducing inflammatory response and improving tissue compatibility.[19]

Recent randomized evidence has demonstrated differences between biologic and synthetic meshes in contaminated ventral hernia repair, further highlighting the importance of appropriate mesh selection.[20]

However, most of these studies are limited to pairwise comparisons or focus on a single mesh type or modification strategy. In contrast, the present study provides a comprehensive head-to-head comparison of polypropylene mesh (Prolene®), tissue adhesive-impregnated polypropylene mesh (Tisseel®), dual mesh (Gore® DualMesh®), and biologic mesh (Permacol®) within a standardized experimental model. This design enables direct comparison of both macroscopic adhesion formation and detailed histopathological responses across multiple mesh types.

Importantly, the present study extends the existing literature by offering a multi-dimensional evaluation that integrates both macroscopic and histopathological outcomes under identical experimental conditions. This approach provides a more robust and clinically relevant comparison than previous studies.

CONCLUSION

This study differs from most previous investigations that have focused on the effects of coating on mesh structure or have evaluated meshes with different pore characteristics.

Given the high cost and technical challenges associated with biological meshes, this study aimed to assess whether these approaches provide a meaningful clinical advantage at the experimental level. Accordingly, we sought to address not only the hypothesis that "different materials yield better outcomes" but also whether the additional cost and complexity are justified.

Although previous studies – particularly those comparing coated meshes with biological meshes – have contributed substantially to the field, experimental studies incorporating a four-group comparison under conditions that preserve mesh structure and evaluate practical applicability remain limited. In this context, the present study contributes to both scientific understanding and potential clinical application.

Unlike previous studies, this work provides a comprehensive comparative evaluation of multiple mesh types under standardized experimental conditions.

This experimental study demonstrated that biological and dual meshes, as well as polypropylene meshes treated with tissue adhesive, resulted in significantly reduced adhesion formation and milder histopathological reactions compared to conventional Prolene mesh. Although no material completely prevented adhesion formation, lower-porosity meshes and anti-adhesive strategies consistently reduced adhesion severity. These findings support the preferential use of biologic or composite meshes in intraperitoneal applications to minimize adhesion-related complications. Further research is required to identify strategies that can completely prevent adhesion formation.

Ethics Committee Approval: This study was approved by the Ankara University Local Ethics Committee for Animal Experiments (Date: 25.09.2013, Decision No: 2013-16-125).

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Authorship Contributions: Concept: Ş.O.; Design: Ş.O.; Supervision: A.Ç.; Resource: Ş.O.; Materials: Ş.O.; Data collection and/or processing: Ş.O.; Analysis and/or interpretation: Ş.O.; Literature review: A.Ç.; Writing: Ş.O.; Critical review: Ş.O.

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DENEYSEL ÇALIŞMA - *ÖZ*

Rat modelinde sentetik, biyosentetik ve biyolojik ağların implantasyonunu takiben karın içi yapışıklık oluşumunun karşılaştırılması

AMAÇ: İntraabdominal adezyonlar, insizyonel herni onarımında bağırsak obstrüksiyonu ve kronik ağrı gibi komplikasyonlara yol açabilen önemli bir sorun olmaya devam etmektedir. Çeşitli prostetik mesh materyalleri geliştirilmiş olmakla birlikte, bu materyallerin adezyon profillerinin karşılaştırmalı değerlendirmesi tam olarak ortaya konulamamıştır. Bu deneysel çalışmada, standartlaştırılmış bir sıçan modelinde sentetik, biyosentetik, biyolojik ve kimyasal olarak modifiye edilmiş meshlerin oluşturduğu intraabdominal adezyon şiddeti ve buna eşlik eden histopatolojik reaksiyonların karşılaştırılması amaçlanmıştır.

GEREÇ VE YÖNTEM: Elli Wistar albino sıçan rastgele beş gruba ayrıldı (her grupta n=10): kontrol, polipropilen mesh (Prolene®), doku yapıştırıcısı emdirilmiş polipropilen mesh (Tisseel®), dual mesh (Gore® DualMesh®) ve biyolojik mesh (Permacol®). Her hayvanda standart 2×2 cm tam kat abdominal duvar defekti oluşturuldu ve ardından meshler intraperitoneal olarak implante edildi. Postoperatif 30. günde makroskopik adezyonlar Modified Diamond Skalası kullanılarak değerlendirildi. Histopatolojik incelemede fibrozis, inflamasyon, vasküler proliferasyon ve dev hücre reaksiyonu derecelendirildi. İstatistiksel analiz Kruskal–Wallis ve çoklu karşılaştırma testleri ile gerçekleştirildi.

BULGULAR: Prolene mesh en yüksek adezyon şiddetini gösterdi (ortalama Modified Diamond Skoru: 2.80±1.23) ve biyolojik mesh (p=0.010), dual mesh (p=0.002) ve doku yapıştırıcısı emdirilmiş Prolene grubuna (p=0.033) kıyasla anlamlı derecede daha yüksek bulundu. Fibrozis ve inflamasyon en belirgin olarak Prolene ve dual mesh gruplarında gözlenirken, biyolojik mesh grubunda daha hafif reaksiyonlar saptandı (Prolene ile karşılaştırıldığında fibrozis için p=0.028; inflamasyon için p=0.033). Vasküler proliferasyon ve dev hücre sayıları biyolojik mesh grubunda anlamlı derecede daha düşüktü (sırasıyla p=0.004 ve p<0.001).

SONUÇ: Biyolojik ve dual meshler ile doku yapıştırıcısı ile modifiye edilmiş meshler, işlenmemiş polipropilen mesh ile karşılaştırıldığında anlamlı derecede daha az adezyon oluşumu ve daha düşük histopatolojik yanıt ile ilişkili bulunmuştur. Hiçbir materyal adezyonları tamamen önleyememiş olsa da, düşük poroziteli meshler ve antiadezif stratejiler intraperitoneal herni onarımında adezyona bağlı morbiditenin azaltılmasında umut verici görünmektedir. Bu bulguların doğrulanması ve optimal mesh seçiminin belirlenmesi için ileri çalışmalara ihtiyaç vardır.

Anahtar sözcükler: Cerrahi mesh; hayvan modeli; insizyonel herni; karın içi yapışıklıklar.

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EXPERIMENTAL STUDY

Mitochondrial transplantation attenuates apoptosis and improves spermatogenic function following testicular torsion-detorsion injury in rats

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ABSTRACT

BACKGROUND: Testicular torsion is a urological emergency that may result in irreversible ischemia-reperfusion injury and long-term impairment of spermatogenic function despite timely surgical detorsion. Mitochondrial dysfunction plays a central role in oxidative stress-induced germ cell damage following torsion. This study aimed to investigate the protective effects of isolated intratesticular mitochondrial transplantation in a rat model of testicular torsion-detorsion injury.

METHODS: Thirty-six adult male Sprague-Dawley rats were randomly allocated into four groups: sham (n=4), torsion (n=10), torsion+vehicle (n=10), and torsion+mitochondria (n=10). Testicular torsion was induced by a 720° rotation for 2 h, followed by surgical detorsion. Isolated mitochondria were administered through intratesticular injection before torsion induction. Histopathological evaluation was performed using hematoxylin–eosin staining and quantified by the Johnsen scoring system. Apoptotic activity was assessed by Caspase-3 immunohistochemistry. Functional outcomes were evaluated through total sperm count, motile sperm count, and detailed sperm motility subtype analysis.

RESULTS: The torsion and vehicle groups demonstrated marked histological damage, significantly reduced Johnsen scores, and increased apoptotic activity compared with the sham group. Mitochondrial transplantation significantly preserved seminiferous tubular architecture and resulted in higher Johnsen scores compared with untreated torsion (9.7±0.4 vs. 6.4±1.0, $p<0.001$). Caspase-3 expression was significantly reduced in the mitochondria-treated group, approaching levels observed in sham animals. Functionally, total and motile sperm counts were significantly higher in mitochondria-treated rats than in torsion and vehicle groups. Detailed motility analysis revealed restoration of progressive sperm motility patterns, whereas progressive motility was completely absent in untreated ischemic groups.

CONCLUSION: Intratesticular mitochondrial transplantation provides significant structural and functional protection against ischemia-reperfusion injury in experimental testicular torsion. By preserving spermatogenic architecture, reducing apoptosis, and restoring progressive sperm motility, mitochondrial therapy represents a promising experimental strategy for fertility preservation in ischemic testicular disorders.

Keywords: Apoptosis; ischemia-reperfusion injury; mitochondrial transplantation; spermatogenesis; testicular torsion.

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INTRODUCTION

Ischemia-reperfusion (I/R) injury remains one of the leading causes of tissue damage in surgical and urological emergencies, such as testicular torsion, renal transplantation, and major vascular procedures.[1] In particular, testicular torsion-detorsion (TTD) represents a time-critical urological emergency that compromises microcirculatory perfusion, leading to germ cell apoptosis, oxidative stress, and impaired spermatogenesis.[2] Even when timely surgical detorsion is achieved, the restoration of blood flow can paradoxically aggravate tissue damage through the excessive generation of reactive oxygen species (ROS), mitochondrial dysfunction, and disruption of the blood–testis barrier.[3] Current therapeutic strategies, including antioxidant and anti-inflammatory agents, have demonstrated only partial success, and no pharmacological approach has yet been proven to fully restore testicular structure and function following I/R injury.[4-6]

Mitochondria play a central role in energy metabolism, redox balance, and cell survival.[7] They are particularly abundant in testicular and sperm cells, where they supply adenosine triphosphate (ATP) required for spermatogenesis and sperm motility.[8] Increasing evidence indicates that mitochondrial injury during reperfusion is a key event driving germ cell apoptosis and testicular atrophy.[9] Therefore, strategies aimed at preserving or restoring mitochondrial function have gained growing attention. Mitochondrial transplantation has recently emerged as a promising therapeutic strategy for ischemic tissue injury.[10] Studies in cardiac, hepatic, and renal models have demonstrated that the delivery of isolated functional mitochondria into damaged tissues can restore bioenergetic capacity, reduce oxidative stress, and improve histological recovery.[11-13] Experimental findings further suggest that transplanted mitochondria are capable of integrating into host cells, maintaining membrane potential, and activating prosurvival signaling pathways.[14] Although mitochondrial transplantation has been successfully applied in several organ systems, its potential role in testicular I/R injury remains largely unexplored.[15] Previous research has mainly focused on mesenchymal stem cell-based or paracrine antioxidant mechanisms, while the direct restoration of mitochondrial integrity in reproductive tissues has not been systematically evaluated.[16] Moreover, the mechanisms by which exogenous mitochondria modulate germ cell apoptosis and spermatogenic recovery following torsion-detorsion injury are not yet fully understood.

In this study, we aimed to investigate the protective and regenerative effects of isolated mitochondrial transplantation in a rat model of TTD injury, focusing on its impact on spermatogenesis, histopathological alterations, and mitochondrial integrity markers.

MATERIALS AND METHODS

All experimental procedures were approved by the Saki Yenilli Experimental Animals Production and Research Laboratory Local Ethics Committee (Approval No: 14, Date: 02.12.2022) and conducted in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals

A total of 36 adult male Sprague-Dawley rats (12–14 weeks old, 250–350 g) were used. Animals were maintained under standard laboratory conditions (temperature 22–24°C, 45–55% humidity, 12-h light/dark cycle) with free access to food and water. Before all procedures, animals were fasted overnight but allowed water ad libitum. Two additional rats were used exclusively for mitochondrial isolation and verification procedures.

Experimental Design

Rats were randomly assigned to four groups: Sham, torsion, torsion+vehicle, and torsion+mitochondria. The sham group underwent scrotal incision and immediate replacement of the testis without torsion. In the torsion group, the left testis was twisted 720° clockwise and fixed for 2 h to induce ischemia, followed by detorsion.[17,18] The vehicle group received intratesticular injection of respiration buffer before torsion, while the mitochondria group received an equal volume containing isolated mitochondria.[12,19] The 2-h torsion period was selected based on prior studies demonstrating reproducible ischemic damage without total necrosis, allowing subsequent evaluation of reperfusion-related recovery.[17,18]

Anesthesia and Surgical Procedure

Anesthesia was induced by intraperitoneal injection of ketamine (90 mg/kg) and xylazine (10 mg/kg). Through a midline scrotal incision, the left testis was gently exteriorized and rotated 720° clockwise, then fixed to the scrotal wall with a 4-0 atraumatic silk suture to maintain ischemia. After 2 h, detorsion was achieved by returning the testis to its natural position, and the incision was closed with interrupted 4-0 silk sutures. In the sham group, only scrotal incision and immediate repositioning were performed without torsion. Postoperative analgesia was ensured with meloxicam (1 mg/kg, s.c.), and all animals were monitored for recovery.

Mitochondrial Isolation

Allogeneic biceps femoris muscle was used as the mitochondrial source. Isolation was carried out at +4°C under hypothermic conditions using a commercial kit (Mitochondria Isolation Kit for Tissue and Cultured Cells, ab288084; Abcam, UK) according to the manufacturer's instructions.[12,19]

Briefly, 200 mg of freshly harvested skeletal muscle was washed twice in isolation buffer, minced into small fragments, and homogenized with a Dounce homogenizer (10 strokes). The homogenate was centrifuged at 600 × g for 10 min to remove debris, followed by centrifugation of the supernatant at 7000 × g for 10 min to obtain the mitochondrial pellet. The pellet was washed with isolation buffer, resuspended in storage buffer, and kept on ice until transplantation.

Mitochondrial protein concentration was quantified using a BCA Protein Assay Kit (Thermo Fisher Scientific, 23225), and

the target transplantation dose was calculated

Mitochondrial Transplantation Procedure

Under sterile conditions, isolated mitochondria (150 µg protein/100 µL respiration buffer) were injected into the left testis using a 30G insulin syringe.[10,12,19] The needle was inserted at a 45° angle from the lower pole toward the upper pole; injection was performed slowly while withdrawing the needle to ensure homogeneous distribution. In the vehicle group, an equivalent volume of respiration buffer was administered. All injections were performed immediately before torsion induction.

Tissue Collection

At 14 days after detorsion, rats were anesthetized and sacrificed by cardiac exsanguination under deep anesthesia (National Research Council, 2011). Bilateral orchiectomy was performed. The left testis and epididymis were dissected, rinsed with isotonic saline, and divided for histopathological, immunohistochemical, and spermatological analyses. Tissues for histology were fixed in 10% neutral-buffered formalin, while samples for molecular assays were snap-frozen in liquid nitrogen and stored at −80°C.

Histopathological Evaluation

Formalin-fixed, paraffin-embedded tissue blocks were sectioned at 5 µm and stained with hematoxylin and eosin. Fifty seminiferous tubules per section were examined under light microscopy at 400× magnification. Spermatogenic activity was scored using the Johnsen scoring system (0–10 scale). Mean Johnsen scores were 3.6±0.8 (vehicle), 6.4±1.0 (torsion), 9.2±0.5 (sham), and 9.7±0.4 (mitochondria), indicating partial to complete recovery in the treatment group.[20]

Immunohistochemical Analysis

Apoptotic activity was assessed by Caspase-3 immunohistochemistry.[21] Sections were deparaffinized, rehydrated, and incubated with primary anti-Caspase-3 antibody (1:100, Abcam, UK), followed by a secondary antibody system. Visualization was achieved using 3,3′-diaminobenzidine substrate, and nuclei were counterstained with hematoxylin. The percentage of Caspase-3-positive cells was semi-quantitatively scored based on staining intensity and localization testis.

Spermatological Evaluation

The epididymis was dissected in accordance with its anatomical structure and minced into small pieces in 5 mL of normal saline at 37°C. Samples were incubated for 15 min, and the supernatant was filtered through gauze. The sperm suspension was examined using a Makler counting chamber under 200× magnification.[22] The epididymal sperm preparation protocol was adapted from Makler's method with minor modifications suitable for rodent models.

Motile and immotile spermatozoa were counted in 100 fields, and three independent counts were averaged per animal. The mitochondria-treated and sham groups exhibited significantly higher total and motile sperm counts compared with the torsion and vehicle groups ($p<0.05$). Sperm motility was evaluated according to the World Health Organization criteria and categorized into fast progressive (Type A), slow progressive (Type B), non-progressive (Type C), and immotile (Type D) spermatozoa. Total motility was calculated as the sum of Types A and B. In addition, sperm concentration ($\times 10^6$/mL) and normal morphology percentage were assessed using standard light microscopy.

Statistical and Power Analysis

Statistical analyses were performed using IBM Statistical Package for the Social Sciences Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Data distribution was assessed for normality using the Shapiro–Wilk test. Continuous variables are presented as mean±standard deviation. For comparisons among more than two independent groups, one-way analysis of variance (ANOVA) was used for normally distributed data, followed by Tukey's post hoc test for multiple comparisons. For non-normally distributed data, the Kruskal-Wallis test was applied, followed by pairwise Mann–Whitney U tests with Bonferroni correction. Categorical variables, including sperm motility subtype distributions, were analyzed using the Chi-square test or Fisher's exact test where appropriate. A two-tailed $p<0.05$ was considered statistically significant. Post hoc power analysis was conducted using G*Power software (version 3.1.9.7; Heinrich Heine University, Düsseldorf, Germany). Based on the observed effect sizes for the primary outcomes, including Johnsen score and motile sperm count, the achieved statistical power exceeded 0.80 for detecting large effect sizes ($f\geq0.45$) at an alpha level of 0.05.

RESULTS

A total of 36 adult male Sprague-Dawley rats were included in the study: sham (n=4), torsion (n=10), torsion+vehicle (n=10), and torsion+mitochondria (n=10) groups. Two additional animals were used exclusively for mitochondrial isolation and verification. All animals survived the procedure, and no perioperative complications or mortality occurred. TTD was successfully completed in all rats, and post-operative recovery was uneventful. Comparative biochemical and histopathological findings are summarized in Table 1, and representative photomicrographs are shown in Figure 1.

After detorsion, ischemic changes such as testicular swelling, discoloration, and vascular congestion were prominent in the torsion and vehicle groups, whereas these changes were notably attenuated in the mitochondria-treated group. No adverse local or systemic reactions were detected following mitochondrial injection.

Histopathological Findings

Light microscopic evaluation revealed marked degeneration of seminiferous tubules, germ cell loss, and interstitial edema in the torsion and vehicle groups. Conversely, the mitochondria-treated group demonstrated well-preserved

Table 1. Comparison of histopathological and spermatological parameters among study groups

Parameter	Sham (n=4)	Torsion (n=10)	Torsion+Vehicle (n=10)	Torsion+Mitochondria (n=10)	p
Johnsen score	9.2±0.5	6.4±1.0	3.6±0.8	9.7±0.4	<0.001[a]
Caspase-3 positivity (% cells)	12.4±3.2	54.1±8.7	58.3±9.1	18.6±4.5	<0.01[b]
Total sperm count (×10⁶/mL)	28±3.8	6±3.4	5±3.2	22±3.6	<0.05[a]
Motile sperm count (×10⁶/mL)	19.9±3.5	1.3±0.2	1.2±0.2	15±2.6	<0.05[a]
Normal morphology (%)†	92	28	24	68	<0.05[a]

[a]One-way analysis of variance with Tukey's post hoc test. [b]Kruskal–Wallis test followed by Mann–Whitney U test. †Normal morphology values are presented as group means. Values are presented as mean±standard deviation (SD).

tubular architecture, intact germinal epithelium, and restored spermatogenic organization similar to that of the sham group. Quantitative analysis based on the Johnsen scoring system showed significantly higher spermatogenic activity in the mitochondria-treated group (9.7±0.4) compared with the torsion (6.4±1.0) and vehicle (3.6±0.8) groups ($p<0.001$). There was no significant difference between the mitochondria-treated and sham (9.2±0.5) groups ($p>0.05$) (Table 1 and Fig. 1a-d).

Apoptotic Activity (Caspase-3 Immunohistochemistry)

Immunohistochemical assessment of Caspase-3 expression demonstrated intense cytoplasmic and nuclear positivity in germ cells and Sertoli cells in the torsion and vehicle groups, indicating heightened apoptotic activity. In contrast, the mitochondria-treated group showed markedly reduced Caspase-3 immunoreactivity, comparable to the sham animals (Fig. 2). Semi-quantitative scoring confirmed a significant reduction in Caspase-3 positivity in the mitochondria group relative to the torsion and vehicle groups ($p<0.01$).

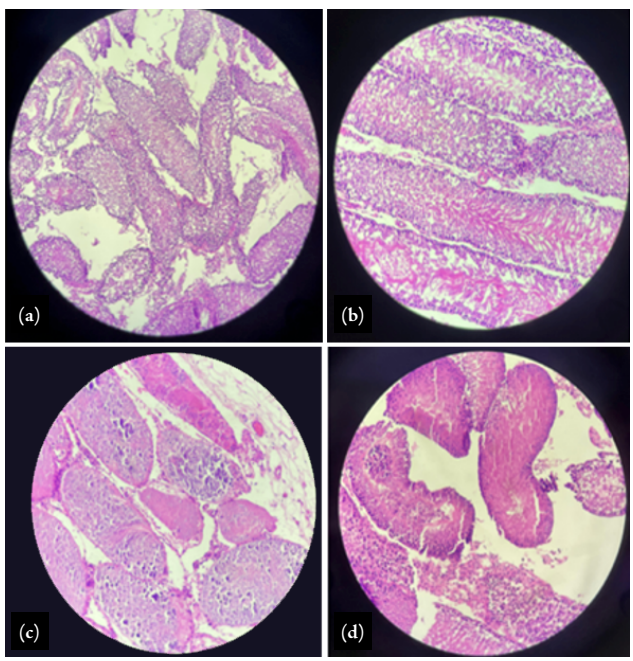


Figure 1. Representative hematoxylin and eosin-stained sections of seminiferous tubules in each group. **(a)** Sham (Johnsen Score: 9.2), **(b)** Torsion+Mitochondria (9.7), **(c)** Torsion+Vehicle (3.6), **(d)** Torsion (6.4).

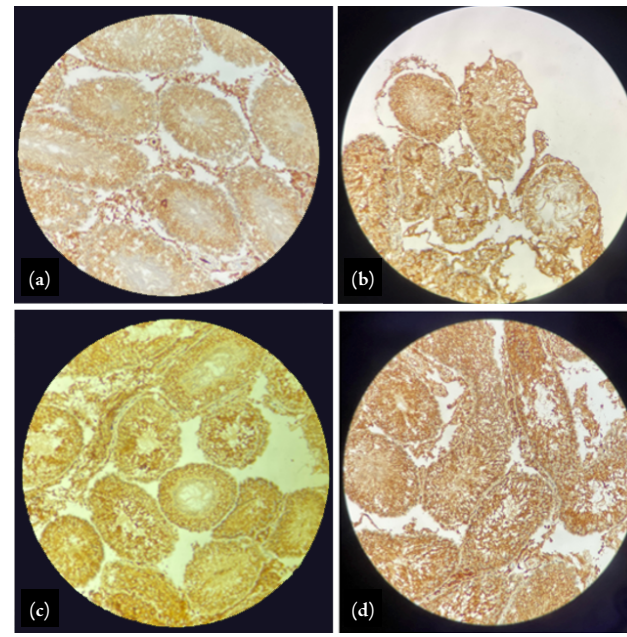


Figure 2. Immunohistochemical Caspase-3 staining in testicular tissue. **(a)** Sham, **(b)** Torsion+Mitochondria, **(c)** Torsion+Vehicle, **(d)** Torsion. Reduced apoptotic staining is observed in the mitochondria-treated group compared with untreated torsion controls.

Functional Sperm Outcomes

Epididymal spermiogram evaluation revealed significantly decreased total and motile sperm counts in the torsion and vehicle groups, whereas both parameters were markedly improved in the mitochondria-treated group (Fig. 3). When histopathological integrity, Johnsen score, Caspase-3 activity, and sperm motility were collectively evaluated, the mitochondria-treated group demonstrated the highest degree of structural and functional recovery among all ischemia-exposed groups (Fig. 4).

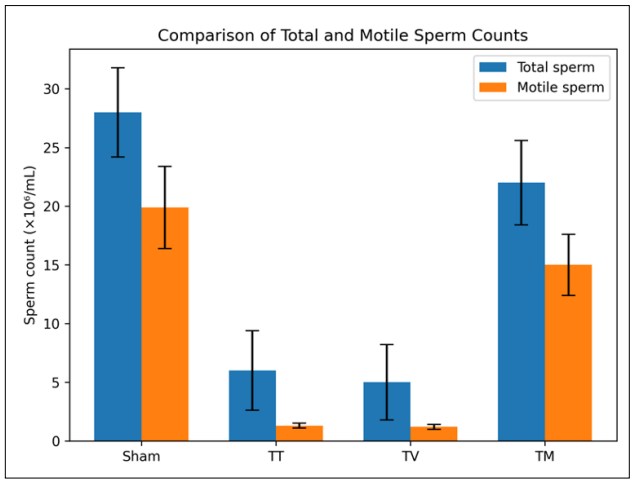


Figure 3. Comparison of total and motile sperm counts among groups. Bar graphs represent mean±standard deviation (SD) of total and motile sperm counts (×10^6/mL) in sham, torsion (TT), torsion+vehicle (TV), and torsion+mitochondria (TM) groups. The mitochondria-treated group shows significantly higher total and motile sperm counts compared with torsion and vehicle groups and demonstrates values comparable to sham controls. Statistical analysis was performed using one-way analysis of variance followed by Tukey's post hoc test.

Detailed evaluation of sperm motility subtypes demonstrated profound alterations in progressive motility following testicular torsion. Fast and slow progressive spermatozoa (Types A and B) were completely absent in both the torsion and vehicle groups, with motility predominantly consisting of non-progressive (Type C) and immotile (Type D) spermatozoa (Table 2). Specifically, immotile sperm accounted for 78% and 82% of total spermatozoa in the torsion and vehicle groups, respectively, resulting in severely diminished total motility rates of 22% and 18% (Table 2).

Assessment of sperm morphology revealed severe structural deterioration in ischemia-exposed groups. The percentage of spermatozoa with normal morphology was reduced to 28% in the torsion group and 24% in the vehicle group, compared with 92% in the sham group (Table 1). Mitochondrial transplantation significantly improved sperm morphological integrity, with 68% normal morphology observed in the treatment group (Table 1), supporting a protective effect on spermatogenic architecture.

Post hoc Statistical Comparisons

Overall ANOVA revealed a significant between-group difference for both Johnsen scores ($F[3,30]=46.2$, $p<0.001$) and motile sperm counts ($F[3,30]=22.8$, $p<0.001$). Tukey's post hoc tests showed that the mitochondria-treated group differed significantly from the torsion and vehicle groups but not from the sham group (Table 3). Post hoc power analysis confirmed >0.80 power for detecting large effects ($f\geq0.45$) in the primary endpoints

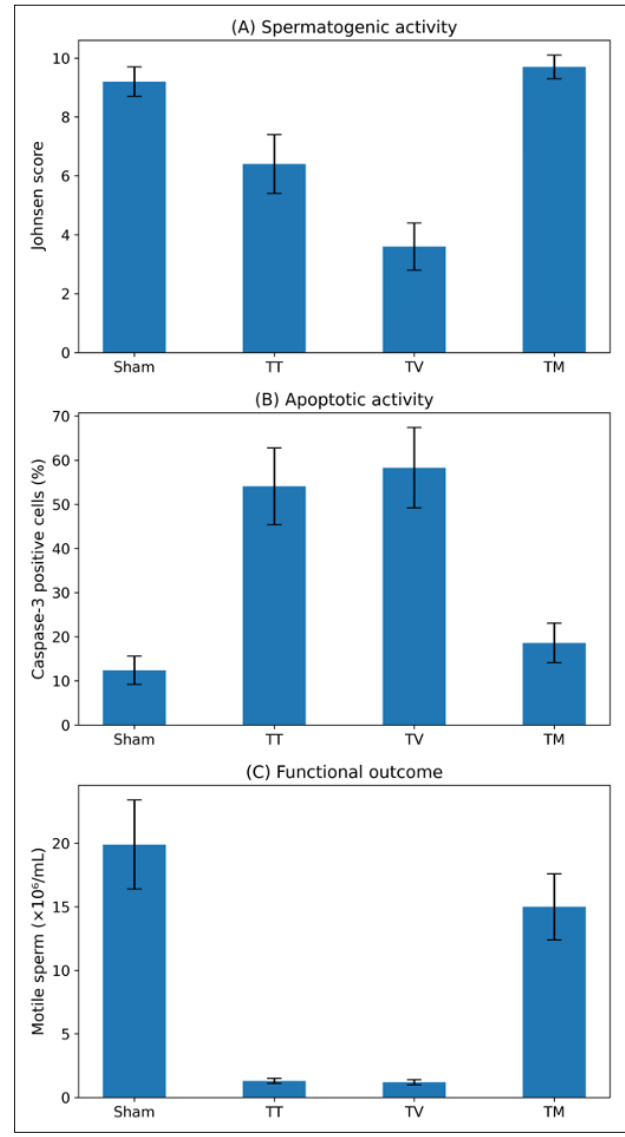


Figure 4. DStructural and functional recovery following mitochondrial transplantation. Composite figure summarizing the structural and functional effects of mitochondrial transplantation in experimental testicular ischemia–reperfusion injury. The mitochondria-treated group demonstrates coordinated recovery across histopathological, apoptotic, and functional sperm parameters compared with torsion and vehicle-treated groups. **(a)** Spermatogenic integrity (Johnsen score). Mean Johnsen scores (± SD) are shown for each experimental group. Mitochondrial transplantation significantly preserved seminiferous tubular architecture and spermatogenic activity compared with torsion and vehicle groups (****$p<0.001$). **(b)** Apoptotic activity (Caspase-3 expression). Percentage of Caspase-3–positive cells in testicular tissue sections. Mitochondria-treated animals exhibit a marked reduction in apoptosis relative to ischemia and vehicle controls. **(c)** Functional outcome (Sperm motility). Mean motile sperm counts (×106/mL±SD) across groups. The mitochondria-treated group shows significant functional recovery compared with torsion and vehicle groups, with values comparable to sham controls ($p>0.05$ vs. Sham). Statistical analysis was performed using one-way analysis of variance with Tukey's post hoc test or non-parametric equivalents where appropriate.

Table 2. Distribution of sperm motility subtypes (%)

Group	Fast progressive (A) (%)	Slow progressive (B) (%)	Non-progressive (C) (%)	Immotile (D) (%)	Total motility (%)
Sham	53	18	14	15	71
Torsion	0	0	22	78	22
Vehicle	0	0	18	82	18
Mitochondria	35	21	17	27	73

Table 3. Post hoc pairwise comparisons of key parameters

Comparison	Johnsen score p	Caspase-3 p	Total sperm p-value	Motile sperm p
TT versus TV	0.042	0.310	0.21	0.18
TT versus TM	<0.001	<0.01	<0.001	<0.001
TV versus TM	<0.001	<0.01	<0.001	<0.001
TT versus Sham	0.006	<0.01	<0.001	0.003
TM versus Sham	0.688	0.770	0.15	0.03

Pairwise comparisons were conducted using Tukey's post hoc or Mann–Whitney U tests as ap-propriate. The significance threshold was set at p<0.05. TT: Torsion, TV: Torsion+Vehicle, TM: Torsion+Mitochondria.

DISCUSSION

The present study demonstrates that intratesticular mitochondrial transplantation significantly preserves spermatogenic activity and reduces apoptotic cell injury in a rat model of TTD. Animals receiving mitochondria before torsion exhibited higher Johnsen scores, improved sperm motility, and reduced Caspase-3 expression compared with untreated torsion and vehicle groups. These findings indicate that exogenous mitochondria can exert a potent cytoprotective and anti-apoptotic effect in I/R injury, contributing to the preservation of testicular function.

I/R injury following testicular torsion remains one of the most destructive events in reproductive physiology. The pathogenesis involves rapid generation of ROS, mitochondrial depolarization, and activation of intrinsic apoptotic pathways within Sertoli and germ cells.[2] Mitochondria play a pivotal role in maintaining testicular energy homeostasis through oxidative phosphorylation and regulation of calcium flux. Therefore, mitochondrial dysfunction following torsion may directly compromise spermatogenesis and Leydig cell steroidogenesis. The current study was designed to evaluate whether targeted mitochondrial transplantation could restore bioenergetic balance and mitigate apoptotic cell death after TTD injury. Mitochondrial delivery was intentionally performed before torsion induction to evaluate its prophylactic cytoprotective capacity and to isolate mitochondrial effects from reperfusion-related confounders. Although pretreatment does not directly reproduce the clinical scenario of testicular torsion, this experimental design has been widely used in previous studies investigating the mechanisms of I/R injury and the protective effects of pharmacological agents. Pretreatment with compounds such as ternatin, L-alanyl-glutamine, and α-lipoic acid has been shown to attenuate testicular I/R injury in rat torsion-detorsion models. Consistent with these proof-of-concept studies, our objective was to determine whether transplantation of healthy mitochondria could confer resistance to subsequent ischemic injury. Future investigations should evaluate mitochondrial transplantation administered at the time of detorsion or during early reperfusion to better reflect the clinical management of testicular torsion.[23-25]

Our findings are consistent with those of Ekşi et al.,[26] who reported that experimental I/R injury in rat testes causes severe germ cell loss, tubular atrophy, and elevated oxidative stress markers, including malondialdehyde and nitric oxide. In their study, antioxidant treatment partially attenuated these effects, but structural recovery remained incomplete. Similarly, Chung et al.[23] demonstrated that mitochondrial dysfunction contributes significantly to testicular damage in torsion models, emphasizing the need for therapeutic approaches targeting mitochondrial integrity. Hu et al.[27] further showed that exogenous mitochondrial therapy can improve organ viability in ischemic conditions by stabilizing ATP production and decreasing cytochrome c release. Our results extend these observations by providing direct histological and functional evidence that intratesticular mitochondrial delivery restores

spermatogenic architecture and improves fertility indices.

The observed improvement in Johnsen scores and sperm parameters aligns with the hypothesis that mitochondrial transplantation replenishes the injured germ cell environment with functional organelles capable of restoring oxidative phosphorylation. Several preclinical studies have demonstrated the feasibility of mitochondrial transfer as a therapeutic tool in different ischemic models. For instance, McCully et al.[19] successfully used autologous mitochondrial injection to reduce myocardial infarct size and improve cardiac contractility following ischemia in porcine models. Similarly, Gollihue et al.[28] reported improved neuronal survival and axonal regeneration following mitochondrial transplantation in spinal cord injury. The current study represents, to our knowledge, the first evidence of this approach applied to testicular I/R injury, highlighting its potential translational relevance to male reproductive preservation.

Apoptosis plays a central role in testicular degeneration following torsion. Our immunohistochemical findings demonstrate a marked reduction in Caspase-3 expression in the mitochondria-treated group compared with untreated controls. This observation suggests that exogenous mitochondria may inhibit the intrinsic apoptotic pathway, possibly through restoration of mitochondrial membrane potential and suppression of cytochrome c release. Previous research has established that torsion induces mitochondrial swelling, loss of cristae, and depolarization of the inner membrane, leading to caspase activation and germ cell apoptosis.[3,17,21] The introduction of healthy mitochondria likely counteracts this process by restoring electron transport chain function and scavenging free radicals.

Another key observation in our study was the significant improvement in sperm motility and total count in the mitochondria-treated animals. The epididymal spermiogram revealed that mitochondrial therapy preserved both quantitative and qualitative sperm parameters, indicating functional recovery beyond mere histological preservation. This is particularly important because motile sperm production reflects the cumulative health of germ cells, Sertoli cell metabolism, and epididymal maturation. Wei et al.[4] also reported a strong correlation between oxidative stress markers and sperm motility decline following torsion, further supporting the hypothesis that mitochondrial damage underlies post-torsion subfertility.

The improved outcomes observed in our model can also be attributed to the metabolic support provided by the transplanted mitochondria. Exogenous mitochondria are capable of transiently integrating into host cells, restoring local ATP concentrations, and stabilizing membrane potential.[27] Studies in hepatic and renal ischemia models have demonstrated that transplanted mitochondria can maintain bioenergetic stability and reduce necroptosis through direct interaction with host organelles.[12,13] Although the persistence of transplanted mitochondria within testicular cells remains to be fully elucidated, previous fluorescence-tracking studies have confirmed mitochondrial uptake by parenchymal cells within hours after administration.

Our study differs from previous approaches primarily in the route and timing of mitochondrial delivery. While the recent studies performed systemic mitochondrial infusion, which may limit local concentration at the injury site,[10,11] our intratesticular injection ensured direct parenchymal distribution and immediate availability of functional organelles before ischemic insult. This strategy contributed to the pronounced preservation of seminiferous architecture observed in histological analyses. Moreover, the use of freshly isolated mitochondria from skeletal muscle – a metabolically robust source – enhanced the likelihood of transplant viability and functional competence.

However, our study has several limitations. The sample size, while statistically adequate for large effect detection, remains relatively small, reflecting ethical constraints inherent to animal research. Furthermore, long-term outcomes such as hormonal profiles, fertility rates, and offspring viability were not evaluated. Future studies should include assessments of mitochondrial integration, lifespan, and genetic stability within recipient testicular tissue, potentially using labeled or fluorescently tagged organelles. In addition, while Caspase-3 expression serves as a reliable apoptotic marker, inclusion of complementary assays such as TUNEL or Western blotting for Bax/Bcl-2 ratio would strengthen mechanistic conclusions. Another limitation is that this study utilized allogeneic mitochondria derived from skeletal muscle, which may elicit mild immunologic responses. However, no inflammatory or fibrotic changes were histologically evident in our specimens, suggesting acceptable biocompatibility. Future investigations may explore the use of autologous mitochondria isolated from less ischemia-prone tissues such as adipose or buccal mucosa, which could enhance translational applicability. Although a full spermatogenic cycle in rats lasts approximately 50 days, early spermatogenic disruption and recovery markers, including Johnsen score and epididymal sperm parameters, have been shown to reflect acute testicular injury and functional trends in short-term torsion models.

A limitation of the present study is that the cellular localization of transplanted mitochondria within the testis was not evaluated. Although our previous studies demonstrated efficient cellular uptake of exogenous mitochondria in kidney and liver tissues.[29,30] whether transplanted mitochondria are internalized by Sertoli, Leydig, or germ cells in the testis remains to be elucidated. Future studies using fluorescently labeled mitochondria together with cell-specific markers will be required to define their cellular fate following intratesticular administration.

Clinically, our results support the potential of mitochondrial therapy as an adjunctive strategy in testicular torsion, especially in cases where surgical detorsion alone may not fully

restore spermatogenic function. Given the narrow therapeutic window after torsion onset, rapid mitochondrial delivery at the time of surgical exploration could serve as a feasible intervention to preserve fertility potential. Advances in organelle isolation and storage technology may further facilitate bedside applications of mitochondrial transplantation.

In addition to testicular torsion, the implications of this approach may extend to other urological and andrological pathologies involving oxidative stress and mitochondrial injury, such as varicocele, cryptorchidism, and chemotherapy-induced gonadotoxicity. Indeed, Costa et al.[8] emphasized that mitochondria-targeted therapeutics might represent a unifying strategy for conditions characterized by energy imbalance and apoptotic dysregulation in male reproductive tissues.

CONCLUSION

Our findings suggest that intratesticular mitochondrial transplantation may offer structural and functional protection against I/R injury. The observed increase in Johnsen score, reduction in Caspase-3 expression, and improvement in sperm motility indicate a potential beneficial effect of this approach in preserving testicular viability. However, to validate these preliminary results and support clinical translation, larger prospective randomized studies incorporating mitochondrial tracking, molecular imaging, and long-term fertility outcomes are needed.

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Ethics Committee Approval: All experimental procedures were approved by the Saki Yenilli Experimental Animals Production and Research Laboratory Local Ethics Committee (Date: 02.12.2022, Decision No: 14).

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Authorship Contributions: Concept: C.Ö., G.B.K., S.G., Ü.Ö.; Design: A.S., U.D.M., M.S., C.Ö.; Supervision: G.B.K., A.M.A., G.Ş., M.M.A.; Resource: C.Ö., G.B.K., S.G., Ü.Ö.; Materials: A.S., U.D.M., M.S., M.M.A.; Data collection and/or processing: G.S.K., A.M.A., G.Ş., M.M.A.; Analysis and/or interpretation: C.Ö., G.B.K., S.G., Ü.Ö., U.D.M.; Literature review: S.G., C.Ö., G.S.K., M.M.A.; Writing: A.S., U.D.M., M.S., A.M.A.; Critical review: G.B.K., G.Ş., C.Ö., S.G., Ü.Ö.

Informed Consent: As this study involves only experimental animals, informed consent is not required.

Conflict of Interest: The authors declare that they have no conflicts of interest.

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DENEYSEL ÇALIŞMA - *ÖZ*

Mitokondriyal transplantasyon, sıçanlarda testis torsiyonu-detorsiyonu yaralanması sonrası apoptozu azaltıcı ve spermatogenez fonksiyonunu iyileştirici etkisi

AMAÇ: Testis torsiyonu, zamanında cerrahi detorsiyon yapılmasına rağmen geri dönüşümsüz iskemi-reperfüzyon hasarına ve spermatogenez fonksiyonunda uzun süreli bozulmaya yol açabilen bir ürolojik acil durumdur. Mitokondriyal disfonksiyon, torsiyon sonrası oksidatif stresin neden olduğu germ hücresi hasarında merkezi bir rol oynar. Bu çalışma, testis torsiyonu-detorsiyon hasarı olan sıçan modelinde izole intratestiküler mitokondriyal transplantasyonun koruyucu etkilerini araştırmayı amaçlamıştır.

GEREÇ VE YÖNTEM: Otuz altı yetişkin erkek Sprague–Dawley sıçanı rastgele dört gruba ayrıldı: sham (n=4), torsiyon (n=10), torsiyon+araç (n=10) ve torsiyon+mitokondri (n=10). Testis torsiyonu, 2 saat boyunca 720° rotasyon ile indüklendi, ardından cerrahi detorsiyon uygulandı. Torsiyon indüksiyonundan önce izole edilmiş mitokondriler intratestiküler enjeksiyon yoluyla uygulandı. Histopatolojik değerlendirme hematoksilen-eozin boyaması kullanılarak yapıldı ve Johnsen skorlama sistemi ile ölçüldü. Apoptotik aktivite, Caspase-3 immünohistokimyası ile değerlendirildi. Fonksiyonel sonuçlar, toplam sperm sayısı, hareketli sperm sayısı ve ayrıntılı sperm hareketliliği alt tip analizi ile değerlendirildi.

BULGULAR: Mitokondri tedavisi uygulanan sıçanlar, tedavi uygulanmayan kontrol grubuna kıyasla önemli ölçüde daha yüksek Johnsen skorları (9.7±0.4'e karşı 6.4±1.0, p<0.001), azalmış Caspase-3 ekspresyonu ve iyileşmiş toplam ve hareketli sperm sayıları sergilemiştir. Sonuçlar, mitokondriyal tedavi sonrasında testis yapısının ve spermatogenik fonksiyonun korunduğunu göstermektedir. Mitokondri ile tedavi edilen sıçanlar, tedavi edilmeyen iskemik kontrol grubuna kıyasla önemli ölçüde daha yüksek Johnsen skorları, azalmış Caspase-3 ekspresyonu, korunmuş sperm konsantrasyonu ve morfolojisi ve ilerleyici sperm hareketliliğinin geri kazanıldığını göstermiştir.

SONUÇ: Mitokondriyal transplantasyon, testis torsiyonuna bağlı iskemi-reperfüzyon hasarında hem testiküler yapıyı hem de spermatogenik fonksiyonu anlamlı düzeyde korumuştur. Mitokondri ile tedavi edilen grupta sperm konsantrasyonu, morfolojisi ve özellikle ilerleyici sperm hareketliliğinin korunması, bu yaklaşımın fertiliteyi sürdürmede potansiyel bir organel temelli tedavi stratejisi olabileceğini göstermektedir.

Anahtar sözcükler: Apoptoz; iskemi-reperfüzyon hasarı; mitokondriyal transplantasyon; spermatogenez; testis torsiyonu.

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ORIGINAL ARTICLE

Clinical predictors of mortality in earthquake victims with crush-related acute kidney injury requiring hemodialysis

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ABSTRACT

BACKGROUND: Major earthquakes frequently cause crush injuries that lead to acute kidney injury (AKI), posing significant challenges for medical teams. Understanding which patients are at the highest risk of mortality can help physicians make better treatment decisions during these disasters. This study examined earthquake victims who developed severe kidney problems requiring dialysis to identify factors that predict survival.

METHODS: A retrospective cohort study was conducted at a major tertiary hospital. Of the 5,338 earthquake victims treated, 1,416 adults developed AKI, of whom 159 required hemodialysis for crush-related injuries. Demographics, clinical features, laboratory parameters, and outcomes were analyzed during logistic regression to identify independent predictors of mortality.

RESULTS: The cohort's mean age was 38.3±14.6 years, with 62.9% male. Mortality was 30.8%. Independent predictors of mortality were septic shock (odds ratio [OR]: 52.148), elevated sodium levels (OR: 1.186), and hypoalbuminemia (OR: 0.877). Prolonged extrication time, systemic infections, and metabolic acidosis were significantly associated with mortality. Demand for hemodialysis peaked in the 1st week, with hyperkalemia and sepsis as major complications.

CONCLUSION: Mortality among earthquake victims with crush-related renal injury depends primarily on overall disease severity rather than renal function alone. Septic shock, blood chemistry imbalances, and prolonged entrapment were the main determinants of survival. Prompt rescue and aggressive treatment of infections and metabolic problems are essential to saving lives in future disasters.

Keywords: Acute kidney injury; Crush syndrome; earthquakes; mortality; renal dialysis.

INTRODUCTION

Natural disasters, such as earthquakes, are catastrophic events with profound human and infrastructural consequences. They often cause complex patterns of trauma, including crush injuries, metabolic disturbances, and multiorgan dysfunction.[1] Among these, acute kidney injury (AKI), particularly crush-related AKI, is a critical condition requiring urgent and specialized medical attention. AKI not only poses an immediate threat to survival but also contributes to long-term morbidity among survivors, underscoring the need for effective and timely interventions.

The pathophysiology of AKI in crush syndrome is well-documented and involves rhabdomyolysis-induced nephrotoxicity, hypovolemia, and systemic inflammation. These processes are further exacerbated by delays in rescue and medical intervention, which are common in disaster settings. Hemodialysis is a cornerstone of the management of crush-related AKI and has the potential to reduce mortality and improve recovery. However, its success depends on early diagnosis, efficient resource allocation, and coordination among multidisciplinary teams. Despite advances in disaster response systems, gaps remain in understanding the predictors of mortality in this vulnerable population.[2,3] Previous studies have focused

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on the epidemiology of AKI and the utility of dialysis during earthquakes, but data on specific clinical and laboratory markers that influence outcomes are limited. Furthermore, there is a need to evaluate how systemic complications, such as sepsis, hypoalbuminemia, and electrolyte imbalances, interact with AKI to determine mortality.[4,5] These insights are critical for optimizing disaster preparedness and improving care for earthquake victims, particularly in tertiary hospitals that serve as referral centers during such crises.

While previous studies have documented AKI patterns in the Marmara and Wenchuan earthquakes, they have primarily focused on epidemiological aspects and basic clinical outcomes. Our study addresses critical gaps by (1) providing a comprehensive multivariate analysis of mortality predictors, including metabolic markers rarely examined together, (2) analyzing the temporal evolution of renal function recovery stratified by pre-existing chronic kidney disease (CKD) status, and (3) examining the interaction between systemic complications and metabolic disturbances in a large contemporary cohort with modern management protocols. Limited data exist on the specific clinical and laboratory predictors of mortality in crush-related AKI, particularly the interplay between systemic complications and metabolic disturbances in determining patient outcomes. In this context, our study aimed to investigate the clinical, demographic, and laboratory characteristics of earthquake victims with AKI, focusing on crush-related injuries requiring hemodialysis (HD). We sought to identify key predictors of mortality to help clinicians manage similar scenarios more effectively. By analyzing a comprehensive dataset from a tertiary hospital, this study contributes to understanding predictors of mortality in earthquake-related crush syndrome.

MATERIALS AND METHODS

Study Design and Setting

This retrospective, cross-sectional study was conducted at a tertiary hospital that served as a major referral center following a devastating earthquake. The study included earthquake victims admitted to the hospital, with a focus on those diagnosed with AKI and requiring HD for crush-related injuries.

Patient Population

A total of 5338 individuals presented to the hospital following the earthquake, of whom 3313 were adults aged 18 years or older. Of these, 1416 patients were diagnosed with AKI, and 159 required HD for crush-related injuries. Demographic data, clinical parameters, laboratory results, and treatment outcomes were extracted from electronic hospital records.

Ethical Considerations

This study was approved by the Adana City Training and Research Hospital Scientific Research Ethics Committee (Date: 25.07.2025, Decision no: 72), and all procedures adhered to the ethical principles of the Declaration of Helsinki. Given the study's retrospective design, informed consent was waived. Patient anonymity and confidentiality were strictly maintained throughout the study.

Data Collection

Among the 3,313 adults, 1,416 were diagnosed with AKI, and 159 patients required hemodialysis for crush-related injuries. Due to the earthquake's impact on most hospitals in the region, many victims were admitted to our hospital within the 1st h after the disaster.

Data were collected retrospectively from patients' medical records. The data included demographic information (age, gender), clinical variables (intensive care unit [ICU] admission, mechanical ventilation, comorbidities), laboratory parameters (e.g., albumin, sodium, lactate, pH), and dialysis session details. Thirty-day mortality was defined as the primary outcome of the study. Mortality was assessed as death from any cause occurring within 30 days after hospital admission.

Disease severity was assessed using two validated scoring systems. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score was calculated within the first 24 h of admission, using the worst values of 12 physiological variables, age, and chronic health status. The Sequential Organ Failure Assessment (SOFA) score was calculated to evaluate multi-organ dysfunction, incorporating assessments of the respiratory, cardiovascular, hepatic, coagulation, renal, and neurological systems. Higher scores indicate greater disease severity in both systems.

Statistical Analysis

Statistical analyses were performed using Statistical Package for the Social Sciences version 27.0 (IBM Corp., Armonk, NY, USA). Categorical variables were summarized as frequencies and percentages, and continuous variables as mean±standard deviation or, where appropriate, as median (minimum-maximum). The Chi-square test was used to compare categorical variables. Data-handling procedures included systematic checks for missing values and outliers. Missing data patterns were assessed, and cases with >20% missing key variables were excluded. Continuous variables were examined for normality using the Shapiro–Wilk test. Retrospective data collection followed a standardized protocol with two independent reviewers extracting data to ensure accuracy. Discrepancies were resolved through consensus or consultation with a third reviewer. For variables that did not follow a normal distribution, comparisons between two groups were conducted using the Mann–Whitney U-test. Factors influencing mortality were evaluated using multivariate logistic regression analysis. Model assumptions were checked, including linearity of continuous variables with log odds, and the final model's goodness-of-fit was assessed using the Hosmer–Lemeshow test. Sensitivity analyses were performed, excluding extreme outliers, to verify model stability. A $p<0.05$ was considered statistically significant for all tests.

RESULTS

A total of 5,338 patients were treated and followed up at our hospital, of whom 3,313 were adults aged 18 years or older. Among these, AKI developed in 1,416 patients, and 199 of them underwent HD treatment. Of these, 159 patients required HD due to AKI associated with crush syndrome.

A total of 159 earthquake victims were included in the study. The mean age of the patients was 38.3±14.6 years, with 100 (62.9%) male and 59 (37.1%) female. Comorbidities were observed in 19 (11.9%) patients: Diabetes mellitus in 5 (26.3%), hypertension in 7 (36.8%), and other comorbidities in 9 (47.4%). The mean time to extrication from the earthquake debris was 41.1±24.0 h. Signs of anuria were observed in 146 (91.8%) patients, with 55 (34.6%) having anuria and 91 (57.2%) oliguria. Amputations were performed in 43 (27%) patients, fasciotomy in 92 (57.9%), and additional complications were identified in 72 (45.3%). Among the amputations, 7 were performed on the upper extremities of 6 patients, while 40 were performed on the lower extremities of 36 patients. ICU admission was required for 92 (57.9%) patients, with a mean ICU stay of 11.8±13.2 days. Endotracheal intubation was performed in 46 (28.9%) patients. Hemodiafiltration (HDF) was applied to 24 (15.1%) patients. The need for HD continued for 72 (45.3%) patients during the 1st week, with a mean of 3.83±3.3 HD sessions per patient. CKD was developed in 8 (5%) patients during follow-up. Mortality was observed in 49 (30.8%) patients (Table 1).

Table 1. Demographic data of patients with crush syndrome

Variables	Number of patients (Total, n=159)	%
Gender		
Male	100	62.9
Female	59	37.1
Comorbidities	19	11.9
Diabetes mellitus	5	26.3
Hypertension	7	36.8
Other	9	47.4
Anuria	55	34.6
Oliguria	91	57.2
Amputation	43	27.0
Lower extremity amputation	40	25.2
Upper extremity amputation	3	1.9
Fasciotomy	92	57.9
Infection complications	87	54.7
Wound infection	58	66.7
Urinary tract infection	14	16.1
Bloodstream infection	24	27.6
Aspiration-associated infection	4	4.6
Other infection	3	3.4
Culture positivity	77	48.4
Sepsis	78	49.1
Septic shock	37	23.3
Acute respiratory distress syndrome	6	3.8
Disseminated intravascular coagulation	13	8.2
Chronic kidney disease developed	8	5.0
Mortality	49	30.8

Patients may have more than one comorbidity or infection; subgroup percentages are calculated within the respective category.

Infection foci were detected in 87 (54.7%) patients. The most common infections were wound infections in 58 (66.7%), urinary tract infections in 14 (16.1%), bloodstream infections in 24 (27.6%), aspiration-associated infections in 4 (4.6%), and other infections in 3 (3.4%). Microorganisms were isolated in 77 (48.4%) patients. The most frequently isolated organisms were Acinetobacter baumannii in 44 (57.1%), Escherichia coli in 5 (6.5%), non-albicans Candida in 2 (2.6%), Candida albicans in 3 (3.9%), Klebsiella pneumoniae in 9 (11.7%), extended-spectrum beta-lactamase-producing E. coli in 3 (3.9%), coagulase-negative staphylococci in 4 (5.2%), and other microorganisms in 21 (27.3%).

No significant differences were found between groups in terms of gender or age ($p>0.05$). Non-survivors had higher rates of amputation, ICU admission, intubation, and HDF ($p=0.026$, $p<0.001$, $p<0.001$, $p<0.001$, respectively). Disease severity scores were calculated for all patients. The mean APACHE II score was 19.53±5.11 in survivors versus 21.31±7.22 in non-survivors ($p=0.254$), showing no significant difference. In contrast, SOFA scores were significantly higher in non-survivors (7.04±2.10) compared to survivors (5.74±1.40, $p=0.001$) (Table 2).

The average extrication time was significantly longer in patients who died ($p=0.019$). In addition, systolic and diastolic blood pressures, albumin, pH, and bicarbonate levels were significantly lower in non-survivors ($p<0.001$, $p<0.001$, $p=0.003$, $p=0.003$, $p=0.002$, respectively). In contrast, pulse rate, glucose, platelet count, sodium, lactate, ferritin, and international normalized ratio (INR) levels were significantly higher in these patients ($p=0.003$, $p=0.013$, $p=0.026$, $p=0.018$, $p<0.001$, $p=0.036$, $p=0.011$, respectively). No significant differences were observed in other laboratory parameters between groups, $p>0.05$ (Table 3).

Urinary infections were less common in non-survivors ($p=0.005$), while bloodstream infections were more frequent ($p=0.028$). Sepsis, septic shock, acute respiratory distress syndrome (ARDS), and disseminated intravascular coagulation (DIC) were significantly more prevalent in non-survivors ($p<0.001$, $p<0.001$, $p=0.005$, $p=0.012$, respectively) (Table 4).

In univariate analysis, amputation, extrication time, albumin, sodium, pH, lactate, INR, sepsis, and septic shock were sig-

Table 2. Comparison of diagnostic features and clinical outcomes between mortality and survival groups among earthquake victims

Variables	Survivors (Total, n=110)	Non-survivors (Total, n=49)	p
Age (years)	36.7±11.9	41.9±18.9	0.325
Gender			
Male (n/%)	66 (60%)	34 (69.4)	0.258
Female (n/%)	40 (40%)	15 (30.6)	0.258
Comorbidity (n/%)	11 (10%)	8 (16.3%)	0.256
	Mean±SD	Mean±SD	p
Urinary output			
Anuria	33 (32.7)	22 (48.9)	0.175
Oliguria	68 (67.3)	23 (51,1)	0.115
Amputation	24 (21.8)	19 (38.8)	0.026*
Fasciotomy	66 (60)	26 (53.1)	0.413
Other problems	50 (45.5)	22 (44.9)	0.948
ICU admission	43 (39.1)	49 (100)	<0.001**
Intubation	6 (5.5)	40 (81.6)	<0.001**
Hemodiafiltration	102 (92.7)	33 (67.3)	<0.001**
1st week hemodialysis	48 (43.6)	24 (49)	0.532
Mean±SD	Mean±SD (Med)	p‡	
Duration under the rubble (hours)	38.5±24	46.9±23.2	0.019*
ICU duration (days)	10.5±10	12.9±15.4	0.770
Hemodialysis sessions	4.16±3.5	3.1±2.7	0.068
APACHE II score	19.53±5.11	21.31±7.22	0.254
SOFA score	5.74±1.40	7.04±2.10	0.001*

ICU: Intensive care unit; CKD: Chronic kidney disease; *p<0.05; †: Chi-square; ‡: Mann–Whitney U.

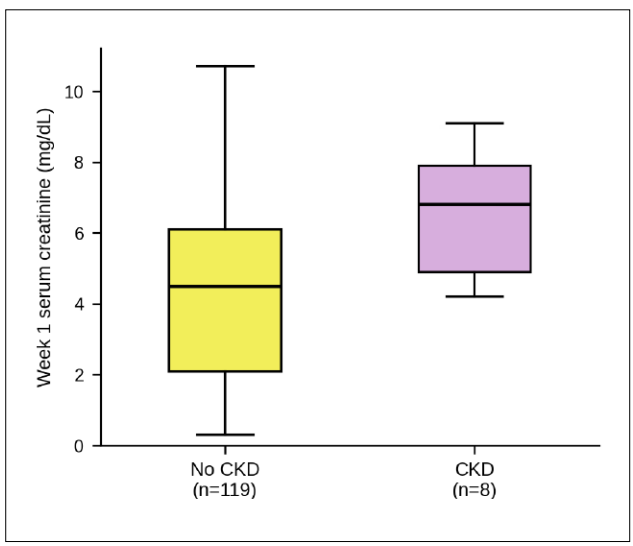


Figure 1. Comparison of week 1 serum creatinine levels between patients who did and did not develop chronic kidney disease (CKD).

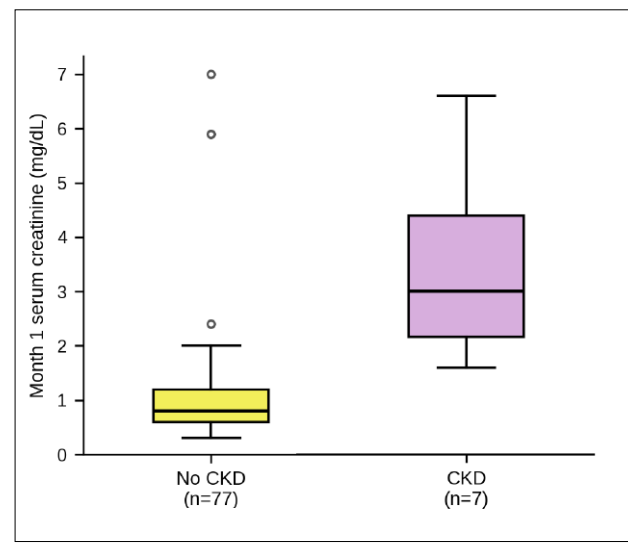


Figure 2. Comparison of month 1 serum creatinine levels between patients who did and did not develop chronic kidney disease (CKD).

Table 3. Comparison of diagnostic features and clinical outcomes between mortality and survival groups among earthquake victims

Variables	Survivors (n=110)	Non-survivors (n=49)	p
Systolic blood pres-sure (mmHg)	118.4±14.8	88.3±15.7	<0.001**
Diastolic blood pres-sure (mmHg)	72.6±8.4	54.3±11.9	<0.001**
Heart rate (beats/minute)	85.5±13.7	100.6±16.6	0.003**
Glucose (mg/dL)	132.3±62.9	170.1±100.3	0.013*
Urea (mg/dL)	116.2±80.7	121.6±78.5	0.600
Creatinine (mg/dL)	3.27±2.1	3.47±2.2	0.576
Albumin (g/L)	30.1±6.8	25.9±7.3	0.003**
Total protein(g/L)	58.3±10.8	54.3±11.6	0.263
C-reactive protein (mg/L)	176.5±84.9	169.1±102.9	0.433
Procalcitonin (ng/mL)	26.2±84.2	31.2±41.5	0.026*
Sodium (mmol/L)	133.1±10.2	135.9±6.3	0.018*
Potassium (mmol/L)	6.46±2.3	6.48±1.1	0.195
Uric acid (mg/dL)	11.7±3.2	12.5±3.2	0.169
Direct bilirubin (mg/dL)	0.14±0.12	0.16±0.16	0.718
Total bilirubin (mg/dL)	0.68±0.54	0.64±0.5	0.735
Alanine aminotrans-ferase (U/L)	419.6±268.5	603.7±564.8	0.346
Aspartate aminotrans-ferase (U/L)	1062.1±643.6	1244.8±929.8	0.426
Calcium (mg/dL)	7.54±0.9	7.22±1.2	0.097
Magnesium (mg/dL)	2.27±0.6	2.27±0.4	0.878
Phosphorus (mg/dL)	8.16±2.8	8.67±2.6	0.157
Creatine phosphoki-nase (U/L)	113471.3±16187.6	104047.7±98557.4	0.419
Amylase (U/L)	253.6±411.5	295.2±258.5	0.434
Myoglobin (ng/mL)	3745.9±743.7	907.4±3706.0	0.678
Leukocyte (×10^9/L)	24.52±27.69	24.58±25.06	0.684
Hemoglobin (g/dL)	15.3±3.6	3.16±15.2	0.595
Hemotocrit (%)	45.5±10.6	10.2±45.5	0.745
Platelets (×10^9/L)	263.25±93.04	260.15±102.70	0.357
pH 7.19±0.10	7.20±0.13	0.003**	
Bicarbonate (mmol/L)	16.1±3.2	15.5 ±3.59	0.002**
Lactate (mmol/L)	36.3±25.4	33.0±55.1	<0.001**
Ferritin (µg/L)	428.4±363.6	1897.6±345.7	0.036*
International normal-ized ratio	1.24±1.2	1.29±0.5	0.011*
1st week creatinine (mg/dL)	4.46±2.9	4.47±1.9	0.977
1st month Ürea (mg/dL)	38.7±27.8	91.3±51.1	<0.001**
1st month creatinine (mg/dL)	1.23±1.4	1.90±1.3	0.004**

*p<0.05; Mann–Whitney U.

nificant variables and included in a multivariate logistic regression model (Table 5). According to the model, albumin (odds ratio [OR]: 0.877), sodium (OR: 1.186), and septic shock (OR: 52.148) were identified as independent predictors of mortality (p<0.05).

Patients with CKD who developed group had significantly higher creatinine levels compared to those without CKD who did not develop at both week 1 and month 1 following the earthquake. These findings are illustrated in Figures 1 and 2, which demonstrate the prolonged recovery of renal function in patients with pre-existing CKD. At week 1, the mean

Table 4. Infection sites and complications in relation to mortality among earthquake victims

Variables	Survivors (n=110)	Non-survivors (n=49)	p
Infection complications	59 (53.6)	28 (57.1)	0.682
Wound infection	41 (69.5)	17 (60.7)	0.417
Urinary tract infection	14 (23.7)	-	0.005**
Blood infection	12 (20.3)	12 (42.9)	0.028*
Aspirate infection	1 (1.7)	3 (10.7)	0.061
Other infection	1 (1.7)	2 (7.1)	0.193
Sepsis	40 (36.4)	38 (77.6)	<0.001**
Septic shock	6 (5.5)	31 (63.3)	<0.001**
ARDS	1 (0.9)	5 (10.2)	0.005**
DIC	5 (4.5)	8 (16.3)	0.012*

ESBL+: Extended-spectrum beta-lactamase positive; ARDS: Acute respiratory distress syndrome; DIC: Disseminated intravascular coagulation.

Table 5. Multivariate analysis of mortality predictors in patients with crush-related acute kidney injury

Variables	p	OR	%95 CI	
			Lower	Upper
Amputation	0.417	1.675	0.482	5.817
Duration under the rubble (hours)	0.146	1.017	0.994	1.040
Albumin	0.004**	0.877	0.803	0.958
Sodium	0.002**	1.186	1.063	1.323
pH	0.158	77.262	0.184	32432.7
Lactate	0.063	1.025	0.999	1.053
International normalized ratio	0.154	0.753	0.511	1.111
Sepsis	0.479	1.676	0.401	6.997
Septic shock	<0.001**	52.148	8.704	312.419

CI: Confidence interval; OR: Odds ratio. *p<0.05; **p<0.01.

creatinine level was 6.59±1.8 mg/dL in the CKD developed group and 4.32±2.7 mg/dL in the non-CKD group (p=0.020). By month 1, the CKD developed group's mean creatinine level remained elevated at 3.47±1.8 mg/dL, while the non-CKD group's mean creatinine level had decreased to 1.09±1.1 mg/dL (p<0.001). These findings highlight the slower recovery of renal function in patients who developed CKD.

DISCUSSION

The devastating earthquakes that struck Türkiye highlighted the critical importance of timely medical interventions in disaster scenarios. In this study, we analyzed one of the largest cohorts of earthquake victims with crush-related AKI, revealing that mortality was influenced by a combination of systemic complications and metabolic disturbances.

AKI in the patients included in this study was predominantly attributed to acute tubular necrosis resulting from rhabdomyolysis, as evidenced by markedly elevated mean levels of creatine kinase and myoglobin. The severity of renal impairment was further underscored by the high proportion of patients (91.8%) presenting with either anuria or oliguria. Among the interventions, fasciotomy was performed on 92 patients (57.9%), a rate lower than the 67.7% reported among HD-treated patients during the 1999 Marmara earthquake.[6] The lower rate of fasciotomy observed in our study compared with the Marmara earthquake may be explained by increased clinical awareness in the diagnosis and monitoring of rhabdomyolysis and compartment syndrome, the implementation of

more selective and indication-based surgical decision-making, and a greater emphasis on limb-sparing approaches. Notably, fasciotomy in our cohort did not demonstrate a significant impact on mortality. In addition, amputations were required in 43 patients (27%), with the majority involving the lower extremities (86.1%) compared to 13.9% in the upper extremities. These findings highlight the vulnerability of the lower extremities to trauma in earthquakes.[7] Larger muscle groups in these regions contribute to extensive rhabdomyolysis and an increased risk of AKI.

For such patients, close monitoring for rhabdomyolysis is critical, and simple measures like urine dipstick tests for hematuria or patient observation of urine color and output can aid in early detection.

A significant relationship was observed between the time to extrication from debris and mortality. These findings emphasize the critical importance of rapid rescue efforts in improving survival outcomes, as delayed extrication increases the risk of systemic complications and mortality.

Our findings align with previous studies that emphasize the profound impact of AKI and electrolyte imbalances on the prognosis of disaster victims, particularly those with crush syndrome. Similar to the Wenchuan earthquake study, where hyponatremia was prevalent in over half of the patients and significantly associated with poor outcomes, our study also identified electrolyte disturbances, such as hypernatremia, as critical predictors of mortality among earthquake victims.[8] In our study, sodium levels in the survivor group were found to be lower compared to the non-survivor group. This finding can be explained by the provision of better hydration to the survivor group. Furthermore, the interplay of systemic complications such as sepsis and septic shock underscores the necessity for early and aggressive interventions to stabilize patients. The consistent association of AKI with crush-related injuries in both studies reinforces the critical role of timely renal replacement therapy and multidisciplinary disaster response strategies in improving survival outcomes. These findings collectively highlight the importance of robust nephrology expertise and resource planning in disaster medicine to mitigate morbidity and mortality in future large-scale emergencies.

The outcomes of our study are consistent with those of previous research emphasizing the critical impact of timely intervention and comprehensive management in earthquake victims, particularly those suffering from crush syndrome and AKI. Similar to the findings in the Kahramanmaraş earthquake study, our data highlight the prevalence of AKI and systemic complications such as sepsis and septic shock among victims.[9] The correlation between the duration of entrapment under rubble and metabolic derangements, including elevated serum lactate, uric acid, and myoglobin levels, underscores the importance of early fluid resuscitation to mitigate ischemia-reperfusion injuries.

The cornerstone of treatment for crush-related AKI is undoubtedly fluid replacement and HD.[10] The indications for HD is these patients are no different from other causes of AKI. Patients underwent HD for hyperkalemia, metabolic acidosis unresponsive to medical treatment, hypervolemia, and uremic symptoms. No prophylactic HD was performed.

In our study, similar to the Kahramanmaraş earthquake study, hyperkalemia was the most common indication.[11] Other HD indications included hypervolemia, medically refractory metabolic acidosis, and uremic symptoms.

In addition, trauma characteristics, such as crush injuries below the knee and the presence of compartment syndrome, were more strongly associated with mortality in the Kahramanmaraş cohort. These differences underscore the importance of context-specific approaches to disaster nephrology, with an emphasis on rapid diagnosis and management of metabolic derangements, compartment syndrome, and systemic complications like sepsis.

The findings of our study contrast with those from the Marmara earthquake, highlighting important advancements in disaster management and nephrology care. The Marmara earthquake reported a significantly higher dialysis need (74.6%) and mortality rates among renal victims compared to our cohort, where improvements in fluid resuscitation strategies and better disaster preparedness likely played a critical role.[12] The Marmara study identified extensive rhabdomyolysis and systemic complications such as DIC and ARDS as key predictors of mortality, emphasizing the severity of crush syndrome complications. While our study also observed high rates of AKI and systemic infections, the streamlined management protocols in the recent disaster, including early fluid administration and potassium-free fluids, likely contributed to improved survival outcomes. Furthermore, surgical interventions such as fasciotomies were performed more frequently in the Marmara cohort, correlating strongly with sepsis and higher mortality rates. This underscores the importance of balancing invasive procedures with medical management strategies like mannitol therapy to mitigate compartment syndrome while minimizing the risk of infections. Variations in patient management between earthquakes reflect evolving disaster response protocols. The implementation of early fluid resuscitation protocols and improved coordination of dialysis resources since the Marmara earthquake likely contributed to the observed differences in outcomes. Regional factors, including proximity to tertiary care centers and speed of international aid response, also influence mortality patterns across different disasters.

Both our study and the analysis of mortality factors in crush syndrome identify low systolic blood pressure upon admission as a significant predictor of mortality among earthquake victims.[13] This shared finding emphasizes the critical importance of early fluid resuscitation in managing crush syndrome patients, as hypotension often indicates delayed or inad-

equate pre-hospital care. In addition, hypotension increases HD complications and the need for vasopressors during HD, which also increases mortality. Another reason may be the addition of hypotension to be complications of crush-related AKI such as sepsis and septic shock. However, while our study primarily focuses on hypervolemia and systemic complications like sepsis as additional contributors to mortality, the other study highlights the role of elevated serum potassium and creatinine levels alongside severe acidosis as key determinants of poor outcomes. Furthermore, while both studies report a significant association between AKI severity and mortality, the frequency of HD was higher in their cohort, likely reflecting differences in rescue and treatment protocols or patient demographics.

In our study, 49 patients (30.8%) died. This mortality rate is comparable to those reported in other major earthquakes. For example, the mortality rate was 23.7% in the Marmara earthquake and 15.1% among AKI patients on HD in the Wenchuan earthquake.[14,15] The high mortality rate observed in our study may be associated with differences in demographic and clinical characteristics of the patients and with the severity of the earthquake.

Although crush-related injuries are associated with significant mortality and morbidity, studies have shown that the risk of developing CKD is relatively low.[16] In our study, CKD developed in 8 patients, and none of them required long-term HD.

This study has several limitations. First, the retrospective design may introduce recall bias and limit the control over data collection, potentially leading to missing or incomplete records. Second, the single-center nature of the study restricts the generalizability of the findings to other regions or populations affected by similar disasters. Third, the lack of certain laboratory and clinical parameters in the dataset constrained the scope of our analyses. Finally, the study cohort was limited to patients who presented to our hospital, potentially excluding victims who either did not reach healthcare facilities or were treated elsewhere. These limitations should be considered when interpreting the findings of this study. Formal collinearity diagnostics were not included in our original analysis protocol; however, the stability of the model was assessed through sensitivity analyses. The high odds ratio for septic shock should be interpreted cautiously, given the wide confidence interval, which may reflect the relatively small number of events in this category.

CONCLUSION

This study highlights the multifactorial determinants of mortality among earthquake victims with crush-related AKI requiring HD. Key findings indicate that prolonged extrication times, systemic complications such as septic shock, and metabolic disturbances, including hypoalbuminemia and elevated sodium levels, were significant predictors of mortality. The high prevalence of complications such as sepsis, amputations, and intensive care admissions underscores the critical importance of early and aggressive interventions. These findings reinforce the need for robust disaster preparedness plans, specialized nephrology expertise, and streamlined protocols for managing crush syndrome and AKI in disaster settings. By addressing these factors, future disaster responses may achieve better survival outcomes and mitigate the long-term impact on affected populations.

Ethics Committee Approval: This study was approved by the Adana City Training and Research Hospital Scientific Research Ethics Committee (Date: 25.07.2025, Decision No: 72).

Peer-review: Externally peer-reviewed.

Informed Consent: Given the study's retrospective design, informed consent was waived.

Authorship Contributions: Concept: D.B.T.; Design: D.B.T., E.O.; Supervision: D.B.T., E.G.; Resource: D.B.T., F.Ü.; Materials: D.B.T., M.H.; Data collection and/or processing: D.B.T., E.O.; Analysis and/or interpretation: D.B.T., E.G.; Literature review: D.B.T., E.O.; Writing: D.B.T.; Critical review: D.B.T.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Hemodiyaliz gerektiren ezilmeye bağlı akut böbrek yaralanması olan deprem mağdurlarında ölümün klinik tahmin edicileri

AMAÇ: Büyük depremler sıklıkla akut böbrek hasarına (ABH) yol açan ezilme yaralanmalarına neden olur ve bu durum sağlık ekipleri için önemli zorluklar oluşturur. Hangi hastaların ölüm riski açısından daha yüksek olduğunu anlamak, afet sırasında hekimlerin daha doğru tedavi kararları vermesine yardımcı olabilir. Bu çalışma, diyaliz gerektiren ağır böbrek hasarı gelişen deprem mağdurlarında sağkalımı öngören faktörleri belirlemeyi amaçlamıştır.

GEREÇ VE YÖNTEM: Bu retrospektif kohort çalışma, bir üçüncü basamak merkezde gerçekleştirilmiştir. Tedavi edilen 5.338 deprem mağdurunun 1.416'sında ABH gelişmiş olup, bunların 159'unda ezilmeye bağlı olarak hemodiyaliz gereksinimi doğmuştur. Demografik özellikler, klinik bulgular, laboratuvar parametreleri ve sonuçlara ilişkin veriler, mortalitenin bağımsız belirleyicilerini tanımlamak için lojistik regresyon kullanılarak analiz edilmiştir.

BULGULAR: Kohortun ortalama yaşı 38.3±14.6 olup, %62.9'u erkektir. Mortalite oranı %30.8 olarak saptanmıştır. Septik şok (OR: 52.148), yüksek sodyum düzeyleri (OR: 1.186) ve hipoalbüminemi (OR: 0.877) mortalitenin bağımsız belirleyicileri olarak tanımlanmıştır. Uzamış kurtarılma süresi, sistemik enfeksiyonlar ve metabolik asidoz mortalite ile anlamlı şekilde ilişkili bulunmuştur. Hemodiyaliz gereksinimi ilk hafta içinde en yüksek seviyedeydi; hiperkalemi ve sepsis başlıca komplikasyonlardı.

SONUÇ: Ezilme ilişkili böbrek hasarı olan deprem mağdurlarında mortalite oranları, yalnızca böbrek fonksiyonundan ziyade genel hastalık ağırlığı ile ilişkilidir. Septik şok, biyokimyasal dengesizlikler ve uzun süreli enkazda kalma süresi sağkalımı belirleyen temel faktörlerdir. Hızlı kurtarma çalışmaları ile enfeksiyon ve metabolik sorunların agresif tedavisi, gelecekteki felaketlerde hayat kurtarmak için kritik öneme sahiptir.

Anahtar sözcükler: Akut böbrek hasarı; depremler; ezilme sendromu; mortalite; renal diyaliz.

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ORIGINAL ARTICLE

Management of renal failure in earthquake-related crush syndrome: Multicenter intensive care outcomes

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ABSTRACT

BACKGROUND: Crush syndrome (CS) is a clinical condition associated with multisystem organ dysfunction that develops after traumatic rhabdomyolysis and primarily affects the kidneys. The aim of this study was to characterize the incidence, risk factors, and treatment patterns of acute kidney injury (AKI) in earthquake victims with CS, with a particular focus on renal replacement therapy (RRT) use and clinical outcomes.

METHODS: In this retrospective multicenter study, 247 adult patients with earthquake-related CS who were admitted to intensive care units (ICUs) in 22 hospitals after the Kahramanmaraş 2023 earthquakes were analyzed. Demographic data, injury patterns, laboratory parameters, treatment protocols, and outcomes were evaluated during the first 15 days following ICU admission.

RESULTS: AKI developed in 78.5% (n=194) of patients, and RRT was required in 62.4% (n=121) of those with AKI. Multiple logistic

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regression analysis demonstrated that myoglobin and creatinine levels were associated with an elevated risk of developing AKI (odds ratio [OR]: 1.001; 95% confidence interval CI: 1.000–1.001 and OR:1.735; 95% CI:1.151–2.615, respectively). Similarly, creatinine level and reasons for ICU admission were identified as factors influencing RRT administration. (OR: 1.7; 95% CI: 1.28–2.15 and OR: 2.9; 95% CI: 1.26–6.90, respectively). The 30-day mortality rate was higher in patients with AKI than in those without AKI. Mortality rates were similar between patients with AKI who received RRT and those who did not.

CONCLUSION: This study demonstrates the high incidence of AKI in earthquake-related CS, underscores the need for improved disaster preparedness with adequate dialysis capacity and early risk stratification using serum myoglobin and creatinine levels for optimal management.

Keywords: Acute kidney injury; adult; crush syndrome; earthquake; renal replacement therapy.

INTRODUCTION

Crush syndrome (CS) is a complex pathophysiological condition characterized by acute kidney injury (AKI) and multisystem organ dysfunction secondary to post-traumatic rhabdomyolysis. The predominant etiological factors include natural disasters such as earthquakes, traumatic accidents, and explosive incidents. The following mechanisms have been proposed to contribute to renal damage: Renal tubular obstruction, oxidative damage, renal artery vasoconstriction, hypovolemia, metabolic acidosis, and myoglobinuria that develop in rhabdomyolysis.[1] Treatment involves the removal of the molecules released by rhabdomyolysis through hydration, diuresis, or renal replacement therapy (RRT).[2]

Earthquakes are one of the most common causes of crush injuries, which are muscle or tissue damage caused by prolonged compressional trauma to the extremities and trunk. Several studies on earthquakes have shown that the incidence of CS and the development of AKI can vary significantly. These differences may be attributable to a variety of parameters, including the time spent under the rubble, the interventions performed after removal from the rubble, and even the type of rubble.[1,3] However, one of the most significant factors influencing the clinical recovery of CS and AKI, as well as the mitigation of disease severity, is the starting time, speed, and type of fluid therapy to be administered. [1] In instances where such measures prove ineffective, RRT emerges as a viable alternative. Nevertheless, close monitoring of clinical and laboratory parameters, in conjunction with rapid decision-making, is imperative within the treatment protocol for these patients.[2]

On February 06, 2023, two earthquakes occurred in Türkiye. The first, measuring 7.8 Mw, was centered in Kahramanmaras-Pazarcık, and was followed 9 h later by a 7.5 Mw in Elbistan. A subsequent 6.4 Mw earthquake in Hatay-Yayladag occurred on February 20, 2023. While many provinces were affected by these earthquakes, a total of 11 provinces sustained severe damage, and more than 48,000 lives were lost.[4]

Earthquakes will continue to occur in our country and around the world, and it is important to share experiences. However, there is a paucity of detailed data in the literature on the demographics, clinical course, laboratory data, treatment protocols, and outcomes of earthquake victims requiring intensive care. The aim of this study was to characterize the incidence, risk factors, and management patterns of AKI in patients admitted to the intensive care unit (ICU) with earthquake-related CS, with particular emphasis on RRT utilization and associated clinical outcomes.

MATERIALS AND METHODS

The study was designed as a retrospective, multicenter study conducted in 22 tertiary referral hospitals following approval by the Local Ethics Committee Çukurova University (Date: 01.09.2023, Decision no: 136). The study included earthquake victims (aged >18 years) admitted to ICUs after the Kahramanmaras and Hatay earthquakes. Exclusion criteria comprised patients (aged <18 years), those with chronic renal failure (CRF), and incomplete medical records preventing outcome assessment. The study period encompassed the initial 15 days (between February 6th, and February 21st, 2023) after admission to the ICU.

Definitions

CS was defined as a systemic disorder resulting from traumatic rhabdomyolysis (creatine kinase [CK] >500 U/L and/or ≥5X reference values) caused by sustained pressure on part or all of the body. CS carries a high mortality rate due to shock, renal failure, and widespread inflammatory responses. [2,5]

AKI was diagnosed according to the Kidney Disease: Improving Global Outcomes (KDIGO) 2012 Clinical Practice Guideline:

• Rise in serum creatinine (SCr) by ×0.3 mg/dL (≥26.5 µmol/L) within 48 h; or

• A 1.5-fold increase in SCr compared to a baseline value known or presumed to have been stable within the previous 7 days; or

• Urine output <0.5 mL/kg/h for 6 h.

The KDIGO guideline delineated the following staging of AKI:

• Stage 1: Creatinine increase of 1.5–1.9 times baseline or ≥0.3 mg/dL (≥26.5 µmol/L) or urine output <0.5 mL/kg/h for 6 h

• Stage 2: Creatinine increase of 2–2.9 times baseline or urine output <0.5 mL/kg/h for 12 h

• Stage 3: Creatinine increase of >3 times baseline or creatinine ≥4 mg/dL or initiation of RRT or urine output <0.3 mL/kg/h for 24 h or anuria for ≥12 h.[6]

Based on the aforementioned criteria, all patients rescued

from under the rubble were considered to have CS due to earthquake-related traumatic rhabdomyolysis. Since the patients' previous SCr values were unavailable, the diagnosis of AKI was based on changes in creatinine levels within the initial 24-h period, along with the assessment of urine output at 6, 12, and 24-h intervals, and RRT initiation. Patients who required RRT at any point during the 15-day follow-up period were also classified as having developed AKI.

Data Collection and Variables

In all centers participating in the study, data were obtained from medical records and subsequently recorded. The dataset included:

- The demographic characteristics (age, sex, weight, comorbidities, and history of cardiac arrest)
- Duration under the rubble
- The location from which the patient was transferred to the ICU and the reason for ICU admission (single vs. multiple reasons)
- Injury patterns and treatment options (central nervous system [CNS], thoracic, abdominal, extremity, and pelvic trauma)
- ICU prognostic scores (Glasgow Coma Scale [GCS]; APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment)
- Vital signs (heart rate, respiratory rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and body temperature) at ICU admission
- Laboratory parameters (complete blood count, comprehensive metabolic panel, muscle injury markers, inflammatory markers, and arterial blood gas analyses)
- Fluid resuscitation (the volume of the initial fluid bolus and 1st-day fluid intake) and urine output
- The treatments administered (nitroglycerin, vasopressor and inotropic support, albumin, diuretics, and blood product replacement)
- The use of RRT and modalities (intermittent hemodialysis [IHD], continuous veno-venous hemodiafiltration [CVVHDF] or continuous single-filter ultrafiltration [SCUF])
- Mechanical ventilation duration
- Length of stay (LOS) in ICU and in hospital, and post-ICU follow-up location.

Outcome Assessment

The primary outcome was defined as the development of AKI and the need for RRT within 15 days of ICU admission. The secondary outcomes included ICU LOS, total hospital LOS, discharge status, and 30-day mortality.

Statistical Analysis

Numbers and percentages were used for categorical data, whereas mean±standard deviation and median (minimum-maximum) used for continuous variables. The Chi-square test was applied for categorical variables, and the Kolmogorov–Smirnov test was used to verify the normality of continuous variables. To comparison continuous variables between two groups, the Student's t-test or Mann–Whitney U test was used depending on normality. Logistic regression analysis was used to identify significant predictors of AKI. The variables that were significant ($p<0.05$) or that were candidate ($p<0.25$) in the univariate analysis were entered in logistic regression analysis. The final model of multiple logistic regression was constructed using the forward LR method. All analyses were performed with IBM Statistical Package for the Social Sciences 20.0 (Armonk, NY: IBM Corp.). For all analyses, the statistical significance level was set at $p<0.05$.

RESULTS

A total of 315 patients who were admitted to the ICU due to being trapped under the rubble were subjected to a comprehensive evaluation for the study. However, six patients were excluded from the study due to CRF and one patient due to missing information. According to laboratory values, 61 patients did not meet the definition of CS due to their CK values, so the final number of patients examined was found to be 247.

The study population had a mean age of 39.8±17.5 years, with 55.9% male predominance. The median duration trapped under rubble and median time from rescue to ICU admission were 16 h (8–36) and 24 h (12–48), respectively. The majority of patients (57.9%) were transferred directly from the emergency departments, 34.4% from other centers, and 7.7% from hospital wards.

The prognostic scores of patients admitted to the ICU are presented below. The median GCS was 15 (interquartile range [IQR]: 12–15); the median APACHE II score was 17 (IQR: 12–26); the median SOFA score was 5 (IQR: 3–7). A total of 65.2% (n=161) of patients exhibited respiratory failure, and 42.7% of these receiving invasive mechanical ventilation. All patients' demographic data are summarized in Table 1.

A total of 74.9% (n=185) of the patients exhibited evidence of extremity trauma, 36.0% (n=89) had thoracic trauma, 17.0% (n=47) had pelvic trauma, 10.5% (n=26) had CNS trauma, 11.3% (n=28) had abdominal trauma, and 2.0% (n=5) exhibited signs of intra-abdominal hypertension. Amputation was performed in 29.7% of patients with extremity trauma, while fasciotomy was performed in 32.4% of these cases. A total of 132 (53.4%) patients in our cohort underwent surgery due to trauma. The distribution of these injuries is shown in Table 2.

AKI was observed in 78.5% (n=194) of the patients, and these patients had a longer duration of stay under the rubble compared with those without AKI (p=0.004). According to the KDIGO classification, approximately 85.9% of patients in the AKI group were classified as Stage 3. Patients in the AKI group exhibited higher ICU admission prognostic scores (GCS, APACHE II, and SOFA) (p=0.025, 0.005, and <0.001,

Table 1. Demographic, clinical, and laboratory data at the time of admission to intensive care

	All patients (n=247)
Age (years)	39.8±17.5
Gender (F/M)	109/138 (44.1/55.9)
Weight (kg) (F/M)	71.4±13.5/76.6±11.7
Comorbidities	
Diabetes mellitus	20 (8.1)
COPD	5 (2.0)
Hypertension	28 (11.3)
Atherosclerosis	12 (4.9)
Cardiac arrest before ICU	12 (4.9)
Reasons for ICU admission	
Sepsis	58 (23.48)
Shock	25 (10.12)
CNS trauma	10 (4.04)
Disturbance of consciousness	35 (14.17)
Respiratory failure	73 (29.55)
Hemodynamic instability	112 (45.3)
Other	82 (33.19)
Laboratory findings at admission	
Creatine kinase (U/L)	5977 (1169–39000)
Blood urea nitrogen (mg/dL)	57.0 (34.0–99.0)
Creatinine (mg/dL)	2.3 (1.03–3.96)
Uric acid (mg/dL)	8.4±3.8
Phosphorus (mg/dL)	5.6 (3.5–7.7)
Potassium (mEq/L)	5.1±1.1
Albumin (g/dL)	28.7±8.2
C-reactive protein (mg/dL)	115 (63.1–197.0)
Procalcitonin (ng/mL)	4.7 (1.0–16.7)
Myoglobin (ng/mL)	2061 (108–4007)
Alanine aminotransferase (U/L)	168.0 (60.6–403.0)
Aspartate aminotransferase (U/L)	350 (110–932)
White blood cell (109/L)	17.4±9.3
Hemoglobin (g/dL)	11.6 (9.4–14.4)
Platelet (109/L)	210 (152–269)
Lactate (mmol/L)	2.1 (1.2–5.3)
Reason for ICU admission	
(Single/multiple reason)	168/79 (68.0/32.0)
Admission-vital signs	
Heart rate (min)	107.7±19.6
Respiratory rate (min)	20.0±5.5
Systolic blood pressure (mmHg)	119.1±24.6
Diastolic blood pressure (mmHg)	67.9±16.5
Mean arterial pressure (mmHg)	84.5±16.4
Body temperature (°C)	36.4±0.6
Treatments administered	
Nitroglycerin	16 (6.5)
Vasopressor	61 (24.7)
Inotrope	42 (17.0)
Albumin	72 (29.1)
Diuretic	106 (42.9)
Fluid loading	179 (72.5)
Blood product replacement	142 (57.5)
Erythrocyte	136(55.1)
Platelet	27 (10.9)
Fresh frozen plasma	33 (13.4)
Cryoprecipitate	3 (1.2)
The volume of the initial fluid bolus (mL)	4554.57±2903.96
The use of RRT	135 (43.8)
Duration of mechanical ventilation (hours)	92.4±107.7 (2-720)
Length of stay in ICU (days)	6.6±7.4 (1-56)
Length of stay in hospital (days)	19.3±34.2 (1-256)
Post-ICU follow-up locations	
Discharged	2 (0.8)
Transfer to ward	147 (59.5)
Transfer to another hospital	53 (21.5)
Mortality	45 (18.2)

Values are presented as mean±standard deviation (minimum-maximum) or median (Q1-Q3) for continuous variables and n (%) for categorical variables. F/M: Female/Male; COPD: Chronic obstructive pulmonary disease; ICU: Intensive care unit; GCS: Glasgow Coma Scale; APACHE II: Acute physiology and chronic health evaluation II; SOFA: Sequential organ failure assessment; CNS: Central nervous system; RRT: Renal replacement therapy.

respectively). DBP and MAP were statistically different in patients with AKI (p=0.009 and p=0.035, respectively). While there was no difference between AKI and non-AKI patients in terms of the volume of the initial fluid bolus and 1st-day fluid intake (p=0.509 and p=0.909, respectively), urine output was lower in patients with AKI (p<0.001) (Table 3).

Laboratory parameters at admission showed statistically differences between the AKI and non-AKI groups. Markers of muscle injury were significantly higher in patients diagnosed with AKI: The median CK level was 9731 U/L versus 2373 U/L (p=0.002), and the median myoglobin level was 3000 ng/mL versus 231 ng/mL (p=0.005). Parameters of kidney function were found to be significantly worse in the AKI group (BUN: 65 mg/dL vs. 39 mg/dL, p=0.001 and SCr: 2.9 vs. 0.83 mg/dL, p<0.001) (Table 3).

According to the multiple logistic regression analysis, myoglobin increased the risk of developing AKI (OR: 1.001; 95% CI: 1.000–1.001), and creatinine level also increased the risk of AKI by approximately 1.7-fold (OR: 1.735; 95% CI: 1.151–2.615) (Fig. 1).

Table 2. Types of trauma

	All patients (n=247)
CNS trauma	26 (10.5)
Intracranial lesions	
Subdural hemorrhage	2 (7.6)
Epidural hemorrhage	2 (7.6)
Subarachnoid hemorrhage	0 (0.0)
Parenchymal contusion	10 (38.4)
Cranium fracture	18 (69.2)
Treatment options	
Follow-up	22 (84.6)
Surgery	4 (15.4)
Thoracic trauma	89 (36.0)
Pleural conditions	
Pneumothorax	28 (31.5)
Hemothorax	9 (10.1)
Hemopneumothorax	10 (11.2)
Pneumomediastinum	8(8.98)
Subcutaneous emphysema	2 (2.2)
Scapular fracture	2 (2.2)
Rib fracture	30 (33.7)
Flail chest	0 (0.0)
Laceration or other	20 (19.1)
Side	
Unilateral	63 (70.8)
Bilateral	26 (29.2)
Treatment options	
Follow-up	56 (63.7)
Tube thoracostomy	31 (35.2)
Surgery	1 (1.1)
Abdominal trauma	28 (11.3)
Affected organs	
Liver	14 (50)
Spleen	4 (14.28)
Small bowel	6 (21.4)
Large bowel	2 (6.89)
Renal	11 (39.2)
Bladder	1 (3.57)
Other (intrauterine ex fetus)	1 (3.57)
Intra-abdominal hypertension	5 (2.0)
Intra-abdominal hypertension treatment	
Follow-up	2 (40.0)
Laparotomy	3 (60.0)
Extremity trauma	185 (74.9)
Affected extremities	
Right upper extremity	54 (29.1)
Right lower extremity	117 (63.24)
Left upper extremity	44 (23.78)
Left lower extremity	87 (47.02)
Other (burn)	1 (0.54)
Type of trauma	
Fracture	50 (27.02)
Open wound	37 (20)
Soft-tissue injury	85 (45.94)
Compartment syndrome	106 (57.29)
Treatment options	
Medical	74 (40)
Surgery	128 (69.2)
Fasciotomy	60 (32.4)
Fixation	15 (7.93)
Debridement	35 (18.91)
Amputation	55 (29.72)
Pelvic trauma	42 (17.0)
Treatment options	
Follow-up	32 (76.2)
Surgery	10 (23.8)

Values are presented as n (%). CNS: Central nervous system.

Among the 194 patients with AKI, 121 (62.4%) required RRT, constituting 49% of the total study cohort. The duration of stay in the rubble was shorter in the non-AKI group (p=0.013). Patients requiring RRT exhibited more severe clinical presentations: The APACHE II score and the SOFA score were higher in the RRT group (both p<0.001). SBP, DBP, and MAP were lowest in the AKI-non-RRT group and highest in the non-AKI group; heart rate, respiratory rate, and body temperature were similar across all groups (p= 0.008, p=0.007, and p=0.011). Patients who underwent RRT were received a greater number of medications (excluding inotropes, diuretics, and fluid loading). Urine output was lower in patients with AKI compared with non-AKI patients (p<0.001). Laboratory markers indicative of tissue damage and organ dysfunction were found to be significantly elevated in the RRT group: the median CK level was 17134 compared with 3322 U/L (p<0.001), and the median SCr level was 3.4 compared with 1.3 mg/dL (p<0.001) (Table 4).

Creatinine level and reasons for ICU admission were identified as factors associated with the need for RRT. An elevated creatinine level was associated with a 1.7-fold (OR: 1.7, 95%CI: 1.28–2.15) increase in the use of RRT, while the reasons for ICU admission were associated with a 2.9-fold increase (OR: 2.9; 95% CI: 1.26–6.90) (Fig. 1).

Patients with AKI had prolonged ICU stays (median 5 days

Table 3. AKI versus non-AKI

	AKI (n=194)	non-AKI (n=53)	p
Age (years)	39.1±17.7	42.0±16.7	0.292
Gender (F/M)	80/114 (41.2/58.8)	29/24 (54.7/45.3)	0.088
Weight (kg)	74.0±12.9	75.7±12.1	0.433
The duration of stay in the rubble (hours)	20.0 (8.5–36.0)*	10 (5.0–24.0)	0.004
The time between patients' rescue from the rubble and ICU admis-sion(hours)	24.0 (10.0–48.0)	24.0 (18.8–72.0)	0.083
Comorbidities			
Diabetes mellitus	15 (7.7)	5 (9.4)	0.776
Hypertension	20 (10.3)	8 (15.1)	0.333
COPD	4 (2.1)	1 (1.9)	0.999
Atherosclerosis	7 (3.6)	5 (9.4)	0.139
Reason for ICU admission			
(Single/multiple reason)	125/69*	43/10	0.021
KDIGO stage			
1	7 (4.1)		
2	17 (10.0)		
3	146 (85.9)		
ICU admission prognostic scores			
GCS	14 (10.8–15.0)*	15 (14–15)	0.025
APACHE II	18.0 (12.0–27.0)*	12 (10–23)	0.005
SOFA	6 (4–8)*	4 (2–6)	<0.001
ICU admission-vital signs			
Heart rate (min)	107.9±20.4	106.7±16.4	0.677
Respiratory rate (min)	20.0 (16.0–24.0)	20.0 (15.0–24.0)	0.770
Systolic blood pressure (mmHg)	120.0 (100.0–131.0)	120.0 (110.0–140.0)	0.074
Diastolic blood pressure (mmHg)	66.0 (56.0–76.5)*	73.0 (60.0–84.0)	0.009
Mean arterial pressure (mmHg)	83.0 (72.0–93.0)*	88.7 (78.0–100.0)	0.035
Body temperature (°C)	36.5 (36.0–36.8)	36.2 (36.0–36.8)	0.442
Respiratory failure	126 (64.9)	35 (66.0)	0.883
Existing traumas			
CNS trauma	20 (10.3)	6 (11.3)	0.803
Thorax trauma	68 (35.1)	21 (39.6)	0.539
Abdominal trauma	24 (12.4)	4 (7.5)	0.326
Intra-abdominal hyperten-sion	5 (2.6)	0 (0.0)	0.588
Extremity trauma	144 (74.2)	41 (77.4)	0.641
Pelvic trauma	33 (17.0)	9 (17.0)	0.996
Treatments administered			
Nitroglycerin	16 (8.3)*	0 (0.0)	0.027
Vasopressor	57 (29.4)*	4 (7.5)	0.001
Inotrope	37 (19.1)	5 (9.4)	0.098
Albumin	60 (31.3)	12 (22.6)	0.223
Diuretic	88 (45.4)	18 (34.0)	0.137
Fluid loading	143 (73.7)	36 (67.9)	0.403
Blood product replacement	117 (60.3)	25 (47.2)	0.086
The volume of the initial fluid bo-lus (mL)	4500 (2500–6500)	5000 (3100–6250)	0.509
1st-day fluid intake (mL)	4850 (3175–6950)	4800 (3225–5900)	0.909
1st-day urine output (mL)	715 (150–1800)*	1500 (1200–2000)	<0.001
Duration of mechanical ventilation (hours)	48.0 (24.0–120.0)	72.0 (48.0–120.0)	0.448

Length of stay in ICU (days)	5.0 (2.0–10.0)*	3.0 (2.0–6.0)	0.010
Length of stay in hospital (days)	11.0 (4.0–16.0)	9.0 (6.0–16.0)	0.641
Post-ICU follow-up location			
Discharged	2 (1.3)	0 (0.0)	
Transfer to ward	102 (67.5)	45(88.2)	0.015
Transfer to another hospital	47 (31.1)	6 (11.8)	
Laboratory findings at admission			
Creatine kinase (U/L)	9731(1180–45920)*	2373 (1100–8579)	0.002
Blood urea nitrogen (mg/dL)	65.0 (38.2–100.0)*	39.0 (26.0–72.0)	0.001
Creatinine (mg/dL)	2.9 (1.59–4.50)*	0.83 (0.57–1.36)	<0.001
Uric acid (mg/dL)	8.9±3.7*	6.1±3.5	<0.001
Phosphorus (mg/dL)	6.3 (4.3-8.0)*	3.4 (2.8–4.2)	<0.001
Potassium (mEq/L)	5.3±1.2*	4.6±0.7	<0.001
Albumin (g/dL)	26.9±7.8*	30.3±8.9	0.016
C-reactive protein (mg/dL)	123 (71.5–202.5)*	86.2 (44.2–169.5)	0.024
Procalcitonin (ng/mL)	8.0 (2.0–19.5)*	0.9 (0.15–4.5)	<0.001
Myoglobin (ng/mL)	3000 (344–4007)*	231 (27.2–2512)	0.005
Alanine aminotransferase (U/L)	219.5 (74.0–443.0)*	93.0 (40.0–182.0)	<0.001
Aspartate aminotransferase (U/L)	619.5 (150–1023)*	130.0 (52.1–292.0)	<0.001
White blood cell (109/L)	18.1±9.3*	14.9±9.1	0.005
Hemoglobin (g/dL)	11.6 (9.2–15.2)	11.7 (9.7–13.0)	0.361
Platelet (109/L)	204.5 (149–256)*	230 (180–293)	0.033
Lactate (mmol/L)	2.2 (1.3–5.8)*	1.48 (1.1–3.0)	0.028
pH	7.29 (7.18–7.36)	7.36 (7.30–7.41)	<0.001
Mortality	43 (22.2)*	2 (3.8)	0.002

Values are presented as mean±standard deviation and/or median(Q1-Q3) for continuous and n (%) for categorical variables. AKI: Acute kidney injury; F/M: Female/Male; COPD: Chronic obstructive pulmonary disease; ICU: Intensive care unit; GCS: Glasgow coma scale; APACHE II: Acute physiology and chronic health evaluation II; SOFA: Sequential organ failure assessment; CNS: Central nervous system; RRT: Renal replacement therapy; KDIGO: Kidney disease improving global outcomes.

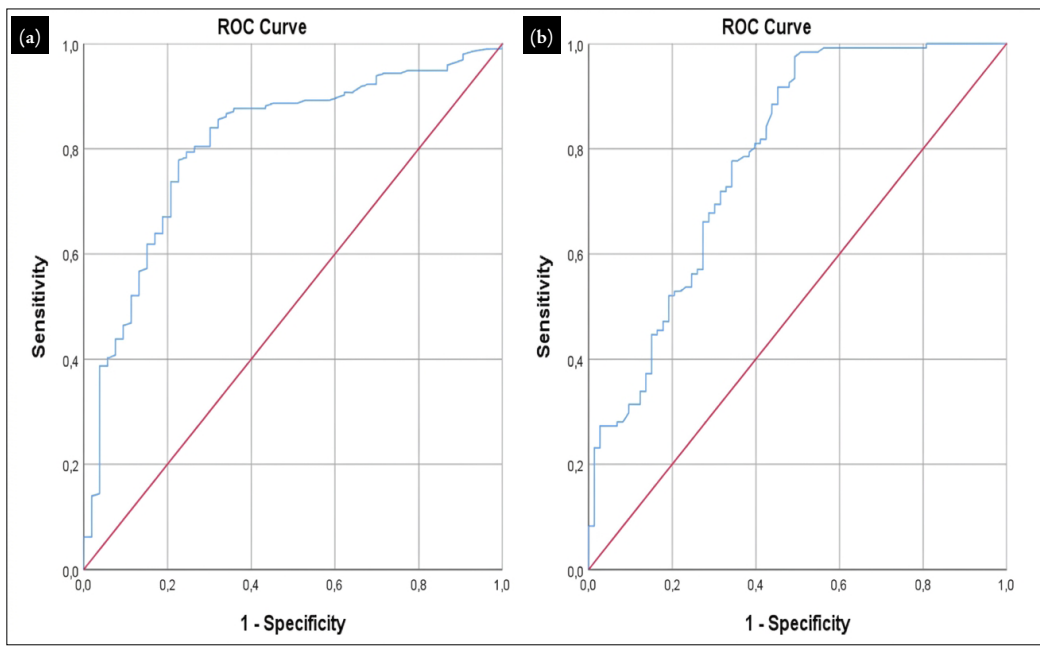


Figure 1. (a) Receiver operating characteristic (ROC) curve for creatinine levels while determining acute kidney injury, **(b)** ROC curve for creatinine levels while determining renal replacement therapy.

Table 4. Renal replacement therapy in patients

	AKI RRT (n=121)	AKI non-RRT (n=73)	non-AKI (n=53)	p
Age (years)	37.0±16.0	42.8±19.8	42.0±16.7	0.074
Gender (F/M)	52/69 (43.0/57.0)	28/45 (38.4/61.6)	29/24 (54.7/45.3)	0.177
Weight (kg)	75.1±12.2	72.4±13.8	75.7±12.1	0.315
The duration of stay in the rubble (hours)	16.0 (10–40)	24 (8–32.5)	10 (5.0–24.0)[a,b]	0.013
The time between patients' rescue from the rubble and ICU admission (hours)	24.0 (9.0–48.0)	24.0 (10.0–48.0)	24.0 (18.8–72.0)	0.095
Comorbidities				
Diabetes mellitus	6 (5.0)	9 (12.3)	5 (9.4)	0.175
Hypertension	6 (5.0)	14 (19.2)	8 (15.1)	0.006
COPD	2 (1.4)	2 (2.7)	1 (1.9)	0.870
Atherosclerosis	1 (0.8)	6 (8.2)	5 (9.4)	0.015
Reason for ICU admission				
(Single/multiple reason)	71(58.7)/50(41.3)	54(74.0)/19(26.0)	43(81.1)/10 (18.9)[a]	0.006
ICU admission prognostic scores				
GCS	14 (11.0–15.0)	14 (10.0–15.0)	15 (14–15)	0.080
APACHE II	20.0 (14.0–29.0)	15.0 (9.0–22.0)[a]	12 (10–23)[a]	<0.001
SOFA	6 (4–8)	4 (2–7)[a]	4 (2–6)[a]	<0.001
ICU admission-vital signs				
Heart rate (min)	106.9±22.2	109.7±16.9	106.7±16.4	0.589
Respiratory rate (min)	20.0 (17.0–24.0)	18.5 (14.0–22.0)	20.0 (15.0–24.0)	0.058
Systolic blood pressure (mmHg)	120.0 (100.0–136.0)	110.0 (98.0–126.0)[a]	120.0 (110–140)[b]	0.008
Diastolic blood pressure (mmHg)	70.0 (60.0–76.0)	65.0 (50.0–78.0)	73.0 (60.0–84.0)[a,b]	0.007
Mean arterial pressure (mmHg)	84.0 (73.0–96.0)	80.0 (68.0–90.0)[a]	88.7 (78.0–100.0)[b]	0.011
Body temperature (oC)	36.5 (36.0–36.8)	36.2 (36.0–36.7)	36.2 (36.0–36.8)	0.129
Respiratory failure	47 (61.2)	52 (71.2)	35 (66.0)	0.357
Existing traumas				
CNS trauma	9 (7.4)	11 (15.1)	6 (11.3)	0.239
Thorax trauma	36 (29.8)	32 (43.8)	21 (39.6)	0.117
Abdominal trauma	15 (12.4)	9 (12.3)	4 (7.5)	0.618
Intra-abdominal hyperten-sion	5 (4.1)	0 (0.0)	0 (0.0)	0.070
Extremity trauma	92 (76.0)	52 (71.2)	41 (77.4)	0.679
Pelvic trauma	20 (16.5)	13 (17.8)	9 (17.0)	0.974
Treatments administered				
Nitroglycerin	14 (11.7)	2 (2.7)	0 (0.0)[a]	0.005
Vasopressor	40 (33.1)	17 (23.3)	4 (7.5)[a]	0.001
Inotrope	20 (16.5)	17 (23.3)	5 (9.4)	0.122
Albumin	51 (42.5)	9 (12.5)a	12 (22.6)[a]	0.001
Diuretic	55 (45.5)	33 (45.2)	18 (34.0)	0.331
Fluid loading	92 (76.0)	51 (69.9)	36 (67.9)	0.457
Blood product replacement	85 (70.2)	32 (43.8)[a]	25 (47.2)[a]	0.001
RRT modalities				
Intermittent hemodialysis	93			

CVVHDF	57			
SCUF	11			
The volume of the initial fluid bo-lus (mL)	4000 (1800–6435)	5000 (3600–6600)	5000 (3100–6250)	0.076
First–day fluid intake (mL)	4800 (3350–7200)	5000 (2800–6500)	4800 (3225–5900)	0.893
First–day urine output (mL)	710 (150–2000)	750 (180–1200)	1500 (1200–2000)a,b	<0.001
Duration of mechanical ventilation (hours)	50.0 (28.0–144.0)	48.0 (24.0–48.0)	72.0 (48.0–120.0)	0.153
Length of stay in ICU (days)	6.0 (3.0–11.0)	2.0 (2.0–5.0)[a]	3.0 (2.0–6.0)[a]	<0.001
Length of stay in hospital (days)	12.0 (7.0–17.0)	8.0 (2.0–15.0)[a]	9.0 (6.0–16.0)	0.045
Post-ICU follow–up location				
Discharged	1 (0.8)	1 (1.4)	0 (0.0)	
Transfer to ward	60 (49.6)	42 (57.5)	45 (88.2)	0.009
Transfer to another hospi-tal	36 (29.8)	11 (15.1)	6 (11.8)	
Laboratory findings at admission				
Creatine kinase (U/L)	17134(1520–68603)	3322(1012–15701)[a]	2373 (1100–8579)[a]	<0.001
Blood urea nitrogen (mg/dL)	74.0 (46.0–107.0)	49.7 (25.0–85.1)[a]	39.0 (26.0–72.0)[a]	<0.001
Creatinine (mg/dL)	3.4 (2.3–4.9)	1.3 (0.7–3.2)[a]	0.83 (0.57–1.36)[a]	<0.001
Uric acid (mg/dL)	9.5±3.3	7.8±4.2[a]	6.1±3.5[a]	<0.001
Phosphorus (mg/dL)	7.0(5.4–8.0)	4.8 (3.2–8.1)[a]	3.4 (2.8–4.2)[a,b]	<0.001
Potassium (mEq/L)	5.6±1.1	4.9±1.2[a]	4.6±0.7[a]	<0.001
Albumin (g/dL)	25.8±7.1	28.8±8.7[a]	30.3±8.9[a]	0.001
C–reactive protein (mg/dL)	128 (76.7–211.7)	109.8 (57.4–180.0)	86.2 (44.2–169.5)[a]	0.025
Procalcitonin (ng/mL)	9.9 (3.2–29.0)	3.2 (0.7–12.0)[a]	0.9 (0.15–4.5)[a,b]	<0.001
Myoglobin (ng/mL)	3000 (421–4007)	3000 (339–4007)	231 (27.2–2512)[a,b]	0.020
Alanine aminotransferase (U/L)	320 (138–519)	91.0 (38.0–254.0)[a]	93.0 (40.0–182.0)[a]	<0.001
Aspartate aminotransferase (U/L)	840.0 (336–1485)	182.0 (63–633)[a]	130.0 (52.1–292.0)[a]	<0.001
White blood cell (109/L)	18.4±8.7	17.7±10.2	14.9±9.1	0.065
Hemoglobin (g/dL)	11.9 (9.1–15.9)	11.3 (9.5–14.5)	11.7 (9.7–13.0)	0.543
Platelet (109/L)	185.0 (131–239)	230.0 (189–275)[a]	230 (180–293)[a]	<0.001
Lactate (mmol/L)	2.5 (1.4–7.1)	1.7 (1.1–3.7)[a]	1.48 (1.1–3.0)[a]	0.005
pH	7.25 (7.17–7.34)	7.32 (7.20–7.39)	7.36 (7.30–7.41)[a,b]	<0.001
Mortality	24 (19.8)	19 (26.0)	2 (3.8)a,b	0.005

Values are presented as mean±standard deviation or median (Q1-Q3) for continuous and n (%) for categorical variables. aDifferent from AKI+RRT group, bDifferent from AKI-non RRT group. RRT: Renal replacement therapy; GCS: Glasgow Coma Scale; APACHE II: Acute physiology and chronic health evaluation II; SOFA: Sequential organ failure assessment; ICU: Intensive care unit; COPD: Chronic obstructive pulmonary disease; CVVHDF: Continuous veno-venous hemodiafiltration; SCUF: Slow continuous ultrafiltration.

vs. 3 days, p=0.010), but there was no significant difference in hospital LOS when compared with non-AKI patients (Table 3). Patients requiring RRT had the longest ICU stays compared with AKI patients not requiring RRT and with non-AKI patients (p<0.001) (Table 4).

The 30-day mortality rate was significantly higher in patients with AKI compared with those without AKI (p=0.002) (Table 3). Among patients with AKI, mortality rates were similar between those requiring RRT (19.8%) and those managed conservatively (26.0%); however, both groups exhibited significantly higher mortality rates than non-AKI patients (p=0.005) (Table 4).

DISCUSSION

This multicenter retrospective analysis of earthquake victims with CS demonstrates an extremely high incidence of AKI (78.5%) and a requirement for RRT (62.4% of AKI patients), significantly exceeding rates reported in previous earthquake series. These findings have important implications for disaster preparedness and the development of clinical management

protocols for future earthquake responses.

The development of AKI due to CS has been reported at varying rates in the literature: 6% (n=30) in the Iranian earthquake, 18.3% (n=87) in the Marmara earthquake, 41.6% (n=62) in the Chinese earthquake, and 30.2% (n=95) in the most recent article.[3,7-9]

The variation in AKI incidence between different disasters can be attributed to several factors, including rescue time, initial treatment protocols, referral patterns, and the severity of cases reaching tertiary care centers. Notably, our findings align more closely with those of a recent report by Aydin et al.,[10] who documented an AKI incidence of 88.7% in ICU patients following the same earthquakes in Türkiye. This suggests that the severity of the disaster and the clinical status of patients referred to tertiary care centers contributed to these unprecedented rates.

The results of this study demonstrate that patients in the AKI group exhibited a prolonged stay in the rubble, elevated GCS, APACHE II, and SOFA scores, diminished MAP, increased use of nitroglycerine and vasopressor medications, and higher laboratory values, which is consistent with many previous studies.[2,11,12] These factors have been shown to accelerate the development of AKI.

Given these factors, is it possible to detect the development of AKI earlier? This process can be explained as follows: Rhabdomyolysis is a clinical condition caused by muscle breakdown. The release of CK and myoglobin from muscle cells reflects this process. CK has been identified as a significant marker of rhabdomyolysis and has been proposed as an important predictor in the development of post-traumatic AKI.[9,12,13] However, the present study discovered that serum myoglobin and creatinine can be used as predictors of AKI development. Consistent with our study, Tarazona et al.[14] reported that myoglobin may be used as an early predictor of post-traumatic AKI, for the following reasons: First, myoglobin acts as a direct mediator of rhabdomyolysis-induced AKI; second, myoglobin levels increase in the blood within a few hours and, in contrast to CK, myoglobin is not transported through the lymphatic system. Similarly, Frelich et al.[15] indicated that myoglobin, creatinine, neutrophil gelatinase-associated lipocalin, and high mobility group box1 can serve as early indicators of post-traumatic AKI.

Hypovolemia constitutes the most significant factor in the pathogenesis of rhabdomyolysis-induced AKI. Therefore, early and aggressive fluid resuscitation represents the primary intervention for preventing AKI in CS.[16] The current study demonstrated no significant difference between AKI and non-AKI groups in terms of fluid administration and effective fluid therapy during the first 24-h period. Furthermore, despite diuretic administration, the AKI group exhibited reduced urine output during this initial 24-h interval. Gunal et al.[17] and Sagheb et al.[1] highlighted that early and vigorous fluid resuscitation combined alkaline diuresis resulted in better outcomes by preventing AKI in crush victims and reducing the need for RRT. However, the results of our study demonstrate that the RRT rate remains high, even in the presence of effective fluid therapy. This observation is in accordance with the recent findings of Aydin et al.,[10] who reported that despite the implementation of standardized fluid protocols, 88.7% of ICU patients developed AKI following the 2023 earthquakes. This suggests that certain injury patterns may be resistant to conventional preventive measures.

Some patients with AKI may have a refractory response to conventional therapeutic interventions, including volume resuscitation and fluid replacement protocols. In such circumstances, the implementation of RRT becomes clinically indicated. This study found that 62.4% of patients who developed AKI received RRT. Patients who underwent RRT had higher APACHE II and SOFA scores, as well as higher CK, BUN, creatinine, and potassium levels. No differences were observed in fluid loading, intake, or output between the RRT and non-RRT groups in patients who developed AKI. Although both groups received identical treatments, only one group required RRT. This raises the question of whether this need could have been anticipated and RRT initiated earlier. According to our regression analysis, the reasons for ICU admission (single/multiple reasons) and creatinine level were identified as predictor parameters of RRT requirement. In our study, SBP, DBP, and MAP tended to be lower in AKI/non-RRT group, which may indicate a milder, potentially reversible form of AKI that responded to supportive management and therefore did not progress to a severity requiring RRT. Unlike our study, Comoglu et al.[9] reported in their recent article that they developed a dialysis score that would facilitate patient follow-up. The authors observed that 95 (30.2%) of patients developed AKI, 68 of these patients (21.6%) requiring RRT. The dialysis score included CK, albumin, and the number of traumatic sites, and exhibited sensitivity and specificity values of 98.5% and 77.6% for a dialysis score of 3 or higher, and 97.1% and 89.4% for a dialysis score of 4 or higher, respectively.[9] In another study in pediatric patients, the authors developed a renal score (comprising glomerular filtration rate, CK level, time under the rubble, presence of amputation or fasciotomy, and urine volume) for RRT, with a cut-off value of 2.5.[5] The authors of the study asserted that renal score, CK level, and myoglobinuria were the most effective markers for RRT. In a similar study, Atmis et al.[18] demonstrated increased CK and phosphorus levels and the percentage of body area that was crushed were valuable predictors of RRT.

In this study, the RRT utilization rate (62.4%, n=121) is one of the highest reported in the disaster literature. RRT rates in patients with AKI have been presented as 68% (n=59) in the Marmara earthquake, 53.2% (n=33) in the Wenchuan earthquake, and 60.9% (n=123) in the Kobe earthquake.[3,8,11] The patients underwent various RRT modalities, including IHD (n=93), CVVHDF (n=57), and SCUF (n=11). The RRT

modality used may vary depending on the clinical needs of the patients; however, Sever et al.[2] suggest IHD as the primary option, which is consistent with our study. New extracorporeal blood purification (EBP) techniques may now be needed. In situations where myoglobin is a predictor of AKI development, as in this study, new EBP modalities such as hemadsorption or high- and medium-cutoff membranes may increase myoglobin clearance and improve outcomes in patients with AKI secondary to CS.[19]

It was not surprising that patients who developed AKI and received RRT had a longer ICU stay. On the other hand, the 30-day mortality rate was higher in patients with AKI than in those without AKI. However, somewhat unexpectedly, mortality rates were similar among patients with AKI who required RRT (19.8%) and those who were managed conservatively (26.0%). This finding, together with previous reports, suggests that AKI itself is a major determinant of poor outcome in CS, whereas the need for RRT more likely reflects underlying disease severity and multiorgan dysfunction rather than directly determining mortality.[20,21] A key implication of these findings is the necessity of working diligently to prevent the development of AKI in the first place.

Our study has several limitations. First, the retrospective design inherently limits the quality and completeness of data collection, as medical records from emergency disasters may be incomplete or inconsistent across participating centers. Second, differences in institutional practices, availability of RRT, and levels of expertise may have resulted in heterogeneous treatment approaches and outcomes. Third, the 15-day observation period was designed to cover the acute injury phase and initial treatment response, but may not have been sufficient to capture long-term renal recovery and chronic complications. Another limitation of the study is the lack of long-term follow-up data on persistent renal dysfunction or recovery patterns.

CONCLUSION

This multicenter study of 247 patients with CS demonstrated that 78.5% of ICU patients developed AKI. Serum myoglobin and creatinine were identified as independent predictors of AKI development, demonstrating the potential for early risk stratification in disaster areas. Concurrently, creatinine level has been identified as a predictor of RRT, with the reasons for admission to ICU also serving as a concomitant predictor. The higher need for RRT and significantly higher mortality in the AKI group highlight the severity of renal complications following earthquake-related crush injuries. Despite fluid loading protocols, the incidence of severe AKI remained high, highlighting the limitations of conventional preventive measures. The optimal timing of RRT in CS management protocols, particularly during disasters, needs to be more clearly defined. These findings have critical implications for disaster preparedness and highlighting the need for adequate dialysis capacity in earthquake-prone areas and rapid rescue operations to minimize duration under rubble.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Depremle ilişkili crush sendromunda böbrek yetmezliğinin yönetimi: Çok merkezli yoğun bakım sonuçları

AMAÇ: Crush sendromu (CS), travmatik rabdomiyoliz sonrası gelişen ve öncelikli olarak böbrekleri etkileyen multisistem organ disfonksiyonu ile ilişkili klinik bir durumdur. Bu çalışmanın amacı, depremzede CS'li hastalarda akut böbrek hasarının (ABH) insidansını, risk faktörlerini ve tedavi modellerini, özellikle renal replasman tedavisi (RRT) kullanımı ve klinik sonuçlarına odaklanarak karakterize etmektir.

GEREÇ VE YÖNTEM: Retrospektif çok merkezli bu çalışmada, Kahramanmaraş-2023 depremlerinden sonra 22 hastanenin yoğun bakım ünitelerine yatırılan depremle ilişkili CS'li 247 yetişkin hasta incelenmiştir. Demografik veriler, yaralanma modelleri, laboratuvar parametreleri, tedavi protokolleri ve sonuçlar, yoğun bakıma yatışı izleyen ilk 15 gün için değerlendirilmiştir.

BULGULAR: Hastaların %78.5'inde (n=194) ABH gelişti ve bu hastaların %62.4'ünde (n=121) RRT gerekti. Çoklu lojistik regresyon analizi, miyoglobin ve kreatinin düzeylerinin ABH gelişme riskinin artmasıyla ilişkili olduğunu göstermiştir (OR: 1.001; %95 CI: 1.000-1.001 ve OR: 1.735; %95 CI: 1.151-2.615). Benzer şekilde, kreatinin düzeyi ve yoğun bakım ünitesine yatış nedenleri, RRT uygulanmasını etkileyen faktörlerdi (OR: 1.7; %95 CI: 1.28-2.15 ve OR: 2.9; %95 CI: 1.26-6.90). ABH'li hastalarda 30 günlük mortalite oranı, ABH olmayan hastalara göre daha yüksekti. RRT uygulanan ve uygulanmayan ABH'li hastalar arasında mortalite oranları benzerdi.

SONUÇ: Bu çalışma, depremle ilişkili CS'de ABH'nin yüksek oranda görüldüğünü ve optimal yönetim için yeterli diyaliz kapasitesi ile serum miyoglobin ve kreatinin düzeyleri kullanılarak erken risk sınıflandırması yapılması ve afetlere karşı daha iyi hazırlık yapılması gerektiğini vurgulamaktadır.

Anahtar sözcükler: Akut böbrek hasarı; Crush sendromu; deprem; renal replasman tedavisi; yetişkin.

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ORIGINAL ARTICLE

Ocular trauma presentations to a tertiary emergency department: Demographic characteristics, injury mechanisms, and clinical outcomes

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ABSTRACT

BACKGROUND: This study aimed to evaluate the demographic characteristics, etiological factors, associated injuries, and clinical outcomes of patients presenting to a tertiary emergency department with ocular trauma.

METHODS: This retrospective observational study included 6,557 patients who presented to the Emergency Department of Süleyman Yalçın City Hospital with ocular trauma between 2022 and 2025. Demographic data, trauma mechanisms, physical examination findings, associated injuries, need for surgical intervention, and clinical outcomes were evaluated. Categorical variables were analyzed using the chi-square test, while Student's t-test and the Mann–Whitney U-test were used for continuous variables.

RESULTS: Of the patients, 85.4% (n=5,598) were male, and 52.9% were aged between 20 and 39 years. The most common reason for presentation was ocular foreign body injury (88.9%), and the most frequent physical examination finding was corneal abrasion (30.9%). Computed tomography (CT) was performed in 8.6% of cases. In 95.9% of patients, ocular trauma occurred without associated injuries, and 1.5% required surgical intervention. Overall, 97.9% of patients were discharged from the emergency department. Ocular foreign body injury (p<0.001), falls (p<0.001), traffic accidents (p=0.004), penetrating or sharp object injuries (p<0.001), and chemical injuries (p=0.002) were more frequent in males. Female sex (p<0.001), age over 60 years (p<0.001), Glasgow Coma Scale (GCS) score below 13 (p<0.001), and the presence of associated injuries (p<0.001) were associated with increased surgical intervention. Female sex (p<0.001), age under 9 years (p<0.001) and over 60 years (p<0.001), GCS score ≤13, presentation due to falls (p<0.001) or traffic accidents (p<0.001), and the presence of orbital or extraocular bone fractures (p<0.001) were associated with higher hospitalization rates.

CONCLUSION: Ocular trauma predominantly affected young males and was most commonly caused by foreign bodies. Corneal abrasion was the most frequent finding. Most cases involved isolated ocular trauma, did not require CT, and were discharged from the emergency department. Female sex, pediatric and geriatric age groups, low GCS scores, and trauma related to falls or traffic accidents were associated with increased surgical intervention and hospitalization.

Keywords: Concomitant injuries; eye trauma; hospitalization; mechanism; outcome; outpatient discharge; surgical intervention.

INTRODUCTION

Ocular trauma is one of the most common causes of visual impairment and preventable blindness and has become a public health problem. Worldwide, approximately 1.6 million people suffer from blindness due to ocular injuries.[1] While serious complications such as blindness are less frequent in developed countries, ocular trauma has been reported as one of the major causes of monocular blindness in African countries.[2,3]

Depending on the severity of trauma, mild injuries such as

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corneal abrasions, eyelid lacerations, and foreign body penetration are frequently observed; however, ocular trauma may also lead to severe complications, including significant loss of visual function and blindness.[4] As with all types of trauma, patients with traumatic eye injuries most commonly present first to emergency departments. In the United States, ocular injuries account for approximately 3% of all emergency department visits.[5] These injuries result from various mechanisms, including motor vehicle accidents, falls from height, industrial accidents, violence, and domestic accidents. In addition, ocular trauma may be accompanied by injuries to other organ systems. Ocular injuries have been reported to accompany approximately 84% of head trauma cases.[6]

The most common ocular injuries occur due to blunt trauma and are generally treated conservatively. In contrast, penetrating ocular injuries usually require surgical intervention and are, therefore, managed with hospital admission.[7]

Young males are more frequently exposed to ocular trauma.[8] The most affected structures are the conjunctiva, retina, cornea, and sclera. Conjunctival injuries are usually minor, such as subconjunctival hemorrhage and conjunctival laceration, whereas optic nerve and retinal injuries threaten visual function and may result in vision loss.[9]

In patients with ocular trauma, ocular evaluation is performed after life-threatening injuries are stabilized within the scope of primary care.[10] However, in patients with major trauma, ocular injuries may be overlooked during the evaluation of life-threatening injuries involving large anatomical regions, such as the head and neck, abdomen, and chest. Factors including altered mental status, distracting injuries, and limited experience in ocular examination may also contribute to delayed recognition of ocular injuries.[11] Systematic evaluation and management of patients with ocular trauma are therefore vital for preserving visual function and preventing morbidity. The ability of emergency physicians to recognize ocular trauma during the initial assessment and manage it appropriately contributes significantly to patient prognosis.

In this study, the demographic characteristics, trauma mechanisms, physical examination findings, presence of associated injuries, radiological findings, surgical interventions, and clinical outcomes of consecutive patients presenting with ocular trauma to the emergency department of Süleyman Yalçın City Hospital between August 1, 2022, and August 1, 2025, were evaluated. The findings are expected to contribute to the identification and reduction of regional risk factors. In addition, this study aims to contribute to the literature on patients presenting to emergency departments and to provide a scientific basis for future preventive and corrective health policies. However, large-scale emergency department-based data guiding clinical decision-making regarding imaging, surgical intervention, and hospitalization in patients with ocular trauma remains limited. Therefore, this large case series study focuses on identifying trauma mechanisms, imaging requirements, associated injuries in adjacent regions, the need for surgical intervention, and factors associated with hospitalization among patients with ocular trauma presenting to a tertiary emergency department.

MATERIALS AND METHODS

Study Design

This study was designed as a retrospective observational study and conducted in the Emergency Department of Süleyman Yalçın City Hospital, a tertiary-level center. Ethical approval was obtained from the Ethics Committee of Süleyman Yalçın City Hospital (Date: 28.08.2025, Decision no: 2025/0142). The study was designed in accordance with the STROBE guideline.

Inclusion and Exclusion Criteria

All patients who presented to the Emergency Department of Süleyman Yalçın City Hospital with ocular trauma between August 1, 2022, and August 1, 2025, were included, except for those with incomplete data in the hospital registry system.

Data Collection

During the study period, a total of 8,890,676 patients presented to all units of Süleyman Yalçın City Hospital, and 1,592,402 patients presented to the emergency department. Among emergency department admissions, 6,623 patients (0.4%) presented with ocular trauma. Patient data were obtained retrospectively through the hospital electronic information system (Nucleus). The collected data were recorded on predefined study forms and subsequently transferred to Excel files.

For consecutive patients presenting with ocular trauma between August 01, 2022, and August 01, 2025, the following variables were evaluated: Demographic characteristics (age, sex, and occupation), Glasgow Coma Scale (GCS) score at presentation, trauma mechanism (traffic accident, penetrating or sharp object injury, assault, foreign body injury, chemical injury, etc.), physical examination findings (complete or partial vision loss, conjunctival hemorrhage, eyelid laceration, eyelid incision, hyphema, retinal detachment, corneal abrasion, lens dislocation, periorbital edema, etc.), presence of associated injuries, radiological findings, ophthalmology consultations, surgical interventions performed, and patient outcomes (hospitalization, discharge, and death).

Trauma mechanisms were classified according to the primary cause of injury recorded in the hospital information system. Foreign body injury refers to superficial or intraocular foreign material entering the ocular surface during occupational or environmental exposure. Blunt trauma refers to impact-related injury without penetration of ocular tissues, whereas penetrating or sharp object injury indicates direct penetration of ocular tissues by sharp instruments.

As this was a retrospective observational study, the prima-

ry outcome was defined as the description of demographic characteristics, clinical findings, and clinical outcomes of patients presenting with ocular trauma.

Sample Size

Previous studies have reported the incidence of ocular trauma to range between 2% and 5%.[7,12] In this study, the expected ocular trauma rate was assumed to be 5%. Using a two-sided standard normal distribution value of 1.96 for a 95% confidence interval and an effect size of 5%, the estimated sample size was calculated as 72. After adding a 10% margin of error, the target sample size was determined to be 80. The sample size calculation was performed to ensure methodological adequacy; however, all eligible patients during the study period were included in the analysis.

Statistical Analysis

Categorical variables are presented as frequencies and percentages. Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed variables are presented as mean±standard deviation, whereas non-normally distributed variables are presented as median (25th–75th percentiles). The Chi-square test was used for categorical variables, Student's t-test for normally distributed continuous variables, and the Mann–Whitney U-test for non-normally distributed continuous variables. For all analyses, $p<0.05$ was considered statistically significant. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0; Armonk, NY: IBM Corp.).

RESULTS

Between August 1, 2022, and August 1, 2025, 6,623 patients presented to the emergency department with ocular trauma. Sixty-six patients were excluded due to missing data, and 6,557 patients were included in the analysis.

Of the patients, 85.4% (n=5,598) were male, and 52.9% were aged between 20 and 39 years. The vast majority of patients had a GCS score of 15 (99.8%); only 11 patients had a GCS score ≤13. The most common trauma mechanisms were ocular foreign body injury (88.9%) and falls (5.2%). In 8 patients (0.1%), the trauma mechanism could not be determined. The most frequently observed physical examination findings were corneal abrasion (30.9%), conjunctival hyperemia (25.6%), and epithelial damage (21.2%). Detailed findings according to sex, age, GCS score at presentation, trauma mechanism, and physical examination findings are presented in Table 1.

During the initial emergency department evaluation, computed tomography (CT) was not required in 91.4% of cases. CT was performed in 567 patients (8.6%). Among those who underwent CT, no pathological findings were detected in 378 patients (66.6%). Overall, the most common CT abnormality in the entire cohort was orbital floor fracture (n=88, 1.3%). In 6,289 cases (95.9%), no associated injury in regions adjacent to the eye was identified. Overall, surgical intervention was

Table 1. Demographic characteristics, trauma mechanisms, and physical examination findings of patients with ocular trauma

Variable	All patients (n=6557)/n (%)
Sex	
Male	5598 (85.4)
Female	959 (14.6)
Age (years)	
0–9	187 (2.9)
10–19	597 (9.1)
20–39	3467 (52.9)
40–59	1879 (28.7)
60–80	427 (6.5)
GCS	
15	6546 (99.8)
13–15	5 (0.1)
10–13	1 (0.01)
8–10	0 (0)
<8	5 (0.1)
Trauma mechanism	
Ocular foreign body	5832 (88.9)
Fall	342 (5.2)
Blunt trauma	227 (3.5)
Traffic accident	71 (1.1)
Penetrating or sharp object injury	47 (0.7)
Chemical injury	29 (0.4)
Unknown mechanism	8 (0.1)
Burn	1 (0.01)
Identified findings	
No finding	30 (0.5)
Any finding	6527 (99.5)
Corneal abrasion	2023 (30.9)
Conjunctival hyperemia	1679 (25.6)
Epithelial injury	1391 (21.2)
Subconjunctival hemorrhage	851 (13)
Periorbital edema	388 (5.9)
Eyelid incision	63 (1)
Eyelid laceration	51 (0.8)
Chemosis	30 (0.5)
Full-thickness eyelid laceration	23 (0.4)
Corneal punctate epitheliopathy	16 (0.2)
Hyphema	6 (0.1)
Gaze limitation	3 (0.04)
Full-thickness corneal laceration	2 (0.03)
Lens dislocation	1 (0.01)

Table 2. Radiological findings, associated injuries, surgical interventions, and clinical outcomes

Variable	All patients (n=6557)/n (%)
Images	
No CT performed	5990 (91.4)
Radiological findings detected in the eye	567 (8.6)
No pathological finding	378 (5.8)
Orbital floor fracture	88 (1.3)
Orbital lateral wall fracture	49 (0.7)
Orbital medial wall fracture	26 (0.4)
Orbital roof fracture	21 (0.3)
Globe perforation	4 (0.1)
Lens dislocation	1 (0.01)
Associated injuries in adjacent regions	
No associated injury	6289 (95.9)
Any associated injury	268 (4.1)
Nasal bone fracture	97 (1.5)
Maxillary fracture	88 (1.3)
Zygomatic fracture	32 (0.5)
Cranial fracture	32 (0.5)
Facial laceration	19 (0.3)
Surgical intervention	
Surgery performed	98 (1.5)
No surgery	6459 (98.5)
Outcome	
Discharge from ED	6421 (97.9)
Hospital admission	136 (2.1)
ICU Admission	10 (0.2)
Ward admission	126 (1.9)
Ophthalmology ward	48 (0.7)
Admission to other clinics	78 (1.2)

required in 98 patients (1.5%) of the entire cohort. Among patients requiring surgical treatment, the most common procedures included repair of full-thickness eyelid lacerations, repair of corneal lacerations, repair of globe perforations, and removal of intraocular foreign bodies. Following emergency department management, 6,421 patients (97.9%) were discharged, while 136 patients (2.1%) required hospitalization, including 10 intensive care unit admissions and 126 ward admissions. Detailed information regarding CT findings, associated injuries, surgical interventions, and patient outcomes is presented in Table 2.

When trauma mechanisms were analyzed by sex, ocular foreign body injury ($p<0.001$), falls ($p<0.001$), traffic accidents ($p=0.004$), penetrating or sharp object injuries ($p<0.001$), and chemical injuries ($p=0.002$) were more frequent in males. A detailed comparison of trauma mechanisms by sex is shown in Table 3.

Surgical intervention was more frequently required in patients who were female ($p<0.001$), aged over 60 years ($p<0.001$), had a GCS score below 13 ($p<0.001$), presented with almost all trauma mechanisms except chemical injuries ($p<0.001$), had positive physical examination findings ($p<0.001$), had direct ocular injury ($p<0.001$), and had associated injuries ($p<0.001$). Except for subconjunctival hemorrhage, chemosis, and corneal punctate epitheliopathy, the presence of positive physical examination findings significantly increased the need for surgical intervention (Table 4). In particular, the presence of an orbital floor fracture was a significant factor associated with surgical treatment. Among extraocular injuries, maxillary and cranial fractures were most frequently associated with surgical intervention (Table 4).

Regarding clinical outcomes, higher hospitalization rates were observed in female patients ($p<0.001$), pediatric patients under 9 years of age ($p<0.001$), geriatric patients over 60 years of age ($p<0.001$), patients with a GCS score of 13 or lower, those presenting due to falls ($p<0.001$) or traffic accidents ($p<0.001$), and patients with orbital or extraocular bone frac-

Table 3. Trauma mechanisms according to sex

Mechanism	Male (n=5598)/n (%)	Female (n=959)/n (%)	p-value
Ocular foreign body	5083 (90.8)	749 (78.1)	<0.001
Falls	216 (3.9)	126 (13.1)	<0.001
Blunt trauma	191 (3.4)	36 (3.8)	0.592
Traffic accidents	52 (0.9)	19 (2)	0.004
Penetrating or sharp object injury	30 (0.5)	17 (1.8)	<0.001
Chemical injuries	18 (0.3)	11 (1.1)	0.002
Unknown mechanism	7 (0.1)	1 (0.1)	1
Burns	1 (0.01)	0 (0)	-

Table 4. Factors associated with surgical intervention in patients with ocular trauma

Variable	Surgical group (n=98)/n (%)	Non-surgical group (n=6459)/n (%)	p-value
Sex			
Male	72 (73.5)	5526 (85.6)	<0.001
Female	26 (26.5)	933 (14.4)	
Age (years)			
0–9	5 (5.1)	182 (2.8)	0.205
10–19	7 (7.1)	590 (9.1)	0.496
20–39	43 (43.9)	3424 (53)	0.072
40–59	25 (25.5)	1854 (28.7)	0.488
60–80	18 (18.4)	409 (6.3)	<0.001
GCS			
15	90 (91.8)	6456 (99.9)	<0.001
13–15	3 (3.1)	2 (0.01)	<0.001
10–13	1 (1)	0 (0)	0.015
8–10	0 (0)	0 (0)	-
<8	4 (4.1)	1 (0.01)	<0.001
Trauma mechanism			
Ocular foreign body	6 (6.1)	5826 (90.2)	<0.001
Falls	43 (43.9)	299 (4.6)	<0.001
Blunt trauma	20 (20.4)	207 (3.2)	<0.001
Traffic accidents	21 (21.4)	50 (0.8)	<0.001
Penetrating or sharp object injury	8 (8.2)	39 (0.6)	<0.001
Chemical injuries	0 (0)	29 (0.4)	1.000
Physical examination findings corneal abrasion	6 (6.1)	2017 (31.2)	<0.001
Conjunctival hyperemia	0 (0)	1679 (26)	<0.001
Epithelial damage	0 (0)	1391 (21.5)	<0.001
Subconjunctival hemorrhage	14 (14.3)	837 (13)	0.698
Periorbital edema	34 (34.7)	354 (5.5)	<0.001
Eyelid incision	8 (8.2)	55 (0.9)	<0.001
Eyelid laceration	4 (4.1)	47 (0.7)	0.007
Chemosis	0 (0)	30 (0.5)	1
Full-thickness eyelid laceration	23 (23.5)	0 (0)	<0.001
Corneal punctate epitheliopathy	0 (0)	16 (0.2)	1
Hyphema	4 (4.1)	2 (0.01)	<0.001
Gaze restriction	2 (2)	1 (0.01)	0.001
Full-thickness corneal laceration	2 (2)	0(0)	<0.001
Ocular injuries			
Orbital floor fracture	20 (20.4)	68 (1.1)	<0.001
Orbital lateral wall fracture	14 (14.3)	35 (0.5)	<0.001
Orbital medial wall fracture	12 (12.2)	14 (0.2)	<0.001
Orbital roof fracture	6 (6.1)	15 (0.2)	<0.001
Globe perforation	4 (4.1)	0 (0)	<0.001
Lens dislocation	1 (1)	0 (0)	0.015
Associated injuries (adjacent regions)			
Nasal bone fracture	3 (3.1)	94 (1.5)	0.177
Maxillary fracture	26 (26.5)	62 (1)	<0.001
Zygomatic fracture	9 (9.2)	23 (0.4)	<0.001
Cranial fracture	16 (16.3)	16 (0.2)	<0.001
Facial laceration	1 (1)	18 (0.3)	0.249

Table 5. Factors associated with hospitalization in patients with ocular trauma

Variables	Hospitalized (n=136)/n (%)	Discharged (n=6421)/n (%)	p-value
Sex			
Male	100 (73.5)	5498 (85.6)	<0.001
Female	36 (26.5)	923 (14.4)	
Age (years)			
0–9	10 (7.4)	177 (2.8)	0.005
10–19	14 (10.3)	583 (9.1)	0.626
20–39	54 (39.7)	3413 (53.2)	0.002
40–59	33 (24.3)	1846 (28.7)	0.252
60–80	25 (18.4)	402 (6.3)	<0.001
GCS			
15	125 (91.9)	6421 (100)	<0.001
13–15	5 (3.7)	0 (0)	<0.001
10–13	1 (0.7)	0 (0)	0.021
8–10	0 (0)	0 (0)	-
<8	5 (3.7)	0 (0)	<0.001
Trauma mechanism			
Ocular foreign body	6 (4.4)	5826 (90.7)	<0.001
Falls	56 (41.2)	286 (4.5)	<0.001
Blunt trauma	27 (19.9)	200 (3.1)	<0.001
Traffic accidents	39 (28.7)	32 (0.5)	<0.001
Penetrating or sharp object injury	8 (5.9)	39 (0.6)	<0.001
Chemical injuries	0 (0)	29 (0.5)	1
Physical examination findings			
Corneal abrasion	6 (4.4)	2017 (31.4)	<0.001
Conjunctival hyperemia	0 (0)	1679 (26.1)	<0.001
Epithelial damage	0 (0)	1391 (21.7)	<0.001
Subconjunctival hemorrhage	20 (14.7)	831 (12.9)	0.545
Periorbital edema	61 (44.9)	327 (5.1)	<0.001
Eyelid incision	11 (8.1)	52 (0.8)	<0.001
Eyelid laceration	6 (4.4)	45 (0.7)	0.001
Chemosis	0 (0)	30 (0.5)	1
Full-thickness eyelid laceration	23 (16.9)	0 (0)	<0.001
Corneal punctate epitheliopathy	0 (0)	16 (0.2)	1
Hyphema	4 (2.9)	2 (0.01)	<0.001
Gaze restriction	2 (1.5)	1 (0.01)	0.001
Full-thickness corneal laceration	2 (1.5)	0 (0)	<0.001
Ocular injuries			
Orbital floor fracture	29 (21.3)	59 (0.9)	<0.001
Orbital lateral wall fracture	19 (14)	30 (0.5)	<0.001
Orbital medial wall fracture	13 (9.6)	13 (0.2)	<0.001
Orbital roof fracture	17 (12.5)	4 (0.1)	<0.001
Globe perforation	4 (2.9)	0 (0)	<0.001
Lens dislocation	1 (0.7)	0 (0)	0.021
Associated injuries (adjacent regions)			
Nasal bone fracture	8 (5.9)	89 (1.4)	0.001
Maxillary fracture	34 (25)	54 (0.8)	<0.001
Zygomatic fracture	11 (8.1)	21 (0.3)	<0.001
Cranial fracture	32 (23.5)	0 (0)	<0.001
Facial laceration	2 (1.5)	17 (0.3)	0.058

tures ($p<0.001$). Detailed comparisons of demographic characteristics, trauma mechanisms, physical examination findings, ocular injuries, associated injuries in adjacent regions, and clinical outcomes are presented in Table 5.

DISCUSSION

Including 6,557 patients, this study represents one of the largest emergency department-based investigations evaluating demographic characteristics, clinical findings, surgical requirements, and hospitalization associated with ocular trauma. In this cohort, 136 patients were admitted to inpatient wards, 10 patients required intensive care unit admission, and surgical treatment was performed in 98 patients. Surgical intervention was more frequently required in patients who were female, of advanced age, had low GCS scores, or sustained ocular injuries related to traffic accidents, falls, penetrating or sharp object injuries, and blunt trauma. The findings indicate that foreign body-related injuries were very common, whereas surgical interventions were mainly associated with high-energy trauma. Advanced age, falls, traffic accidents, orbital fractures, associated injuries, and low GCS scores were important factors influencing hospitalization. From a trauma and emergency medicine perspective, these findings highlight that although ocular trauma is frequently encountered in the emergency department, only a small proportion of patients require advanced imaging, surgical intervention, or hospitalization. Because the primary aim of this study was to provide a descriptive epidemiological overview of ocular trauma presentations in the emergency department, multivariable predictive modeling was not performed.

In our study, CT was required in a small proportion of patients, and the majority of scans revealed no pathological findings. These findings suggest that imaging decisions in ocular trauma should be guided by clinical examination, trauma mechanism, and the presence of associated injuries rather than routine CT.

Previous studies have consistently reported that ocular trauma is most commonly observed in young adults. Many recent studies have shown that patients are predominantly between 20 and 50 years of age and that males constitute the most frequently affected sex.[13-16] In our study, more than half of the patients were between 20 and 39 years of age, which is consistent with the existing literature. Male patients comprised 85% of our cohort, confirming that young males remain the population at highest risk for ocular trauma. However, when trauma mechanisms were analyzed, ocular trauma caused by foreign bodies was more common in males, whereas injuries due to falls, blunt trauma, traffic accidents, penetrating or sharp object injuries, and chemical injuries were more frequent in females. This difference may be related to occupational exposure, as young males are more often employed in labor-intensive jobs.

Studies conducted in different populations have identified several causes of ocular trauma, including penetrating foreign bodies, traffic accidents, falls, occupational accidents, and domestic accidents.[17-21] Lu et al. retrospectively analyzed 1,019 ocular injuries in 2025 and reported that metallic objects were the most common cause requiring surgical treatment.[8] In another retrospective study including 83 patients, foreign bodies accounted for 40% of cases, whereas falls accounted for 22%.[21] In our study, trauma mechanisms were defined in detail, and foreign body injury was identified as the reason for presentation in 88% of cases. In a study by Anguita et al. evaluating intraocular foreign bodies in patients presenting to an ocular trauma unit, 57% of patients underwent surgical removal.[22] In contrast, in our cohort, foreign bodies were removed during ophthalmology consultation in the emergency department in 99% of 5,832 patients presenting with foreign-body injuries, and surgical removal was required in only six patients. The relatively low number of globe perforation cases in our cohort may be explained by the predominance of superficial foreign body injuries presenting to the emergency department.

Numerous positive physical examination findings were documented in patients presenting with ocular trauma. Approximately one-third of patients had corneal abrasion, one-quarter had conjunctival hyperemia, and one-fifth had epithelial damage. The cornea and conjunctiva were the most commonly affected anatomical structures, likely related to the high proportion of foreign-body-related injuries. A retrospective study published in 2024 reported corneal abrasion and contusion as the most frequent findings in 855 patients with ocular trauma.[23] These pathologies generally do not require surgical treatment. Consistent with this, 99% of patients with corneal abrasion and all patients with conjunctival hyperemia or epithelial damage in our study were treated conservatively and discharged after ophthalmology consultation in the emergency department. In contrast, all patients with full-thickness eyelid lacerations, full-thickness corneal lacerations, globe perforations, and lens dislocations underwent surgical treatment. Surgical treatment rates in ocular trauma vary widely depending on the study population.[24,25] In a recent study conducted in our country by Erkan Pota et al., surgical treatment was required in 8.5% of 380 patients with open-globe injuries.[25] In our study, surgical treatment was performed in 1.5% of patients, a lower rate that may be explained by the large sample size and the predominance of foreign body-related injuries.

Orbital fractures were detected in 2.7% of patients in our study, which is consistent with previous reports. Ostadian et al. retrospectively evaluated ocular trauma over 10 years and reported orbital fractures in 2.5% of 927 patients.[26] Peacock et al. put forward that high-energy trauma involving the maxillofacial region may also result in fractures of adjacent facial bones.[27] They reported nasal bone fractures in 58% of patients with bilateral orbital fractures, maxillary fractures in 38%, zygomatic fractures in 27%, and frontal bone fractures

in 20%. In that study, the high rate of associated injuries was attributed to severe maxillofacial trauma. In contrast, our cohort, which included a more heterogeneous patient population and a substantially larger sample size, identified nasal bone fractures in 1.5% of patients, with lower rates of maxillary, zygomatic, and cranial fractures accompanying ocular injuries.

The overall hospitalization rate in our study was 2.1%. Hospitalized patients were more likely to have sustained high-energy trauma mechanisms, including blunt trauma, penetrating or sharp object injuries, falls, and traffic accidents. Previous studies have shown that more than half of orbital injuries caused by high-energy trauma are accompanied by adjacent injuries, which increases the likelihood of hospitalization.[28] A higher proportion of elderly patients was also observed among hospitalized cases in our study. This may be explained by increased bone fragility and delayed protective reflexes in older individuals,[29] and our findings are consistent with the existing literature.

The proportion of female patients among those requiring hospitalization was significantly higher than that of males, suggesting a potential influence of sex on trauma severity and outcomes. This finding may be related to the increased risk of osteoporosis with advancing age in female patients. Werning et al. demonstrated that osteoporosis is an independent risk factor for fracture development in patients with maxillofacial trauma.[30] Furthermore, osteoporosis rates are known to increase significantly in postmenopausal women, contributing to bone fragility.[31] In our study, while foreign body-related ocular injuries were more frequent in males, high-energy trauma mechanisms such as falls, traffic accidents, and penetrating or sharp object injuries were more common in females. The higher hospitalization rates observed among female patients may be explained by the greater exposure to high-energy trauma mechanisms, such as falls and traffic accidents, combined with an increased risk of osteoporosis. In addition, age-related factors, including reduced bone density and delayed protective reflexes, may contribute to greater injury severity and subsequent hospitalization, particularly in elderly patients.

Only 11 patients in our cohort had a GCS score of 13 or lower, and all required hospitalization. The low proportion of such cases reflects the predominance of isolated ocular trauma, particularly foreign body injuries. Nevertheless, these findings indicate that ocular trauma, although infrequent, may be associated with severe adjacent injuries. Previous studies have also shown that low GCS scores are associated with facial trauma and increased morbidity.[32] This underscores the importance of systematic trauma evaluation in patients presenting with ocular injuries, in addition to focused orbital assessment.

The retrospective design, single-center setting, predominance of foreign body-related ocular trauma, and lack of data on hospitalization duration and long-term outcomes should be considered limitations of this study. Standardized ocular trauma classification systems such as the Birmingham Eye Trauma Terminology and the Ocular Trauma Score could not be applied because the retrospective registry data did not consistently include the clinical parameters required for these classifications. Furthermore, because the study relied on retrospectively recorded hospital registry data, coding inaccuracies or documentation bias cannot be completely excluded. Visual acuity measurements and long-term visual outcomes were not consistently available in the emergency department registry system and, therefore, could not be analyzed in this study.

CONCLUSION

This large emergency department-based study demonstrates that the majority of ocular trauma patients can be managed without advanced imaging, surgical intervention, or hospitalization. High-energy trauma mechanisms, older age, and female sex were associated with increased injury severity and the need for hospitalization. These findings may assist emergency physicians in risk stratification and in the more efficient use of imaging and hospital resources in the management of ocular trauma.

Ethics Committee Approval: This study was approved by the Ethics Committee of Süleyman Yalçın City Hospital (Date: 28.08.2025, Decision No: 2025/0142).

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ORİJİNAL ÇALIŞMA - *ÖZ*

Üçüncü basamak bir acil servise başvuran oküler travmalar: Demografik özellikler, yaralanma mekanizmaları ve klinik sonuçlar

AMAÇ: Bu çalışmanın amacı, üçüncü basamak bir acil servise oküler travma nedeniyle başvuran hastaların demografik özelliklerini, etiyolojik faktörlerini, eşlik eden yaralanmalarını ve klinik sonuçlarını değerlendirmektir.

GEREÇ VE YÖNTEM: Bu retrospektif gözlemsel çalışmaya, 2022–2025 yılları arasında Süleyman Yalçın Şehir Hastanesi Acil Servisi'ne oküler travma nedeniyle başvuran toplam 6.557 hasta dâhil edildi. Hastaların demografik verileri, travma mekanizmaları, fizik muayene bulguları, eşlik eden yaralanmaları, cerrahi müdahale gereksinimi ve klinik sonuçları değerlendirildi. Kategorik değişkenlerin analizinde ki-kare testi kullanılırken, sürekli değişkenler için Student t-testi ve Mann–Whitney U testi uygulandı.

BULGULAR: Hastaların %85.4'ü (n=5.598) erkekti ve %52.9'u 20–39 yaş aralığındaydı. En sık başvuru nedeni oküler yabancı cisim yaralanması (%88.9) olup, en yaygın fizik muayene bulgusu korneal abrazyon (%30.9) olarak saptandı. Olguların %8.6'sına bilgisayarlı tomografi çekildi. Hastaların %95.9'unda oküler travma izole olarak görülürken, %1.5'inde cerrahi müdahale gereksinimi oluştu. Olguların %97.9'u acil servisten taburcu edildi. Oküler yabancı cisim yaralanması ($p<0.001$), düşmeler ($p<0.001$), trafik kazaları ($p=0.004$), penetran veya kesici-delici alet yaralanmaları ($p<0.001$) ve kimyasal yaralanmalar ($p=0.002$) erkek hastalarda daha sık görüldü. Kadın cinsiyeti ($p<0.001$), 60 yaşın üzerinde olmak ($p<0.001$), Glasgow Koma Skoru'nun 13'ün altında olması ($p<0.001$) ve eşlik eden yaralanmaların varlığı ($p<0.001$) cerrahi müdahale gereksinimi ile ilişkili bulundu. Kadın cinsiyeti ($p<0.001$), 9 yaşın altında olmak ($p<0.001$) ve 60 yaşın üzerinde olmak ($p<0.001$), Glasgow Koma Skoru ≤13, düşme ($p<0.001$) veya trafik kazası ($p<0.001$) nedeniyle başvuru ve orbital ya da ekstraoküler kemik kırıklarının varlığı ($p<0.001$) daha yüksek hastaneye yatış oranları ile ilişkiliydi.

SONUÇ: Oküler travmalar en sık genç erkek hastaları etkilemekte olup, en yaygın neden yabancı cisim yaralanmalarıdır. Korneal abrazyon en sık saptanan klinik bulgudur. Olguların büyük çoğunluğu izole oküler travma niteliğinde olup, bilgisayarlı tomografi gereksinimi olmadan acil servisten taburcu edilmiştir. Kadın cinsiyet, pediatrik ve geriatrik yaş grupları, düşük Glasgow Koma Skoru ve düşme veya trafik kazalarına bağlı travmalar, artmış cerrahi müdahale gereksinimi ve hastaneye yatış ile ilişkili bulunmuştur.

Anahtar sözcükler: Ayaktan taburculuk; cerrahi müdahale; eşlik eden yaralanmalar; göz travması; hastaneye yatış; klinik sonuçlar; mekanizma.

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ORIGINAL ARTICLE

Clinical burden and predictors of hospitalization in extremity gunshot wounds: A single-center retrospective study

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ABSTRACT

BACKGROUND: This study aimed to retrospectively evaluate the clinical characteristics, temporal admission patterns, and clinical outcomes of patients with extremity gunshot wounds (GSW) presenting to a tertiary care teaching and research hospital.

METHODS: A total of 123 patients presenting with GSWs affecting at least one extremity between January 2024 and December 2025 were retrospectively analyzed. Injury characteristics, interventions, and clinical outcomes were evaluated. Factors independently associated with hospital length of stay (LOS) and intensive care unit (ICU) admission were identified using negative binomial regression and multivariate logistic regression analyses, respectively.

RESULTS: Of the patients, 116 (94.3%) were male, with a mean age of 29.9±11.9 years. The lower extremity was the most frequently affected region (69.1%), and 42 of 43 fractures (97.7%) were open fractures. The ICU admission rate was 26.0% (n=32), and in-hospital mortality was 4.1% (n=5). A total of 43.1% of admissions occurred between 18:00 and 23:59. In negative binomial regression, concomitant injury (incidence rate ratio [IRR]=6.93; 95% confidence interval [CI]: 3.82–12.57; p<0.001), fracture (IRR=5.02; 95% CI: 2.82–8.93; p<0.001), and reoperation (IRR=2.73; 95% CI: 1.44–5.16; p=0.002) were independently associated with length of hospital stay. In logistic regression, neurovascular injury (odds ratio [OR]=28.12; 95% CI: 7.60–104.09; p<0.001) and concomitant injury (OR=20.36; 95% CI: 5.62–73.81; p<0.001) independently predicted ICU admission.

CONCLUSION: Extremity GSWs predominantly affect young males and cluster during evening hours. Concomitant injury and fracture were independently associated with length of hospital stay, whereas reoperation was associated with prolonged hospitalization during the clinical course, while neurovascular injury and concomitant injury independently predict ICU admission.

Keywords: Extremity; gunshot wound; hospital length of stay; intensive care unit.

INTRODUCTION

Gunshot wounds (GSW) remain a significant public health problem worldwide, causing considerable morbidity and mortality. According to the Global Burden of Disease 2016 data, the annual number of firearm-related deaths worldwide is estimated to range from 195,000 to 276,000, with the majority attributed to homicide.[1] These injuries disproportionately affect males and young adults.[2] From an anatomical distribution perspective, the extremities are the most commonly affected region, and orthopedic surgeons frequently encounter these injuries in trauma practice.[3]

Extremity GSWs present across a broad clinical spectrum ranging from isolated soft-tissue injuries to Gustilo type 3C open fractures, and are frequently associated with serious orthopedic complications including fractures, neurovascular injuries, and compartment syndrome.[4,5] The lower extremity is the most commonly affected anatomical region, account-

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ing for approximately 46% of all ballistic fractures.[6] These injuries impose a significant resource burden on healthcare systems due to prolonged hospital stays, repeated surgical interventions, and intensive care requirements.[6,7] Although several epidemiological studies have evaluated firearm injuries in Türkiye, including emergency department-based cohorts,[8,9] studies evaluating extremity GSWs specifically from an orthopedic perspective remain limited.

The aim of this study was to retrospectively evaluate the epidemiological and clinical characteristics, temporal admission patterns, orthopedic interventions, and clinical outcomes of GSWs in which at least one extremity was affected, including concomitant injuries, in patients presenting to a tertiary care teaching and research hospital.

MATERIALS AND METHODS

This study was conducted by reviewing the medical records of patients who presented to the emergency department of a tertiary care teaching and research hospital with GSWs between January 01, 2024 and December 31, 2025. Patients with GSWs affecting at least one extremity were included. Demographic data, injury characteristics, concomitant injuries, applied orthopedic interventions, and clinical outcomes were retrospectively evaluated through the hospital information management system and electronic medical records. This study was approved by the Ethics Committee for Non-Interventional Clinical Research Gaziantep City Hospital (Date: 05.06.2026, Decision no: 2026/34) and conducted in accordance with the principles of the Declaration of Helsinki.

Patients who presented with GSWs during the specified period, were 18 years of age or older, had at least one extremity injury, and whose basic demographic and clinical data were fully accessible through the hospital record system were included. Injuries without extremity involvement affecting only the trunk, head, or neck region, cases admitted as deceased, patients under 18 years of age, cases miscoded for reasons other than ballistic trauma, and patients whose basic clinical data were unavailable were excluded.

Patient data were obtained by reviewing the hospital information management system, emergency department records, operative notes, anesthesia records, and discharge summaries. Patients were screened through the hospital information management system using all GSW diagnosis codes under the International Classification of Diseases, 10th Revision: W32, W33, W34, X93, X94, and X95. Collected data were categorized as demographic characteristics (age, sex), temporal parameters related to admission time (date, time, day, and season of admission), injury characteristics (affected extremity region, anatomical subregion, fracture presence and open/closed fracture status, Gustilo classification, joint involvement, neurovascular injury), concomitant injuries, type of orthopedic intervention, type of anesthesia, presence and number of reoperations, and clinical outcomes (emergency department disposition, intensive care unit [ICU] admission, length of hospital stay, development of complications, and in-hospital mortality). Combined intervention was defined as the performance of two or more orthopedic and/or vascular procedures during the same surgical episode. This category comprised patients with complex extremity gunshot injuries requiring multiple procedures, most commonly combinations of external fixation, debridement, and neurovascular repair, according to the injury pattern. Patients undergoing a single surgical procedure were classified according to that specific intervention. Open fractures were classified according to the Gustilo-Anderson classification by an orthopedic surgeon with at least 5 years of trauma surgery experience, based on review of operative notes, operation records, and discharge summaries.[10] Reoperation was defined as additional surgical interventions performed within the same hospitalization episode following the initial surgical intervention. Neurovascular injury was recorded based on clinical examination, imaging modalities, and specialist consultations. Hospital length of stay (LOS) was calculated as zero days for patients discharged from the emergency department, and as the number of days between admission and discharge for hospitalized patients. Admission times were evaluated in four time intervals for temporal analysis: 00:00–05:59, 06:00–11:59, 12:00–17:59, and 18:00–23:59.

Data were analyzed using the Statistical Package for the Social Sciences statistical software (version 26.0; IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation or median (interquartile range [IQR]), and categorical variables as number and percentage. Normality of distribution was assessed using the Shapiro–Wilk test. The Mann–Whitney U test was used for comparisons of non-normally distributed continuous variables between two groups, and the Kruskal–Wallis test for comparisons among more than two groups. Associations between categorical variables were evaluated using the Chi-square test or Fisher's exact test when the expected cell count was <5. Negative binomial regression analysis was applied to identify independent predictors of hospital LOS, and multivariate logistic regression analysis was used to identify independent predictors of ICU admission. Statistical significance was set at $p<0.05$ for all analyses.

RESULTS

A total of 123 patients meeting the inclusion criteria were included in the analysis. Of these, 94.3% (n=116) were male, with a mean age of 29.9±11.9 years (range: 18–64 years). Demographic characteristics, injury features, and clinical findings of all patients are presented in Table 1.

Regarding the anatomical distribution of injuries, lower extremity involvement was identified in 85 patients (69.1%), upper extremity in 30 (24.4%), and both extremities in 8 (6.5%). The most frequently affected anatomical region was the leg (n=35, 28.5%), followed by the femur/hip (n=27, 22.0%) and

Table 1. Demographic, clinical, and treatment characteristics of patients (n=123)

Variable	n	Percentage
Age (years), mean±SD (range)	29.9±11.9 (18–64)	
Sex		
Male	116	94.3
Female	7	5.7
Affected extremity region		
Lower extremity	85	69.1
Upper extremity	30	24.4
Both	8	6.5
Anatomical subregion		
Leg	35	28.5
Femur/hip	27	22.0
Multiple anatomical regions	20	16.3
Knee	11	8.9
Shoulder-humerus	10	8.1
Hand-wrist	7	5.7
Foot-ankle	7	5.7
Forearm	4	3.3
Elbow	2	1.6
Clinical findings		
Fracture	43	35.0
Open fracture	42	34.1
Joint involvement	28	22.8
Neurovascular injury	27	22.0
Reoperation	27	22.0
Gustilo-Anderson classification*		
Gustilo 1	7	5.7
Gustilo 2	8	6.5
Gustilo 3A	3	2.4
Gustilo 3B	0	0.0
Gustilo 3C	24	19.5
Concomitant injury†		
None	95	77.2
Present – thorax	9	7.3
Present – abdomen	9	7.3
Present – head/neck	5	4.1
Present – other extremity	5	4.1
Intervention type‡		
Conservative	70	56.9
Combined	26	21.1
Debridement	8	6.5
Neurovascular surgery	6	4.9
Internal fixation	6	4.9
Amputation	6	4.9
External fixator	1	0.8
Emergency department disposition		
Discharged	57	46.3
Admitted – ward	34	27.6
Admitted – ICU	32	26.0
Clinical outcomes		
ICU admission	32	26.0
In-hospital mortality	5	4.1
Osteomyelitis	9	7.3
Hospital length of stay (days), median (IQR)	2 (0–9)	
Hospital length of stay (days), mean±SD	6.0±9.2	

Mean: Mean; SD: Standard deviation; IQR: Interquartile range; ICU: Intensive care unit. *Gustilo 3B was not observed in any case. †Each patient was classified according to the most severe injury site; all patients were assigned to a single category. ‡Combined intervention: application of more than one orthopedic or vascular intervention within the same surgical episode.

multiple anatomical regions (n=20, 16.3%). Fractures were identified in 43 patients (35.0%); of these, 42 (97.7%) were open fractures, reflecting the high-energy nature of civilian ballistic trauma. Gustilo 3C was the most common type with 24 cases (19.5%), and Gustilo 3B was not observed in this series. Joint involvement was identified in 28 patients (22.8%) and neurovascular injury in 27 (22.0%). Concomitant injury was present in 28 patients (22.8%); thoracic involvement was detected in 9 (7.3%) and abdominal involvement in 9 (7.3%).

Regarding intervention type, conservative management was applied in 70 patients (56.9%). Of the 53 patients who underwent surgical intervention, combined procedures were performed in 26 (21.1%), debridement in 8 (6.5%), neurovascular surgery in 6 (4.9%), internal fixation in 6 (4.9%), and amputation in 6 (4.9%). The reoperation rate was 22.0% (n=27).

Of all patients, 57 (46.3%) were discharged from the emergency department, 34 (27.6%) were admitted to the ward, and 32 (26.0%) were admitted to the ICU. The overall ICU admission rate was 26.0% (n=32), and in-hospital mortality was 4.1% (n=5). Osteomyelitis was the most common complication (n=9, 7.3%). The median hospital LOS for all patients was 2 days (IQR: 0–9), with a mean LOS of 6.0±9.2 days.

Regarding temporal distribution, A total of 43.1% of admissions (n=53) occurred between 18:00 and 23:59, while 7.3% (n=9) were concentrated in the 06:00–11:59 interval (Fig. 1). The weekend admission rate was 39.8% (n=49). Monthly distribution showed that the highest number of admissions occurred in April (n=20, 16.3%) and the lowest in March (n=4, 3.3%); however, no statistically significant evidence of non-homogeneous monthly distribution was detected (χ^2=19.341,

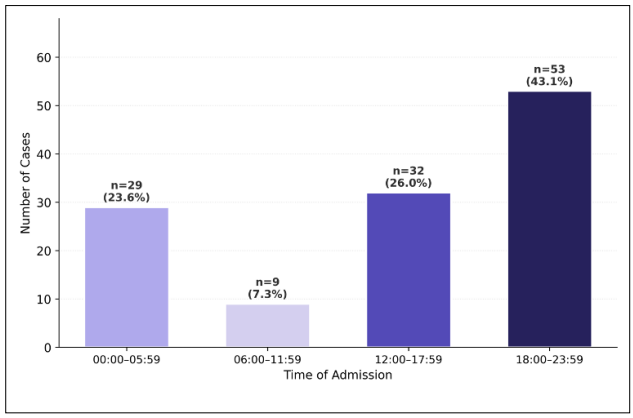


Figure 1. Temporal distribution of emergency department admissions by time interval (n=123).

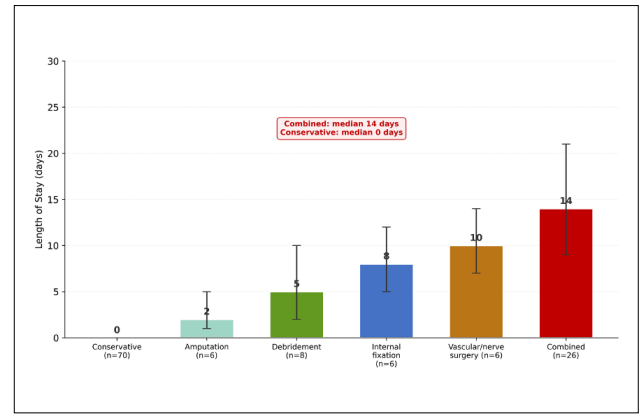


Figure 2. Hospital length of stay by intervention type. Values represent the median (days); error bars indicate the interquartile range.

df=11, p=0.055). Seasonal distribution showed the highest admissions in spring (n=37, 30.1%) and the lowest in autumn (n=23, 18.7%); no statistically significant difference was found between seasons (χ^2=3.276, df=3, p=0.351). Fracture rates (37.5%) and LOS (median 4 days) were higher in winter compared to other seasons, although this difference did not reach statistical significance.

Factors affecting hospital LOS were evaluated using the Mann–Whitney U test (Table 2). Fracture presence (median 9 vs. 0 days, p<0.001), neurovascular injury (median 9 vs. 0 days, p<0.001), reoperation (median 10 vs. 0 days, p<0.001), and concomitant injury (median 10 vs. 0 days, p<0.001) significantly prolonged LOS. Median LOS was 6 days in patients with joint involvement versus 0 days in those without (p=0.005). When comparing median LOS by intervention type, the longest LOS was observed in patients requiring combined intervention (median 14 days), while the conservative treatment group had a median LOS of zero days (Fig. 2).

In multivariate negative binomial regression analysis, concomitant injury (incidence rate ratio [IRR]=6.93; 95% confidence interval [CI]: 3.82–12.57; p<0.001), fracture presence (IRR=5.02; 95% CI: 2.82–8.93; p<0.001), and reoperation (IRR=2.73; 95% CI: 1.44–5.16; p=0.002) were independently associated with hospital LOS (Table 3). Neurovascular injury and joint involvement did not reach statistical significance in the multivariate analysis.

In multivariate logistic regression analysis, neurovascular injury (odds ratio [OR]=28.12; 95% CI: 7.60–104.09; p<0.001) and concomitant injury (OR=20.36; 95% CI: 5.62–73.81; p<0.001) were identified as independent predictors of ICU admission (Fig. 3, Table 4). In-hospital mortality occurred exclusively in patients admitted to the ICU.

Table 2. Factors affecting hospital length of stay

Variable	Present – median (IQR)	Absent – median (IQR)	p
Fracture	9 (3–18)	0 (0–2)	<0.001
Joint involvement	6 (0–14)	0 (0–7)	0.005
Neurovascular injury	9 (4–15)	0 (0–6)	<0.001
Reoperation	10 (7–16)	0 (0–3)	<0.001
Concomitant injury	10 (5–15)	0 (0–6)	<0.001
Length of stay by interven-tion type	Median (IQR)		
Conservative	0 (0–0)		
Debridement	5 (2–10)		
Internal fixation	8 (5–12)		
Neurovascular surgery	10 (7–14)		
Combined	14 (9–21)		
Amputation	2 (1–5)		

IQR: Interquartile range. Comparisons among intervention types were performed using the Kruskal–Wallis test.

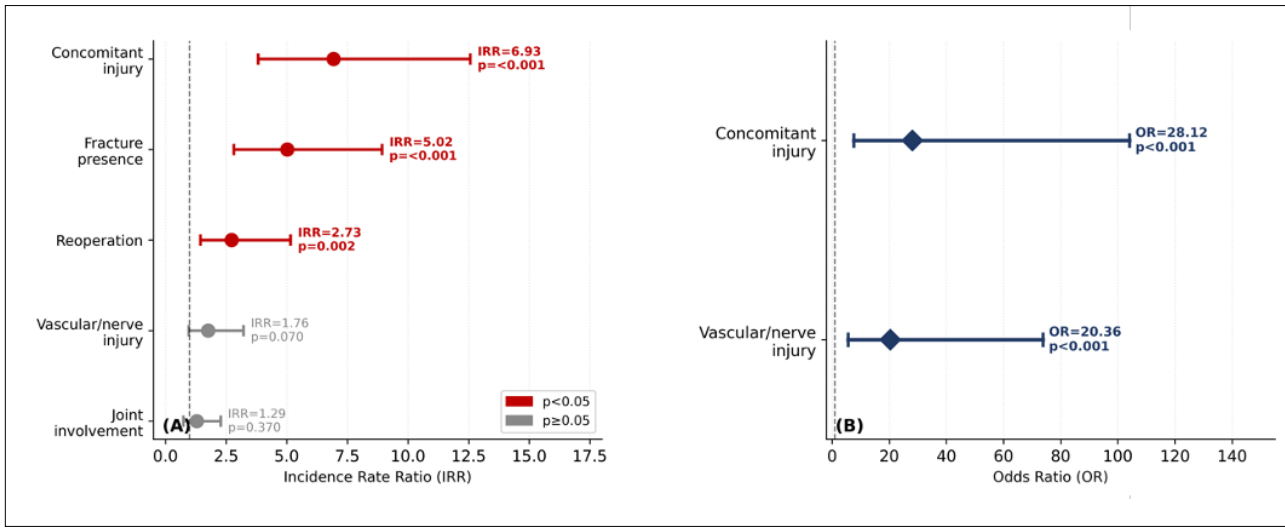


Figure 3. (a) Factors independently associated with hospital length of stay assessed by negative binomial regression. Red circles indicate statistically significant variables (p<0.05). IRR: Incidence rate ratio; CI: Confidence interval. **(b)** Independent predictors of intensive care unit admission assessed by multivariate logistic regression. OR: Odds ratio; CI: Confidence interval.

Table 3. Independent predictors of hospital length of stay

Variable	IRR	95% CI	p
Concomitant injury	6.93	3.82–12.57	<0.001
Fracture	5.02	2.82–8.93	<0.001
Reoperation	2.73	1.44–5.16	0.002
Neurovascular injury	1.76	0.96–3.22	0.070
Joint involvement	1.29	0.74–2.28	0.370

IRR: Incidence rate ratio; CI: Confidence interval. Bold text: p<0.05.

Table 4. Independent predictors of ICU admission

Variable	OR	95% CI	p
Neurovascular injury	28.12	7.60–104.09	<0.001
Concomitant injury	20.36	5.62–73.81	<0.001

OR: Odds ratio; CI: Confidence interval; ICU: Intensive care unit.

DISCUSSION

GSWs represent a significant clinical and healthcare system burden in trauma surgery practice. However, the majority of existing literature consists of data from high-income countries and military series.[7,11] Studies evaluating civilian extremity GSWs from an orthopedic perspective that include hospital LOS and ICU requirements as primary outcome variables remain limited.[5,6] Furthermore, it has been reported that injury patterns and clinical outcomes in centers with different socioeconomic and geographical characteristics may differ from Western series.[11] Therefore, our study aims to contribute to the literature on the orthopedic and clinical characteristics of extremity GSWs using contemporary single-center data from Turkey. Unlike previous epidemiological reports, our study also evaluates independent factors associated with hospital LOS and ICU admission from an orthopedic perspective, thereby providing clinically relevant information for trauma resource allocation and surgical decision-making.

The predominance of young male patients in our series is consistent with demographic patterns reported in civilian GSW series.[12-15] Large civilian trauma series have consistently demonstrated that firearm injuries predominantly affect young males and are associated with considerable healthcare resource utilization. Benton et al.[15] analyzed more than 6,000 GSW patients at a Level I trauma center and similarly reported that extremity injuries were among the most common anatomical locations and that a substantial proportion of patients required surgical intervention.[15] Similarly, Ertekin et al.[9] reported comparable demographic characteristics among firearm injury patients presenting to the emergency department in Türkiye, with most patients being young males; however, their study included all anatomical injury locations rather than focusing specifically on extremity injuries. The predominance of male sex and young adult age group in these injuries has been associated with increased outdoor exposure and more frequent involvement in violence-related events.[2] The finding that the lower extremity was the most frequently affected anatomical region is also consistent with previous series, as injuries around the femur and tibia have been reported to be prominently represented in civilian ballistic trauma.[13,16] The fact that the vast majority of fractures identified in our series were open fractures can be explained by the high-energy nature of ballistic trauma causing widespread damage to bone and surrounding soft tissue.[5,6,17]

In multivariate analysis, concomitant injury (IRR=6.93), fracture presence (IRR=5.02), and reoperation requirement (IRR=2.73) were independently associated with hospital LOS. These findings are consistent with the existing literature, which has reported that the coexistence of bone and vascular injury significantly prolongs hospital LOS compared with isolated soft-tissue injuries.[18,19] The effect of concomitant injuries on LOS may be related to multidisciplinary management requirements, additional surgical interventions, and increased complication risk. The observed association between reoperation and prolonged LOS may be explained by the staged debridement, wound care, and definitive fixation processes frequently required in the management of complex open fractures.[5,19] Because reoperation occurs after the initial hospital admission, its association with prolonged LOS should be interpreted cautiously and does not imply a causal or baseline predictive relationship. Rather, reoperation is likely a surrogate marker of injury complexity, treatment intensity, and the need for staged surgical management during hospitalization.

Neurovascular injury (OR=28.12) and concomitant injury (OR=20.36) were identified as independent predictors of ICU admission. The strong predictive value of neurovascular injury for ICU requirement may be explained by hemodynamic instability, the need for hemorrhage control, and close postoperative monitoring in vascular injuries.[19,20] Previous studies have also reported that ballistic trauma with vascular injury is associated with higher morbidity and a more complex clinical course.[20] Similarly, the independent association of concomitant injuries with ICU admission in our study suggests increased respiratory and circulatory support requirements in multisystem trauma patients. All mortality cases occurred in patients admitted to the ICU, further supporting the substantial clinical burden associated with this patient group.

A substantial proportion of admissions were concentrated in the evening hours, with approximately 40% occurring on weekends. Similar temporal distributions have been reported in previous trauma series, emphasizing that GSWs create additional burden on emergency services and trauma teams during evening and nighttime hours.[11] This finding has practical implications for the organization of emergency orthopedic on-call services, operating room scheduling, and management of intensive care resources. The absence of statistically significant differences between seasons indicates that the seasonal increase pattern described in Western literature was not observed in this series, suggesting that injury incidence may be shaped more by regional and sociodemographic dynamics than by climatic factors.[11]

Osteomyelitis was the most frequent complication in our series (7.3%), and the reoperation rate was 22.0%. Previous studies have reported that osteomyelitis rates in ballistic fractures vary depending on the degree of associated soft-tissue injury and contamination, and our rate is consistent with these data.[5,21,22] Previous series have also reported high reoperation rates in cases where open fractures predominate, due to the need for repeated debridement, temporary stabilization, and staged reconstruction.[21] The frequent coexistence of severe soft tissue and vascular injury in patients undergoing amputation reflects the challenges of limb-salvage surgery in high-energy ballistic trauma.[5,19,23] These findings indicate that extremity GSWs constitute a significant clinical burden not only in terms of acute trauma management but also with respect to multi-stage orthopedic reconstruction processes.

This study has several limitations. First, the retrospective and single-center design limits the generalizability of the results. As the study is based on data from a tertiary trauma center, it should be noted that the patient population may reflect a higher trauma severity and may contain selection bias. The retrospective design inherently carries the risk of incomplete documentation, misclassification of variables, and unmeasured confounders that could not be controlled for in the analyses. Furthermore, as data were derived from a single tertiary trauma center with specific institutional protocols and patient referral patterns, the findings may not be directly generalizable to other settings, including lower-volume centers or regions with different sociodemographic characteristics and mechanisms of injury. The low case numbers in certain subgroups such as Gustilo 3A, amputation, and mortality limit the statistical power of the analyses. The absence of validated trauma severity scores, such as the ınjury severity score, prevented adjustment for overall injury severity and may have resulted in residual confounding in the multivariate analyses. In addition, the American Society of Anesthesiologists score was unavailable for all patients and therefore could not be evaluated as a potential confounder. In addition, the inability to evaluate the time from injury to hospital admission and long-term functional outcomes is among the other important limitations of this study. Furthermore, reoperation was analyzed as a hospitalization-related variable rather than a baseline characteristic. Therefore, its association with prolonged LOS should be interpreted as reflecting injury complexity and the clinical course during hospitalization rather than a true baseline predictor. Our findings need to be supported by larger-scale, multicenter, and prospective studies.

CONCLUSION

This study demonstrated that extremity GSWs most frequently affect young male individuals, with the lower extremity being the most commonly involved anatomical region. Multivariate analyses showed that concomitant injury and fracture presence were independently associated with prolonged hospital LOS, whereas reoperation was associated with prolonged hospitalization during the clinical course, while neurovascular injury and concomitant injury were independent predictors of ICU admission. The concentration of admissions, particularly during evening hours and on weekends has practical importance for the organization of emergency orthopedic services and trauma resources. Our

findings highlight the determinant role of injury severity and concomitant trauma on clinical course in extremity GSWs, and contribute to clinical awareness regarding the management of this patient group. Beyond describing regional epidemiological patterns, these findings may assist orthopedic trauma teams in identifying patients at increased risk for prolonged hospitalization and intensive care requirements. Our results need to be supported by larger-scale, multicenter, and prospective studies.

Ethics Committee Approval: This study was approved by the Ethics Committee for Non-Interventional Clinical Research Gaziantep City Hospital (Date: 05.06.2026, Decision No: 2026/34).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: O.K.; Design: O.K.; Supervision: O.K.; Data collection and/or processing: M.Y., H.A.; Analysis and/or interpretation: O.K., T.Y.; Literature review: B.B.; Writing: O.K.; Critical review: O.K., E.B.

Informed Consent: Retrospective study.

Conflict of Interest: The authors declare no conflicts of interest.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Ekstremite ateşli silah yaralanmalarında klinik yük ve hastanede yatış belirleyicileri: Tek merkezli retrospektif çalışma

AMAÇ: Bu çalışma, üçüncü basamak bir eğitim ve araştırma hastanesine başvuran ekstremite ateşli silah yaralanmalı hastaların klinik özelliklerini, zamansal başvuru paternlerini ve klinik sonuçlarını retrospektif olarak değerlendirmeyi amaçlamaktadır.
GEREÇ VE YÖNTEM: Ocak 2024 ile Aralık 2025 tarihleri arasında, en az bir ekstremitenin etkilendiği ateşli silah yaralanması nedeniyle başvuran 123 hasta retrospektif olarak incelendi. Yaralanma özellikleri, uygulanan girişimler ve klinik sonuçlar değerlendirildi. Hastane yatış süresi ve yoğun bakım ünitesi yatışı ile bağımsız olarak ilişkili faktörler sırasıyla negatif binom regresyon ve çok değişkenli lojistik regresyon analizleri ile belirlendi.
BULGULAR: Hastaların %94.3'ü (n=116) erkek olup yaş ortalaması 29.9±11.9 yıl idi. Alt ekstremite en sık etkilenen bölgeydi (%69.1); 43 kırığın 42'si (%97.7) açık kırık niteliğindeydi. Yoğun bakım ünitesine yatış oranı %26.0 (n=32), hastane içi mortalite oranı ise %4.1 (n=5) olarak saptandı. Başvuruların %43.1'i 18:00–23:59 saatleri arasında gerçekleşti. Negatif binom regresyon analizinde eşlik eden yaralanma (insidans hızı oranı=6.93; %95 güven aralığı: 3.82–12.57; p<0.001), kırık varlığı (insidans hızı oranı=5.02; %95 güven aralığı: 2.82–8.93; p<0.001) ve reoperasyon (insidans hızı oranı=2.73; %95 güven aralığı: 1.44–5.16; p=0.002) hastane yatış süresi ile bağımsız olarak ilişkili bulundu. Lojistik regresyon analizinde nörovasküler yaralanma (odds oranı=28.12; %95 güven aralığı: 7.60–104.09; p<0.001) ve eşlik eden yaralanma (odds oranı=20.36; %95 güven aralığı: 5.62–73.81; p<0.001) yoğun bakım ünitesine yatışı bağımsız olarak öngördü.
SONUÇ: Ekstremite ateşli silah yaralanmaları ağırlıklı olarak genç erkek popülasyonu etkilemekte ve akşam saatlerinde yoğunlaşmaktadır. Eşlik eden yaralanma ve kırık varlığı hastane yatış süresi ile bağımsız olarak ilişkiliyken, reoperasyon klinik seyir süresince uzamış hastanede kalış ile ilişkili bulundu; nörovasküler yaralanma ve eşlik eden yaralanma ise yoğun bakım ünitesine yatışı bağımsız olarak öngördü.

Anahtar sözcükler: Ateşli silah yaralanması; ekstremite; hastane yatış süresi; yoğun bakım ünitesi.

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ORIGINAL ARTICLE

Cumulative soft-sign burden is associated with clinically significant injury in hemodynamically stable penetrating neck trauma

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ABSTRACT

BACKGROUND: Risk stratification remains challenging in hemodynamically stable patients with penetrating neck trauma and no hard signs. We evaluated the association between cumulative soft-sign burden and clinically significant injury (CSI) requiring therapeutic intervention.

METHODS: This retrospective cohort study included adults with penetrating neck trauma who were hemodynamically stable, had no hard signs, and underwent cervical computed tomography angiography (CTA). CSI was defined as a vascular or aerodigestive injury requiring therapeutic surgical or endovascular intervention. Soft-sign count was assessed using receiver operating characteristic analysis and logistic regression.

RESULTS: Of 109 patients, 33 (30.3%) had CSI. The median soft-sign count was higher among patients undergoing therapeutic surgery (2 vs. 1; p<0.001). Soft-sign count showed good discrimination for CSI (AUC, 0.81; 95% CI, 0.71–0.90). A threshold of ≥1 soft sign yielded 93.9% sensitivity and a 91.7% negative predictive value, whereas ≥2 soft signs yielded 89.5% specificity and a 73.3% positive predictive value. Each additional soft sign was independently associated with higher odds of CSI (adjusted OR, 4.83; 95% CI, 2.42–9.64; p<0.001). Gunshot mechanism was also strongly associated with CSI (OR, 10.58; 95% CI, 2.68–41.75).

CONCLUSION: Increasing soft-sign burden was strongly associated with CSI. The absence of soft signs reduced but did not eliminate the risk, whereas multiple soft signs identified a higher-risk group. Soft-sign count may support imaging prioritization and early surgical consultation but should not replace CTA.

Keywords: Clinically significant injury; computed tomography angiography; penetrating neck trauma; risk stratification; soft signs.

INTRODUCTION

Penetrating neck injury is an uncommon but potentially fatal form of trauma because major vascular and aerodigestive structures are concentrated within a small anatomical region.[1,2] Historically, wounds penetrating the platysma—particularly in Zone II—were managed with mandatory surgical exploration. However, the high frequency of non-therapeutic pro-

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cedures and advances in computed tomography angiography (CTA) have led to selective management and the contemporary "no-zone" approach.[3-5] Current management therefore relies primarily on physiological status, clinical findings, injury mechanism, and CTA rather than the external anatomical zone alone.[4-6]

Patients with hemodynamic instability or hard signs generally require urgent intervention, whereas stable patients without hard signs present a more difficult diagnostic problem. Hard signs, including active arterial bleeding, expanding hematoma, shock, airway compromise, pulse deficit, or bruit/thrill, are highly suggestive of major vascular and/or aerodigestive injury and generally mandate immediate operative management. In contrast, soft signs are less specific clinical findings that suggest, but do not confirm, the presence of significant underlying injury and therefore usually warrant further evaluation with CTA.[4,7,8] In this population, soft signs such as stable hematoma, venous bleeding, dysphonia, dysphagia, subcutaneous emphysema, minor hemoptysis, and pulse asymmetry may indicate underlying vascular or aerodigestive injury. Previous studies have demonstrated that physical examination can support selective management, particularly when no soft signs are present.[9-12] Nevertheless, most studies have assessed soft signs as binary findings or broad clinical categories, and the potential value of their cumulative burden remains insufficiently defined.

The number of concurrent soft signs may provide more clinically relevant risk information than the presence of an isolated finding. Such an assessment would not replace CTA but could assist in determining imaging priority, the urgency of surgical consultation, and the intensity of observation. This study therefore aimed to evaluate the association between cumulative soft-sign burden and clinically significant injury (CSI) requiring therapeutic surgical or endovascular intervention in hemodynamically stable patients with penetrating neck trauma and no hard signs. We also assessed the diagnostic performance of different soft-sign thresholds and examined the contributions of injury mechanism and initial hemodynamic variables.

MATERIALS AND METHODS

Study Design and Setting

This single-center retrospective cohort study was conducted in the Ankara Etlik City Hospital, Emergency Medicine Department of a tertiary care center with a high volume of trauma admissions. Consecutive adult patients evaluated for penetrating neck trauma between January 1, 2023, and May 1, 2026, were screened for eligibility. During the study period, 205 patients were assessed, of whom 96 were excluded and 109 were included in the final analysis (Fig. 1). The study was designed and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations.

Penetrating neck injury was defined as a wound that violated the platysma muscle, as confirmed by clinical examination and/or imaging. Superficial wounds that did not penetrate the platysma were classified as non-penetrating and were excluded.

Clinical and outcome data were obtained retrospectively from the hospital information management system, emergency department records, radiology reports, operative reports, inpatient records, discharge summaries, and available follow-up documentation. Data collection and clinical classification were performed under the supervision of specialists in emergency medicine, otorhinolaryngology–head and neck surgery, and general surgery. Records containing ambiguous clinical, imaging, or procedural information were jointly reviewed by the relevant specialists before final classification.

Ethics

This retrospective, observational, single-center study was approved by the Clinical Research Ethics Committee of the Ministry of Health Ankara Etlik City Hospital (Approval No: AEŞH-BADEK1-2026-626; Date: 29/07/2026). The study was conducted in accordance with the principles of the Declaration of Helsinki. Given the retrospective design and use of anonymized data, the requirement for informed consent was waived by the ethics committee.

Study Population

Patients aged 18 years or older who presented to the emergency department with penetrating neck trauma were screened for eligibility. Patients were included if they were hemodynamically stable at the initial assessment, had no hard signs of major vascular or aerodigestive injury, underwent cervical computed tomography angiography as part of their diagnostic evaluation, and had sufficient clinical, imaging, procedural, and outcome information to determine the study endpoints.

Hemodynamic stability was defined as an initial systolic blood pressure of at least 90 mmHg without vasopressor support, ongoing massive transfusion, or persistent signs of shock requiring immediate operative management.

Patients were excluded if they were younger than 18 years; had blunt neck trauma or a clinically documented superficial wound; presented with hemodynamic instability, cardiopulmonary arrest, or a hard sign requiring immediate intervention; were transferred after definitive diagnosis or surgical treatment at another institution; proceeded directly to emergency surgical exploration without CTA; did not undergo cervical CTA; were pregnant; or had insufficient clinical, imaging, procedural, or outcome data.

Laboratory and physiological parameters were recorded as part of routine clinical care. Patients whose core records or vital signs could not be retrieved were excluded at the screening stage (see Figure 1). Among the 109 patients included in the analysis, the extent of missing data was assessed

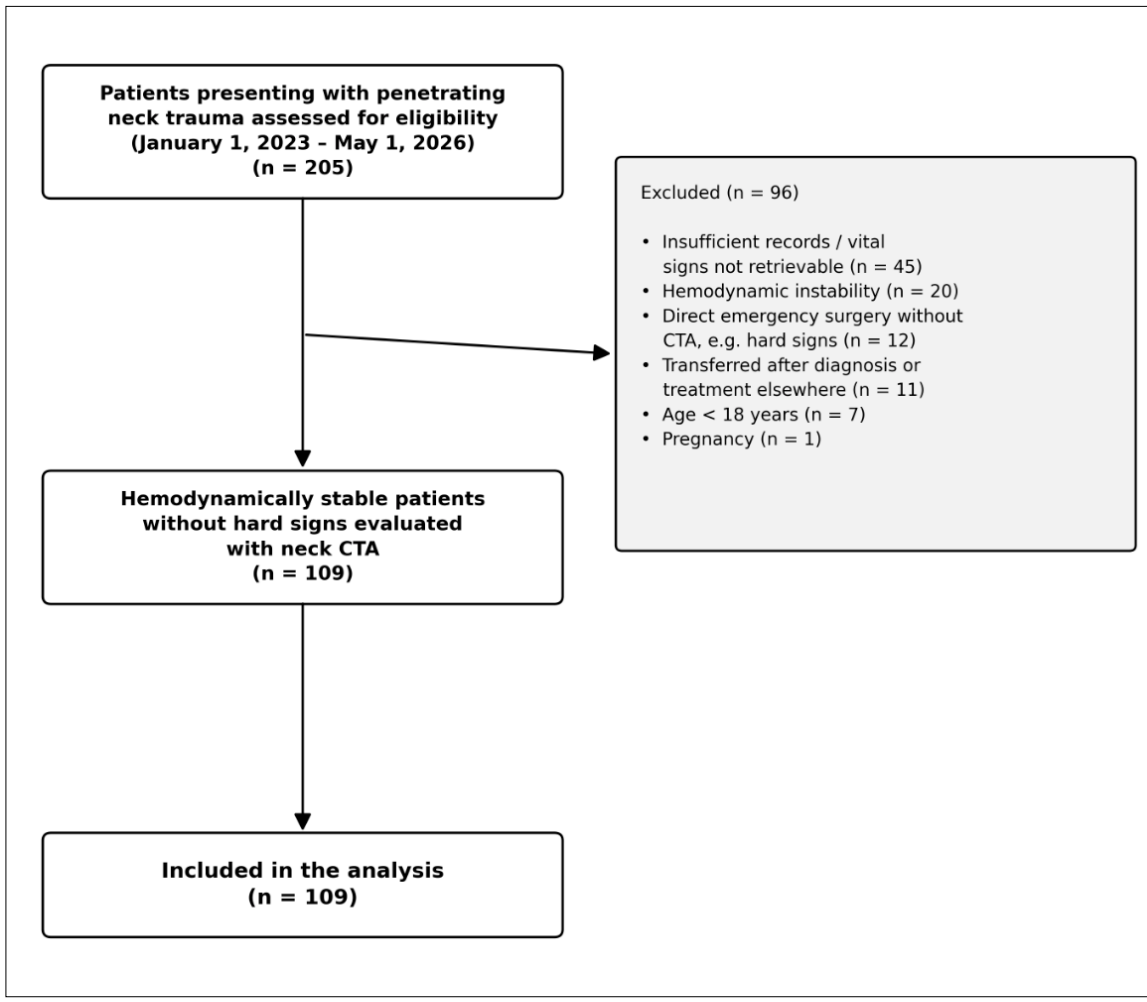


Figure 1. Study flow diagram. Of 205 patients assessed for eligibility, 96 were excluded and 109 were included in the analysis.

for every analyzed variable (demographics, mechanism, vital signs, laboratory values, each individual soft sign, and outcomes). Missing data were negligible: only hemoglobin had a missing value in a single patient (1/109, 0.9%); all remaining 25 variables were complete (0% missing). A complete-case analysis was therefore used, and no imputation was performed.

Data Collection

A structured data collection form was used to extract demographic characteristics, medical history, injury-related variables, initial physiological measurements, clinical examination findings, laboratory results, CTA findings, therapeutic procedures, and clinical outcomes.

Age, sex, hypertension, diabetes mellitus, coronary artery disease, malignancy, and current anticoagulant or antiplatelet treatment were recorded. Comorbidities and medication use were determined from admission records, previous diagnoses, medical history, and available medication lists.

The injury mechanism was categorized as a stab or other sharp-object injury, gunshot wound, glass-related injury or laceration, or another penetrating mechanism. The circumstance of injury was classified as assault, self-harm, or accident. The number of external neck wounds was recorded from the initial examination and consultation records.

The external wound location was classified according to the traditional anatomical neck zones. Zone I extended from the clavicles and sternal notch to the cricoid cartilage, Zone II from the cricoid cartilage to the angle of the mandible, and Zone III from the angle of the mandible to the skull base. Injuries involving more than one anatomical zone or wounds with trajectories crossing zonal boundaries were classified as multiple-zone injuries. Zonal classification was used for anatomical description and was not considered the primary basis for clinical risk stratification.

Physiological and Laboratory Variables

Initial vital signs recorded during the emergency department assessment were collected, including systolic and diastolic blood pressure, heart rate, respiratory rate, peripheral oxygen saturation, and Glasgow Coma Scale score. Shock index

was calculated as the initial heart rate divided by the systolic blood pressure. When available, pre-intervention values were used, and measurements obtained after major resuscitation, transfusion, intubation, surgery, or vasopressor therapy were excluded.

Laboratory parameters obtained before surgical or endovascular intervention were recorded, including hemoglobin, hematocrit, platelet count, serum lactate, and base excess. If multiple measurements were available, the earliest valid pre-intervention result was analyzed.

Assessment of Soft Clinical Signs

Soft signs were identified from the history and physical examination documented during the initial emergency department assessment before CTA or therapeutic intervention. Evaluated soft signs included stable hematoma, a history or observation of venous bleeding, dysphagia, odynophagia, hoarseness or dysphonia, clinically detected subcutaneous emphysema, minor hemoptysis or hematemesis, and peripheral pulse asymmetry.

Stable hematoma was defined as non-pulsatile and non-expanding. Minor hemoptysis or hematemesis referred to limited bleeding without respiratory compromise, hemodynamic instability, or massive ongoing hemorrhage. Only subcutaneous emphysema identified on physical examination was considered a soft sign; findings detected solely on CTA were classified as imaging findings. Neck tenderness was excluded because of its limited specificity in penetrating neck trauma.

For each patient, the soft-sign count was calculated as the unweighted sum of individual findings. In addition to the presence of any soft sign, thresholds of ≥1, ≥2, and ≥3 were analyzed.

CT Angiography and Injury Classification

According to the institutional trauma protocol at our center, neck CTA was obtained in all hemodynamically stable patients with penetrating neck injury, irrespective of the presence or absence of soft signs; imaging was therefore not selectively ordered on the basis of clinical suspicion. All included patients underwent contrast-enhanced neck CTA accordingly. CTA examinations were reviewed for vascular and aerodigestive injuries. Arterial injuries included contrast extravasation, occlusion, dissection, pseudoaneurysm, arteriovenous fistula, or other traumatic arterial abnormalities. Venous injuries included extravasation, thrombosis, occlusion, vessel disruption, or other traumatic venous abnormalities. Aerodigestive injuries were classified as laryngeal, tracheal, or esophageal.

Final injury classification was based on CTA findings together with operative or endovascular findings, additional diagnostic investigations when available, and the documented clinical course. Operative findings were considered definitive when present.

Study Outcomes

The primary outcome was clinically significant injury (CSI), defined as a confirmed vascular or aerodigestive injury requiring therapeutic surgical or endovascular intervention during the index hospitalization.

Therapeutic surgical exploration was defined as an operation in which an injured vascular or aerodigestive structure was repaired, ligated, reconstructed, drained, controlled, or otherwise treated. An operation limited to exploration without a therapeutic procedure was not classified as CSI solely because surgery had been performed. Endovascular intervention included embolization, stent placement, vascular occlusion, or another catheter-based therapeutic procedure performed for a traumatic cervical vascular injury.

Therapeutic surgical exploration and endovascular intervention were additionally recorded as separate components of the primary outcome. Thirty-day all-cause mortality was evaluated as a secondary outcome. Deaths occurring during the index hospitalization or within 30 days of the initial emergency department presentation were included.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA). All tests were two-sided, and $p<0.05$ was considered statistically significant.

Continuous variables were assessed for normality using the Shapiro–Wilk test and are presented as mean±standard deviation or median (interquartile range), as appropriate. Categorical variables are reported as frequencies and percentages.

Patients with and without therapeutic surgical exploration were compared using the independent-samples t test or Mann–Whitney U test for continuous variables and the chi-square or Fisher's exact test for categorical variables.

The diagnostic performance of the soft-sign count for CSI was evaluated using receiver operating characteristic (ROC) analysis. The area under the curve (AUC), optimal cutoff (Youden index), sensitivity, specificity, predictive values, and likelihood ratios were calculated for the predefined thresholds (≥1, ≥2, and ≥3).

Univariable logistic regression was used to identify candidate predictors of CSI, and clinically relevant variables were entered into the multivariable model. Soft-sign count was analyzed as a continuous variable. Results are presented as odds ratios (ORs) with 95% confidence intervals (CIs). Model discrimination was assessed using the AUC and calibration using the Hosmer–Lemeshow goodness-of-fit test.

Gunshot mechanism was excluded from the multivariable model because the high proportion of CSI among patients with gunshot wounds resulted in sparse data and potentially unstable estimates; therefore, its association with CSI was evaluated only in the univariable analysis.

Table 1. Baseline demographic, clinical, and outcome characteristics (N=109).

Variable	Value
Demographics	
Age (years)	31.00 [21.00–45.00]
Female sex	15 (13.76%)
Anticoagulant/antiplatelet use	1 (0.92%)
Hypertension	4 (3.67%)
Diabetes mellitus	4 (3.67%)
Coronary artery disease	2 (1.83%)
Malignancy	0 (0.00%)
Injury characteristics	
Mechanism	
Stab/sharp	59 (54.13%)
Gunshot	13 (11.93%)
Glass/laceration	10 (9.17%)
Other	27 (24.77%)
Cause	
Assault	43 (39.45%)
Self-harm	33 (30.28%)
Accident	33 (30.28%)
Zone	
Zone I	32 (29.36%)
Zone II	30 (27.52%)
Zone III	11 (10.09%)
Multiple	36 (33.03%)
Number of wounds	1.00 [1.00–2.00]
Vital signs	
Systolic BP (mmHg)	115.00 [110.00–125.00]
Diastolic BP (mmHg)	70.64±15.26
Heart rate (/min)	84.97±16.33
Respiratory rate (/min)	17.00 [15.00–18.00]
SpO2 (%)	97.00 [95.00–98.00]
GCS	15.00 [15.00–15.00]
Shock index	0.71 [0.61–0.78]
Soft clinical signs	
Any soft sign	85 (77.98%)
Soft sign count	1.00 [1.00–2.00]
Stable hematoma	27 (24.77%)
Venous bleeding history	21 (19.27%)
Dysphagia	1 (0.92%)
Odynophagia	0 (0.00%)
Hoarseness/dysphonia	3 (2.75%)
Subcutaneous emphysema	73 (66.97%)
Minor hemoptysis/hematemesis	1 (0.92%)
Peripheral pulse asymmetry	0 (0.00%)
Laboratory	
Hemoglobin (g/dL)	14.01±1.81
Hematocrit (%)	42.47±4.98
Platelet (10^3/μL)	268.00 [224.00–314.00]
Lactate (mmol/L)	2.20 [1.56–3.03]
Base excess	-2.10 [-4.10–0.30]
Imaging/Injury (CTA)	
Arterial injury	4 (3.67%)
Venous injury	13 (11.93%)
Laryngeal injury	3 (2.75%)
Tracheal injury	9 (8.26%)
Esophageal injury	1 (0.92%)
Outcomes	
Therapeutic surgical exploration	32 (29.36%)
Endovascular intervention	1 (0.92%)
CSI (therapeutic surgical/endovascular)	33 (30.28%)
30-day mortality	3 (2.75%)

Continuous: mean ± SD (normal) or median [IQR] (non-normal), per Shapiro–Wilk. Categorical: n (%). CSI, clinically significant injury.

Sample Size

Because of the retrospective design, no a priori sample size calculation was performed. All consecutive eligible patients were included. The multivariable model contained two predictors for 33 CSI events (16.5 events per variable), exceeding the conventional minimum of 10 events per variable.

RESULTS

A total of 109 hemodynamically stable patients with penetrating neck injury without hard signs who underwent CTA were included. The median age was 31 years [interquartile range (IQR), 21–45]; 15 (13.76%) were female. The most common mechanism was stab/sharp injury (59, 54.13%), followed by gunshot injury (13, 11.93%). At least one soft sign was present in 85 patients (77.98%). Baseline demographic, clinical, and injury characteristics are summarized in Table 1.

A clinically significant injury (CSI), defined as an injury requiring therapeutic surgical or endovascular intervention, occurred in 33 patients (30.28%). Therapeutic surgical exploration was performed in 32 (29.36%), and endovascular intervention was performed in 1 (0.92%). Thirty-day mortality was 2.75% (3).

Because only one patient underwent endovascular intervention, the group requiring therapeutic surgical exploration was virtually identical to the CSI group; the between-group comparison is therefore presented according to therapeutic surgical exploration. When compared according to therapeutic surgical exploration (Table 2), patients requiring surgery had significantly higher soft-sign counts (median, 2.00 vs 1.00;

Table 2. Comparison by therapeutic surgical exploration

Variable	Therapeutic (n=32)	No therapeutic (n=77)	Effect size (95% CI)[a]	p
Soft signs				
Any soft sign	30 (93.75%)	55 (71.43%)	22.32 (9.20 to 35.44)	0.021
Soft sign count	2.00 [1.00–3.00]	1.00 [0.00–1.00]	Δmed 1.00	<0.001
Stable hematoma	14 (43.75%)	13 (16.88%)	26.87 (7.75 to 45.98)	0.007
Venous bleeding history	12 (37.50%)	9 (11.69%)	25.81 (7.57 to 44.06)	0.004
Dysphagia	0 (0.00%)	1 (1.30%)	-1.30 (-3.83 to 1.23)	1.000
Hoarseness/dysphonia	3 (9.38%)	0 (0.00%)	9.38 (-0.72 to 19.47)	0.024
Subcutaneous emphysema	30 (93.75%)	43 (55.84%)	37.91 (24.00 to 51.81)	<0.001
Vitals & demographics				
Shock index	0.72 [0.66–0.90]	0.71 [0.61–0.77]	Δmed 0.01	0.146
Systolic BP	112.00 [105.00–119.75]	118.00 [112.00–125.00]	Δmed -6.00	0.008
Heart rate	86.75 ± 18.42	84.23 ± 15.45	2.52 (-4.74 to 9.77)	0.500
Age	37.00 [19.00–52.00]	31.00 [22.00–44.00]	Δmed 6.00	0.790
Gunshot mechanism	10 (31.25%)	3 (3.90%)	27.35 (10.72 to 43.99)	<0.001

Categorical: χ^2 or Fisher's exact; continuous: t-test or Mann–Whitney U. Note: non-therapeutic explorations and conservatively managed patients are grouped as 'no therapeutic surgery'. [a]Effect size denotes the risk difference (%) with 95% CI for categorical variables and the difference in means or medians for continuous variables.

Table 3. Diagnostic performance for CSI (therapeutic surgical/endovascular intervention).

Predictor / cut-off	AUC (95% CI)	Cut-off	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV %	NPV %	LR+	LR−
Soft sign count	0.81 (0.71–0.90)	≥2	66.67 (49.61–80.25)	89.47 (80.58–94.57)	73.33	86.08	6.33	0.37
Gunshot mechanism	0.63 (0.51–0.75)	≥1	30.30 (17.38–47.34)	96.05 (89.03–98.65)	76.92	76.04	7.68	0.73
Systolic BP	0.68 (0.56–0.79)	≤115	72.73 (55.78–84.93)	59.21 (47.98–69.56)	43.64	83.33	1.78	0.46
Soft count ≥1		≥1	93.94 (80.39–98.32)	28.95 (19.96–39.96)	36.47	91.67	1.32	0.21
Soft count ≥2		≥2	66.67 (49.61–80.25)	89.47 (80.58–94.57)	73.33	86.08	6.33	0.37
Soft count ≥3		≥3	27.27 (15.07–44.22)	97.37 (90.90–99.28)	81.82	75.51	10.36	0.75

Variables significant in Table 2 included. AUC by ROC; cut-off by Youden index; soft-count thresholds shown for reference. Wilson 95% CIs.

p<0.001) and higher rates of stable hematoma (p=0.007), a history of venous bleeding (p=0.004), hoarseness/dysphonia (p=0.024), and subcutaneous emphysema (p<0.001). Gunshot mechanism (p<0.001) and lower SBP (p=0.008) were also associated with therapeutic surgery.

On ROC analysis (Table 3, Fig. 2), soft-sign count discriminated CSI with an AUC of 0.81, which was higher than that of gunshot mechanism (AUC, 0.63) and SBP (AUC, 0.68). On DeLong comparison (Table 3b), soft-sign count showed significantly better discrimination than gunshot mechanism (p=0.004). At a threshold of ≥1 soft sign, sensitivity was 93.94%, and the negative predictive value was 91.67%, indicating that patients with no soft signs had a low probability of CSI.

On logistic regression analysis (Table 4), soft-sign count was independently associated with CSI (adjusted odds ratio [aOR], 4.83; 95% CI, 2.42–9.64; p<0.001) in a model that included SBP (model AUC, 0.84; Hosmer–Lemeshow p=0.16). Gunshot mechanism, a strong univariable predictor (OR, 10.58; 95% CI, 2.68–41.75; p=0.001), was therefore reported separately; because most patients with gunshot wounds sustained CSI (10 of 13), the resulting sparse data precluded stable adjusted estimation.

Table 3b. Pairwise comparison of AUCs (DeLong test)

Comparison	AUC vs AUC	ΔAUC	z	p
Soft sign count vs Gunshot mechanism	0.81 vs 0.63	+0.18	2.86	0.004
Soft sign count vs Systolic BP	0.81 vs 0.68	+0.13	1.71	0.088
Gunshot mechanism vs Systolic BP	0.63 vs 0.68	-0.05	-0.64	0.522

DeLong test for correlated ROC curves.

Table 4. Univariable and multivariable logistic regression for CSI

Predictor	Univariable OR (95% CI)	p	Multivariable aOR (95% CI)	p
Soft sign count	5.19 (2.63–10.23)	<0.001	4.83 (2.42–9.64)	<0.001
Gunshot mechanism	10.58 (2.68–41.75)	0.001		
Systolic BP	0.96 (0.93–0.99)	0.020	0.98 (0.95–1.01)	0.241
Age	1.02 (0.99–1.05)	0.199		

Multivariable model: soft sign count + systolic BP (33 events, EPV≈16). Model AUC = 0.84; Hosmer–Lemeshow p = 0.16. Gunshot mechanism (univariable OR 10.58 (2.68–41.75), p=0.001) was reported separately as its strong association approached separation.

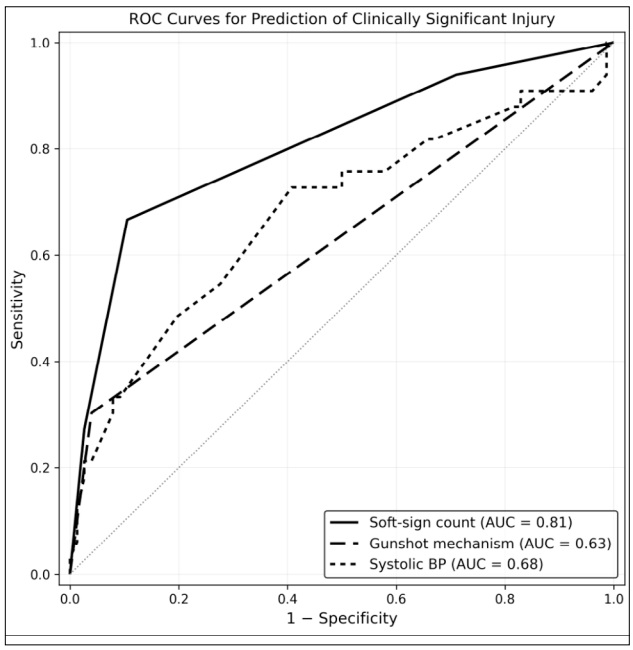


Figure 2. Receiver operating characteristic (ROC) curves for the prediction of clinically significant injury by soft-sign count, gunshot mechanism, and systolic blood pressure.

DISCUSSION

The principal finding of this study was that cumulative soft-sign burden was strongly associated with clinically significant injury in hemodynamically stable patients with penetrating neck trauma and no hard signs. Approximately one-third of the cohort required therapeutic surgical or endovascular intervention, demonstrating that the absence of hard signs does not define a uniformly low-risk population. Patients requiring intervention had more soft signs, and each additional soft sign was associated with a substantial increase in the odds of CSI. Soft-sign count also provided better overall discrimination than either systolic blood pressure or gunshot mechanism alone. Nevertheless, none of the evaluated thresholds achieved sufficient performance to safely replace CTA.

The transition from mandatory neck exploration to selective management has considerably reduced non-therapeutic procedures without an apparent increase in missed clinically important injuries.[3,10,13] Contemporary algorithms distinguish patients with hard signs or physiological instability, who generally require immediate intervention, from stable patients who can undergo clinical assessment and CTA.[4,6,7] However, this second group remains heterogeneous. In our cohort, 30.3% of patients required therapeutic intervention despite being hemodynamically stable and having no hard signs. This finding emphasizes that physiological stability should be interpreted as a prerequisite for structured investigation rather than as evidence that a significant injury is absent.

Previous studies have primarily examined whether any soft sign is present. Isaza-Restrepo et al.[9] reported that the presence of any soft sign had a sensitivity of 97.4% and a negative predictive value of 98.7% for injuries requiring surgical repair. Other studies have similarly suggested that a normal physi-

cal examination may identify patients at relatively low risk of clinically important vascular injury.[11,14] In our study, the presence of at least one soft sign showed a sensitivity of 93.9% and a negative predictive value (NPV) of 91.7%. Although these findings support the value of physical examination, two patients without documented soft signs still had CSI. Accordingly, the absence of soft signs reduced the probability of therapeutic intervention but did not exclude it with sufficient certainty to justify omitting CTA.

Our results extend the binary present-versus-absent approach by demonstrating that the accumulation of soft signs carries additional risk information. Soft-sign count achieved an AUC of 0.81, indicating good but incomplete discrimination. A threshold of at least two soft signs provided 89.5% specificity, a positive predictive value of 73.3%, and a positive likelihood ratio of 6.33. Thus, patients with two or more soft signs represented a distinctly higher-risk group that may warrant expedited CTA, early surgical consultation, and closer monitoring. By contrast, the sensitivity of this threshold was only 66.7%, meaning that approximately one-third of patients with CSI would not be identified. The threshold should therefore be considered a risk-enrichment criterion rather than a rule for determining whether imaging is required.

The presence of at least three soft signs was highly specific for CSI, with a specificity of 97.4%, a positive predictive value (PPV) of 81.8%, and a positive likelihood ratio of 10.36. This degree of risk concentration may be clinically useful when prioritizing patients and mobilizing surgical or endovascular resources. However, its low sensitivity precludes its use as a screening threshold. Taken together, the threshold analyses suggest two different clinical functions: the absence of soft signs identifies a relatively lower-risk group but does not safely rule out CSI, whereas multiple concurrent signs identify patients with an increasingly high probability of requiring therapeutic intervention. This graded interpretation is more informative than treating all soft signs as equivalent binary findings.

Several individual findings were also associated with therapeutic surgery. Stable hematoma and a history of venous bleeding may reflect underlying vascular injury, whereas dysphonia and subcutaneous emphysema raise concern for laryngeal or tracheal involvement. The accumulation of these findings may therefore represent either increasing injury severity or involvement of more than one anatomical compartment. However, rare findings such as dysphonia should be interpreted cautiously because estimates based on small numbers are inherently unstable. Moreover, a simple count assigns equal importance to clinically different findings. The present results support cumulative assessment but should not be interpreted as validation of a definitive clinical score.

Gunshot mechanism was another important indicator of CSI. Ten of the 13 patients with gunshot wounds required therapeutic intervention, and gunshot injury was associated with more than a tenfold increase in the unadjusted odds of CSI. This is consistent with previous reports showing a higher frequency of significant injury after gunshot wounds than after stab wounds, which likely reflects greater energy transfer, tissue cavitation, and less predictable wound trajectories.[2,3,15] The AUC of gunshot mechanism was lower than that of soft-sign count because it identified only a relatively small subgroup and therefore had limited sensitivity. Nevertheless, its high specificity and positive likelihood ratio indicate that it remains clinically important. Soft-sign burden and injury mechanism should therefore be viewed as complementary rather than competing sources of risk information. Our findings further support the need for careful evaluation of civilian cervical gunshot injuries, complementing a recent Turkish case series emphasizing individualized management of vertebral artery injuries in this setting.[16]

Systolic blood pressure was lower among patients requiring therapeutic surgery, but its association was no longer significant after adjustment for soft-sign count. Heart rate and shock index were also not significantly different between the groups. These findings suggest that clinically important localized vascular or aerodigestive injuries may be present before overt systemic hemodynamic deterioration develops. Normal vital signs should therefore not override concerning examination findings. Conversely, modest differences in systolic blood pressure within the conventionally stable range should not be used as an independent indication for intervention.

The role of clinical examination in this setting should be considered complementary to CTA. Multidetector CTA offers high diagnostic accuracy for vascular injury and provides valuable information regarding the wound trajectory and structures at risk.[6,17] It has also contributed to the decline in mandatory exploration and conventional angiography.[5,6] Nevertheless, CTA can be affected by metallic artifacts and may be less reliable for subtle pharyngeal or esophageal injuries, for which additional endoscopic or contrast evaluation may be necessary when clinical suspicion persists.[7,8] Our findings do not support replacing CTA with a soft-sign threshold. Instead, soft-sign burden may help determine how urgently imaging should be obtained and which patients require early multidisciplinary evaluation despite apparently stable physiology.

The anatomical zone of entry was not central to the present analysis. Although traditional zone classifications remain useful for describing injury location and planning operative exposure, external wounds may not accurately reflect the trajectory or internal structures involved.[5,18] This limitation has supported the adoption of the no-zone approach, in which the entire neck is assessed according to clinical findings and CTA results. Accordingly, our results suggest that cumulative clinical findings and injury mechanisms may be more relevant for initial risk stratification than the external zone alone.

Limitations

This study has several limitations. First, its retrospective,

single-center design carries an inherent risk of incomplete or inconsistent documentation. In particular, soft signs were recorded during routine clinical care rather than through a standardized, prospectively applied examination protocol, and their assessment may therefore have varied among clinicians; subtle findings such as minor subcutaneous emphysema or minor bleeding are especially susceptible to this variability. Second, subcutaneous emphysema was more frequent than the other individual soft signs and may have contributed disproportionately to the performance of the cumulative soft-sign count. Third, missing data were minimal (hemoglobin was missing in one patient [0.9%], with all other analyzed variables complete). Although a patient-flow diagram is provided (Fig. 1), the retrospective design means that residual selection effects cannot be entirely excluded. Fourth, the cohort comprised only patients who underwent CTA. At our institution, neck CTA is obtained in all hemodynamically stable patients with penetrating neck injury according to the trauma protocol, which mitigates selection based on clinical severity; nevertheless, stable patients discharged without imaging or managed at other facilities would not have been captured, and this may have contributed to the observed rate of clinically significant injury. Fifth, the CSI outcome was defined by therapeutic surgical or endovascular intervention and may therefore have been influenced by local practice and surgeon decision-making. Sixth, several individual soft signs were uncommon, and the diagnostic thresholds were derived and evaluated in the same cohort, which may have produced optimistic performance estimates. Finally, the relatively small number of events limited the multivariable analysis; notably, gunshot mechanism could not be incorporated into the adjusted model because most patients with gunshot wounds sustained CSI, and the resulting sparse data would have yielded unstable estimates. These findings should therefore be regarded as hypothesis-generating and require prospective, multicenter validation before clinical application.

CONCLUSION

In conclusion, clinically significant injuries were common among hemodynamically stable patients with penetrating neck trauma despite the absence of hard signs. Increasing soft-sign burden was independently associated with therapeutic intervention and provided good discrimination for CSI. The absence of soft signs identified a lower-risk group but did not safely exclude significant injury, whereas two or more concurrent findings substantially increased the probability of intervention. Soft-sign burden should therefore be regarded as a tool for risk stratification, imaging prioritization, and early surgical consultation rather than as a substitute for CTA.

Ethics Committee Approval: This study was approved by the Clinical Research Ethics Committee of the Ministry of Health Ankara Etlik City Hospital (Date: 29.07.2026, Decision No: AEŞH-BADEK1-2026-626).

Informed Consent: Given the retrospective design of the study and the use of anonymized data, the requirement for written informed consent was waived by the institutional ethics committee.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: H.H.C., M.A., Ö.A.; Design: S.A.T., İ.Ş., F.Y.; Supervision: H.H.C., M.A., Ö.A.; Resource: S.A.T.; Materials: S.A.T., F.Y.; Data collection and/or processing: İ.Ş., F.Y., İ.B.; Analysis and/or interpretation: H.H.C., M.A., S.A.T.; Literature review: İ.B.; Writing: İ.Ş., İ.B.; Critical review: H.H.C., M.A., Ö.A.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Kümülatif yumuşak bulgu yükü, hemodinamik olarak stabil penetran boyun travmasında klinik olarak önemli yaralanma ile ilişkilidir

AMAÇ: Hemodinamik olarak stabil, ciddi bulgusu olmayan penetran boyun travmalı hastalarda risk sınıflaması güçlüğünü korumaktadır. Bu çalışmada, kümülatif yumuşak bulgu yükü ile terapötik girişim gerektiren klinik olarak önemli yaralanma (KÖY) arasındaki ilişki değerlendirildi.
GEREÇ VE YÖNTEM: Bu retrospektif kohort çalışmasına, hemodinamik olarak stabil olan, ciddi bulgusu bulunmayan ve servikal bilgisayarlı tomografi anjiyografi (BTA) uygulanan penetran boyun travmalı erişkin hastalar dahil edildi. KÖY, terapötik cerrahi veya endovasküler girişim gerektiren vasküler ya da aerodigestif yaralanma olarak tanımlandı. Yumuşak bulgu sayısı, alıcı işlem karakteristik (ROC) analizi ve lojistik regresyon ile değerlendirildi.
BULGULAR: Toplam 109 hastanın 33'ünde (%30,3) KÖY saptandı. Terapötik cerrahi uygulanan hastalarda ortanca yumuşak bulgu sayısı daha yüksekti (2'ye karşı 1; p<0,001). Yumuşak bulgu sayısı KÖY için iyi ayırt edicilik gösterdi (EAA, 0,81; %95 GA, 0,71–0,90). ≥1 yumuşak bulgu eşiği %93,9 duyarlılık ve %91,7 negatif prediktif değer sağlarken; ≥2 yumuşak bulgu %89,5 özgüllük ve %73,3 pozitif prediktif değer sağladı. Her bir ilave yumuşak bulgu, KÖY olasılığında bağımsız artışla ilişkiliydi (düzeltilmiş OO, 4,83; %95 GA, 2,42–9,64; p<0,001). Ateşli silah mekanizması da KÖY ile güçlü şekilde ilişkiliydi (OO, 10,58; %95 GA, 2,68–41,75).
SONUÇ: Artan yumuşak bulgu yükü KÖY ile güçlü şekilde ilişkiliydi. Yumuşak bulgu yokluğu riski azaltmakla birlikte tamamen ortadan kaldırmadı; buna karşın çok sayıda yumuşak bulgu daha yüksek riskli bir grubu tanımladı. Yumuşak bulgu sayısı, görüntüleme önceliklendirmesini ve erken cerrahi konsültasyonu destekleyebilir; ancak BTA'nın yerini almamalıdır.

Anahtar sözcükler: Bilgisayarlı tomografi anjiyografi; hafif bulgular; klinik olarak önemli yaralanma; penetran boyun travması; risk sınıflaması.

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ORIGINAL ARTICLE

Association between mean platelet volume and acute cholecystitis in pregnant patients with right upper quadrant pain: A multicenter retrospective cohort study

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ABSTRACT

BACKGROUND: Physiological and hematological changes during pregnancy may complicate the interpretation of conventional inflammatory markers in patients with suspected acute cholecystitis (AC). This study aimed to evaluate the association between mean platelet volume (MPV), derived from routine complete blood count analysis, and AC in pregnant patients and to investigate whether this association remained consistent across pregnancy trimesters.

METHODS: This retrospective multicenter exploratory cohort study included 112 pregnant patients presenting with right upper quadrant pain between 2022 and 2025. According to retrospective classification based on the Tokyo Guidelines 2018 criteria, 89 patients were classified as AC and 23 as non-cholecystitis (NC). MPV and other hematological parameters were compared between the groups. Logistic regression analysis adjusted for pregnancy trimester was performed to evaluate the association between MPV and AC. Receiver operating characteristic (ROC) curve analysis with confidence intervals (CIs) was performed to assess the exploratory discriminative performance of MPV.

RESULTS: MPV levels were significantly higher in the AC group than in the NC group (10.6 fL vs. 10.3 fL, p=0.034). In univariable logistic regression analysis, MPV was significantly associated with AC (odds ratio [OR]: 1.734, 95% CI: 1.203–2.500, p=0.003), and this association remained significant after adjustment for pregnancy trimester (OR: 1.870, 95% CI: 1.251–2.794, p=0.002). No significant associations were observed for white blood cell, neutrophil-to-lymphocyte ratio, platelet count, or platelet-to-lymphocyte ratio. ROC analysis demonstrated limited discriminative performance for MPV (area under the curve: 0.655). At the identified cut-off value of 8.70 fL, sensitivity was 95.2% and specificity was 36.4%.

CONCLUSION: MPV was significantly associated with AC in pregnant patients; however, its limited discriminative performance and low specificity suggest that it should not be used as an independent diagnostic marker. MPV may provide supportive diagnostic value when interpreted together with clinical and ultrasonographic findings. Larger prospective studies including standardized MPV measurements and pregnancy-specific diagnostic frameworks are needed to better define the diagnostic role of MPV in pregnant patients with suspected AC.

Keywords: Acute cholecystitis; inflammatory markers; mean platelet volume; pregnancy; right upper quadrant pain.

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INTRODUCTION

Acute cholecystitis (AC) is one of the most common non-obstetric surgical emergencies encountered during pregnancy, with an estimated incidence of 0.02–0.05%.[1,2] Pregnancy-related hormonal changes, particularly progesterone-induced gallbladder hypomotility, increase biliary stasis and gallstone formation, predisposing pregnant patients to biliary diseases including AC.[3] Delayed or missed diagnosis may lead to adverse maternal and fetal outcomes; therefore, early and accurate diagnosis remains clinically important.[4,5]

The Tokyo Guidelines 2018 (TG18) provide widely accepted diagnostic criteria for AC by combining clinical findings, systemic inflammatory markers, and imaging results.[6] However, physiological hematological changes during pregnancy may complicate the interpretation of conventional inflammatory markers. Physiological leukocytosis and trimester-related variations in inflammatory parameters may reduce the diagnostic specificity of routine laboratory tests in symptomatic pregnant patients.[7-9] Therefore, imaging studies play a central role in the diagnostic evaluation of suspected AC during pregnancy.

Ultrasonography is considered the first-line imaging modality in pregnant patients with suspected AC because of its accessibility and lack of ionizing radiation.[10,11] Nevertheless, ultrasonographic findings may occasionally be inconclusive, particularly in early-stage disease or in patients with nonspecific clinical presentation.[12,13] In routine clinical practice, some pregnant patients presenting with right upper quadrant pain may have biliary colic or other symptomatic biliary conditions rather than definite AC. Therefore, interest has increased in additional laboratory parameters that may support clinical evaluation.

Mean platelet volume (MPV) is an inexpensive and easily accessible parameter obtained from routine complete blood count analysis. It reflects platelet size and activation and has been investigated as an inflammatory marker in several inflammatory and surgical conditions.[14] Larger platelets are considered metabolically and enzymatically more active and may be associated with systemic inflammatory response.[15,16] However, the clinical significance of MPV in pregnant patients remains unclear.

Previous studies evaluating the role of MPV in AC have reported inconsistent results.[17-19] In addition, most available studies have been conducted in non-pregnant populations, and data regarding pregnant patients remain limited. Pregnancy-related hematological changes may further complicate the interpretation of MPV in this population.

Therefore, this study aimed to investigate the association between MPV and AC in pregnant patients presenting with right upper quadrant pain and to evaluate whether this association remained consistent across pregnancy trimesters. In addition, MPV was compared with conventional inflammatory parameters including white blood cell count (WBC), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and platelet count (PLT).

MATERIALS AND METHODS

Study Design and Ethical Approval

This retrospective multicenter exploratory cohort study was conducted in four hospitals located in different regions of Türkiye, including three tertiary referral training and research hospitals and one secondary care hospital, between 2022 and 2025. All participating centers provided emergency and obstetric care services. Laboratory data were obtained as part of routine clinical practice.

The study was approved by the Ethics Committee of Etlik City Hospital (Date: 10.02.2026, Decision no: AEŞH-BADEK2-2026-095) and was conducted in accordance with the principles of the Declaration of Helsinki. Patient data were retrospectively collected from electronic medical records and anonymized before analysis. Written informed consent was waived because of the retrospective nature of the study.

Patient Selection

Pregnant patients presenting with right upper quadrant pain and evaluated for hepatobiliary pathology during the study period were retrospectively screened using emergency department records, obstetric and surgical consultation notes, imaging reports, and electronic medical records. Case identification was not based solely on diagnostic codes, and all potentially eligible patients were confirmed by manual chart review.

The inclusion criteria were as follows: (1) Age ≥18 years, (2) ongoing pregnancy, (3) presentation with right upper quadrant pain, (4) availability of complete blood count parameters at admission, and (5) completed abdominal ultrasonographic evaluation.

The exclusion criteria were as follows: (1) Known hematological disease or thrombocytopenia, (2) active malignancy or immunosuppressive therapy, (3) autoimmune disease, and (4) concomitant infectious or systemic inflammatory conditions that could affect inflammatory laboratory parameters.

A total of 129 patients were initially screened. Seventeen patients were excluded because of missing laboratory data (n=5), insufficient imaging documentation (n=9), or predefined exclusion criteria (n=3). Consequently, 112 patients were included in the final analysis. No data imputation was performed for missing data.

Diagnostic Classification

All eligible patients were retrospectively reclassified according to the diagnostic principles of the TG18 using available clinical, laboratory, and imaging findings. This approach was used to reduce inter-center variability in diagnostic classification.

TG18 diagnostic criteria included local inflammatory findings (right upper quadrant pain and/or Murphy's sign), systemic inflammatory findings (fever and/or leukocytosis; C-reactive

protein [CRP] when available), and imaging findings including gallbladder wall thickening ≥3 mm, pericholecystic fluid, or ultrasonographic Murphy's sign.

Patients with clinical, laboratory, and imaging findings compatible with TG18 criteria were classified as the AC group. Patients presenting with right upper quadrant pain who did not meet TG18 diagnostic criteria for AC and were considered compatible with biliary colic were classified as the non-cholecystitis (NC) group.

Gestational age was determined according to obstetric records. Pregnancy trimesters were defined as 1st trimester (1–13 weeks), second trimester (14–27 weeks), and third trimester (≥28 weeks).

Variables

The primary study variable was MPV, fL measured at admission. Secondary variables included age, pregnancy trimester, (WBC, $\times 10^3/\mu L$), neutrophil count, lymphocyte count, NLR, (PLT, $\times 10^3/\mu L$), PLR, length of hospital stay, and treatment modality.

All laboratory measurements were obtained during the initial emergency department evaluation. Complete blood count parameters, including MPV, were analyzed using automated hematology analyzers routinely used at each participating center. Laboratory data were retrospectively extracted from electronic medical records.

Because CRP measurements were not consistently available in all patients because of the retrospective multicenter design, CRP was not included in the primary comparative analyses.

Statistical Analysis

All statistical analyses were performed using Python software (version 3.12) with the SciPy, NumPy, scikit-learn, and statsmodels libraries. The distribution of continuous variables was assessed using the Shapiro–Wilk test. Non-normally distributed variables were expressed as median and interquartile range (IQR) (Q1–Q3).

Continuous variables were compared using the Mann–Whitney U test, whereas categorical variables were analyzed using the Chi-square test or Fisher's exact test, as appropriate.

The association between MPV and AC was evaluated using univariable and pregnancy trimester-adjusted logistic regression analyses. Results were presented as odds ratios with 95% confidence intervals (CIs).

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the discriminative performance of MPV for AC. The area under the curve (AUC) and 95% CI were calculated using a bootstrap method with 2000 resamples. The optimal cut-off value was determined using the Youden index, and sensitivity and specificity were reported.

No formal sample size or power calculation was performed because all eligible patients meeting the inclusion criteria during the study period were included in the analysis.

A two-sided $p<0.05$ was considered statistically significant.

RESULTS

Patient Characteristics

A total of 112 pregnant patients were included in the study. Of these, 89 patients (79.5%) were classified as AC and 23 patients (20.5%) as NC.

The median age was 29.0 years (IQR: 25.0–34.0) in the AC group and 30.0 years (IQR: 25.5–32.5) in the NC group, with no significant difference between the groups (p=0.837). Pregnancy trimester distribution was also similar between the groups (p=0.286). In both groups, most patients were in the third trimester (AC: 48.3%; NC: 56.5%). Demographic and clinical characteristics are presented in Table 1.

The median length of hospital stay was 4.0 days (IQR: 3.0–7.0) in the AC group and 3.0 days (IQR: 2.0–5.5) in the NC group (p=0.087). Conservative medical treatment was the most common management approach in the AC group (n=73, 82.0%), followed by laparoscopic cholecystectomy (n=9, 10.1%), open cholecystectomy (n=5, 5.6%), and percutaneous drainage (n=2, 2.2%).

Inflammatory Laboratory Parameters

Comparisons of inflammatory laboratory parameters are presented in Table 2. No significant differences were observed between the AC and NC groups regarding WBC, neutrophil count, lymphocyte count, NLR, PLT, or PLR (all p>0.05).

MPV was the only hematological parameter that differed significantly between the groups. Median MPV was significantly higher in the AC group than in the NC group (10.6 fL [IQR: 9.8–11.3] vs. 10.3 fL [IQR: 8.3–10.8], p=0.034).

Additional exploratory analyses performed within the AC group demonstrated a moderate negative correlation between MPV and PLT (rho=−0.49, p<0.001). A weaker negative correlation was observed between MPV and PLR (rho=−0.33, p=0.002). No significant correlations were identified between MPV and other inflammatory parameters (Supplementary Table 1).

MPV values did not differ significantly between pregnancy trimesters in the AC group (p=0.551) (Supplementary Table 2).

Logistic Regression Analysis

In univariable logistic regression analysis, MPV was significantly associated with AC (OR: 1.734, 95% CI: 1.203–2.500, p=0.003). This association remained significant after adjustment for pregnancy trimester (OR: 1.870, 95% CI: 1.251–2.794, p=0.002).

No significant associations were observed for age, WBC, NLR, PLT, or PLR in either unadjusted or trimester-adjusted analyses. Logistic regression results are presented in Table 3.

Table 1. Demographic and clinical characteristics of study participants

Variable	Non-cholecystitis (n=23) (%)	Acute cholecystitis (n=89) (%)	p
Age (years) – median (IQR)	30.0 (25.5–32.5)	29.0 (25.0–34.0)	0.837
Gestational age (trimester)			0.286
1st trimester	2 (8.7)	21 (23.6)	—
2nd trimester	8 (34.8)	25 (28.1)	—
3rd trimester	13 (56.5)	43 (48.3)	—
Length of hospital stay (days) – Median (IQR)	3.0 (2.0–5.5)	4.0 (3.0–7.0)	0.087
Treatment (AC group), n (%)			—
Medical management	—	73 (82.0)	—
Laparoscopic cholecystectomy	—	9 (10.1)	—
Open cholecystectomy	—	5 (5.6)	—
Percutaneous drainage	—	2 (2.2)	—

IQR: Interquartile range; AC: Acute cholecystitis. Group comparisons were performed using Mann–Whitney U test for continuous variables and Chi-square or Fisher's exact test, where appropriate, for categorical variables. Treatment data are presented only for the acute cholecystitis group.

Table 2. Comparison of inflammatory laboratory parameters between groups

Parameter	Non-cholecystitis (n=23) median (IQR)	Acute cholecystitis (n=89) median (IQR)	p
WBC (×10³/μL)	10.7 (8.3–13.0)	10.7 (9.3–12.4)	0.513
Neutrophil (×10³/μL)	7.6 (6.1–9.9)	8.0 (6.6–9.6)	0.469
Lymphocyte (×10³/μL)	2.0 (1.5–2.5)	1.6 (1.3–2.2)	0.337
NLR	4.6 (3.0–5.6)	4.2 (3.2–7.1)	0.426
PLT (×10³/μL)	264.0 (225.4–288.0)	251.0 (222.0–311.0)	0.674
PLR	128.1 (104.6–170.5)	148.8 (115.4–200.5)	0.186
MPV (fL)	10.3 (8.3–10.8)	10.6 (9.8–11.3)	0.034*

Values are expressed as median (IQR). WBC: White blood cell count; NLR: Neutrophil-to-lymphocyte ratio; PLT: Platelet count; PLR: Platelet-to-lymphocyte ratio; MPV: Mean platelet volume; IQR: Interquartile range. Group comparisons were performed using Mann–Whitney U test. *p<0.05 indicates statistical significance.

Table 3. Logistic regression analysis of factors associated with acute cholecystitis

Variable	Univariable analysis OR (95% CI)	p	Trimester-adjusted Analysis OR (95% CI)	p
Age (years)	1.019 (0.937–1.109)	0.659	1.015 (0.933–1.103)	0.734
WBC (×103/μL)	1.064 (0.916–1.235)	0.417	1.081 (0.924–1.265)	0.330
NLR	1.110 (0.940–1.311)	0.219	1.131 (0.948–1.350)	0.172
PLT (×103/μL)	1.003 (0.996–1.010)	0.460	1.002 (0.995–1.009)	0.566
PLR	1.003 (0.996–1.010)	0.368	1.003 (0.996–1.010)	0.375
MPV (fL)	1.734 (1.203–2.500)	0.003*	1.870 (1.251–2.794)	0.002*

OR: Odds ratio; CI: Confidence interval; WBC: White blood cell count; NLR: Neutrophil-to-lymphocyte ratio; PLT: Platelet count; PLR: Platelet-to-lymphocyte ratio; MPV: Mean platelet volume. *p<0.05 indicates statistical significance.

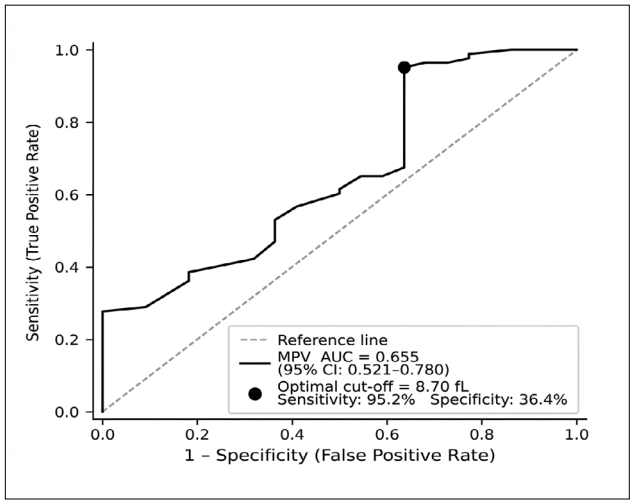


Figure 1. Receiver operating characteristic curve of mean platelet volume for acute cholecystitis in pregnancy (AUC=0.655; 95% CI: 0.521–0.780). The optimal cut-off value was 8.70 fL; at this threshold, sensitivity was 95.2% and specificity was 36.4%

ROC Analysis

ROC curve analysis was performed to evaluate the discriminative performance of MPV for AC (Fig. 1). The AUC was 0.655 (95% CI: 0.521–0.780).

The optimal cut-off value determined using the Youden index was 8.70 fL. At this threshold, sensitivity was 95.2%, specificity was 36.4%, positive predictive value was 85.3%, and negative predictive value was 57.1%.

DISCUSSION

In this retrospective multicenter cohort study, MPV was the only hematological parameter significantly associated with AC in pregnant patients presenting with right upper quadrant pain, and this association remained significant after adjustment for pregnancy trimester. In contrast, conventional inflammatory parameters including WBC, NLR, PLT, and PLR did not differ significantly between the groups. Although statistical significance was achieved, the absolute intergroup difference was modest (10.6 fL vs. 10.3 fL), and ROC analysis demonstrated limited discriminative performance (AUC: 0.655) with high sensitivity but low specificity at the identified cut-off value. Accordingly, MPV should not be used as an independent diagnostic marker in this population; rather, it may serve as a supportive parameter when interpreted together with clinical and ultrasonographic findings.

The evaluation of biliary disease during pregnancy may be challenging because of physiological and hematological changes associated with gestation.[3] Physiological leukocytosis and trimester-related variations in inflammatory markers may reduce the diagnostic value of conventional laboratory parameters in pregnant patients.[7-9] Previous studies have demonstrated that pregnancy-specific reference ranges may be necessary for inflammatory markers such as WBC and CRP.[8,20] In the present study, the absence of significant differences in traditional inflammatory parameters between groups likely reflects these pregnancy-related physiological changes. Ultrasonography remains the primary imaging modality in this population because of its safety and lack of ionizing radiation;[10,12,13] however, findings may occasionally be inconclusive, particularly in early-stage disease or nonspecific presentations. In this context, investigation of additional routine complete blood count-derived parameters that may complement clinical evaluation appears clinically reasonable.

MPV has been investigated as a potential inflammatory marker in several inflammatory and surgical diseases.[14] Larger platelets are considered metabolically and enzymatically more active and may contribute to increased platelet activation and proinflammatory mediator release.[15,21] In the present study, higher MPV levels in the AC group may suggest a role for platelet activation in the inflammatory process. Nevertheless, the biological behavior of MPV during acute inflammation remains complex and may be influenced by disease severity, platelet consumption dynamics, laboratory methodology, and patient characteristics.[14,17] However, a statistically significant association does not necessarily translate into sufficient clinical diagnostic utility, and the modest absolute difference observed in this study should be considered accordingly.

Previous studies evaluating MPV in AC have reported conflicting results. Sayit et al.[18] reported lower MPV values in AC, whereas Eroğlu et al.[17] suggested that MPV may be associated with inflammatory activity. More recent studies have also demonstrated heterogeneous findings regarding platelet indices in AC.[19,22] These discrepancies may reflect differences in study design, patient populations, disease severity, laboratory standardization, and comparator group selection. Unlike most prior studies using healthy volunteers as controls, the present study employed a symptomatic comparison group of pregnant patients with right upper quadrant pain who did not fulfill TG18 criteria for AC. This design better reflects real-world clinical practice, where the differential diagnosis frequently includes biliary colic and other biliary disorders. Notably, because the NC group consisted primarily of symptomatic patients with biliary colic rather than healthy controls, some biological overlap between groups was expected, which may partly explain the modest discriminative performance of MPV.

In addition, MPV values did not differ significantly across pregnancy trimesters within the AC group (p=0.551), suggesting that the observed association was not substantially confounded by gestational age. This consistency across trimesters may be considered a methodological strength of the present study. The trimester-adjusted logistic regression further confirmed this finding, with the association between MPV and AC remaining significant after adjustment (OR: 1.870, 95% CI: 1.251–2.794, p=0.002).

Several limitations should be acknowledged. The retrospec-

tive design may have introduced selection bias and limited control over confounding variables. The multicenter structure may have resulted in methodological heterogeneity, particularly regarding preanalytical variables known to influence MPV measurements, including anticoagulant exposure time, analyzer platform differences, and sample processing delays. The relatively small and imbalanced comparison groups may have limited statistical precision. CRP measurements were not consistently available because of the retrospective multicenter design and could not be incorporated into the primary analyses. These findings should therefore be interpreted within an exploratory rather than confirmatory framework.

Despite these limitations, this study provides one of the few multicenter evaluations of MPV in pregnant patients with suspected AC. The use of trimester-adjusted analyses and a symptomatic real-world comparator cohort enhances the clinical relevance of the findings. Larger prospective studies with standardized MPV measurement protocols and pregnancy-specific diagnostic frameworks are needed to better define the diagnostic role of MPV in this population.

CONCLUSION

In this retrospective multicenter exploratory cohort study, MPV was significantly associated with AC in pregnant patients presenting with right upper quadrant pain. However, its limited discriminative performance and low specificity suggest that MPV should not be used as an independent diagnostic marker. MPV may be considered a complementary parameter within a multimodal diagnostic approach incorporating clinical evaluation and ultrasonographic assessment. Larger prospective studies including standardized MPV measurements and pregnancy-specific clinical evaluation are needed to better define the diagnostic value of MPV in pregnant patients with suspected AC.

Ethics Committee Approval: This study was approved by the Ethics Committee of Etlik City Hospital (Date: 10.02.2026, Decision No: AEŞH-BADEK2-2026-095).

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ORİJİNAL ÇALIŞMA - *ÖZ*

Sağ üst kadran ağrısı olan gebe hastalarda ortalama trombosit hacmi ile akut kolesistit arasındaki ilişki: çok merkezli retrospektif kohort çalışması

AMAÇ: Gebelikte ortaya çıkan fizyolojik ve hematolojik değişiklikler, akut kolesistit (AK) şüphesi olan hastalarda geleneksel inflamatuvar belirteçlerin yorumlanmasını güçleştirebilir. Bu çalışmada, rutin tam kan sayımı analizinden elde edilen ortalama trombosit hacminin (MPV), sağ üst kadran ağrısıyla başvuran gebe hastalarda akut kolesistit ile ilişkisini değerlendirmek ve bu ilişkinin gebelik trimesterleri boyunca tutarlı olup olmadığını araştırmak amaçlandı.

GEREÇ VE YÖNTEM: Bu retrospektif çok merkezli kohort çalışmasına, 2022–2025 yılları arasında sağ üst kadran ağrısıyla başvuran 112 gebe hasta dahil edildi. Tokyo Kılavuzu 2018 (TG18) tanı kriterlerine göre hastalar akut kolesistit (AK, n=89) ve non-kolesistit (NK, n=23) olarak sınıflandırıldı. MPV ve diğer hematolojik parametreler gruplar arasında karşılaştırıldı. MPV ile akut kolesistit arasındaki ilişkiyi değerlendirmek amacıyla tek değişkenli ve gebelik trimesterine göre düzeltilmiş lojistik regresyon analizleri yapıldı. MPV'nin tanısal performansı ROC eğrisi analizi ile değerlendirildi.

BULGULAR: AK grubunda MPV düzeyi NK grubuna göre anlamlı olarak daha yüksekti (10.6 fL'ye karşı 10.3 fL, p=0.034). Tek değişkenli analizde MPV, akut kolesistit ile anlamlı ilişkili bulundu (OR: 1.734, %95 GA: 1.203–2.500; p=0.003) ve bu ilişki gebelik trimesterine göre düzeltme sonrasında da anlamlılığını korudu (OR: 1.870, %95 GA: 1.251–2.794; p=0.002). Beyaz küre sayısı, nötrofil/lenfosit oranı, trombosit sayısı ve trombosit/lenfosit oranı açısından anlamlı ilişki saptanmadı. ROC analizinde MPV'nin ayırt edici performansı sınırlı bulundu (EAA=0.655). Belirlenen 8.70 fL kesim değerinde duyarlılık %95.2, özgüllük %36.4 olarak hesaplandı.

SONUÇ: MPV, akut kolesistit şüphesi olan gebe hastalarda akut kolesistit ile anlamlı ilişkili bulunmuştur; ancak sınırlı ayırt edici performansı ve düşük özgüllüğü nedeniyle bağımsız bir tanı belirteci olarak kullanılmamalıdır. MPV, klinik değerlendirme ve ultrasonografik bulgular ile birlikte yorumlandığında destekleyici tanısal katkı sağlayabilir. Gebelikte akut kolesistitin tanısal değerlendirmesindeki rolünün daha iyi belirlenmesi için standartlaştırılmış MPV ölçümleri ve gebeliğe özgü tanısal yaklaşımlar içeren geniş ölçekli prospektif çalışmalara ihtiyaç vardır.

Anahtar sözcükler: Akut kolesistit; gebelik; enflamatuvar belirteçler; ortalama trombosit hacmi; sağ üst kadran ağrısı.

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Supplementary Table 1. Spearman correlation analysis between MPV and other inflammatory parameters in the acute cholecystitis group (n=89)

Parameter	Spearman's rho	p
PLT (Platelet count)	−0.49	<0.001
PLR (Platelet-to-lymphocyte ratio)	−0.33	0.002
NLR (Neutrophil-to-lymphocyte ratio)	−0.10	0.329
WBC (White blood cell count)	−0.10	0.330
Neutrophil count	−0.11	0.310
Lymphocyte count	−0.00	0.984
Length of hospital stay (days)	−0.03	0.720
Age (years)	0.04	0.672

MPV: Mean platelet volume; PLT: Platelet count; PLR: Platelet-to-lymphocyte ratio; NLR: Neutrophil-to-lymphocyte ratio; WBC: White blood cell count. Bold rows indicate statistically significant correlations (p<0.05).

Supplementary Table 2. MPV values by trimester in the acute cholecystitis group

Variable	1st trimester (n=21)	2nd trimester (n=25)	3rd trimester (n=43)	p
MPV (fL)-Median (IQR)	10.6 (9.6–11.3)	10.7(10.2–11.3)	10.5(9.7–11.3)	0.551
MPV (fL)-Mean±SD	10.6±1.6	10.8±1.1	10.5 ± 1.2	—
MPV (fL)-Min-Max	7.5–13.1	8.2–13.3	8.1–13.6	—

MPV: Mean platelet volume; SD: Standard deviation; IQR: İnterquartile range. The Kruskal–Wallis test was used for between-group comparisons. No statistically significant difference was observed across trimesters (p=0.551).

ORIGINAL ARTICLE

Pre-hospital fluid resuscitation and return of spontaneous circulation in earthquake victims with cardiac arrest during the first 24 hours after the 2023 Kahramanmaraş earthquakes: Implications for disaster risk management

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ABSTRACT

BACKGROUND: Earthquakes can cause crush injuries and post-extrication deaths. Hyperkalemia, metabolic acidosis, hypovolemia, and circulatory failure are key mechanisms of cardiac arrest in victims at risk of crush syndrome. Although intravenous fluid resuscitation is recommended in disaster care, evidence on resuscitation outcomes remains limited. This study evaluated earthquake victims with cardiac arrest during the first 24 h after the 2023 Kahramanmaraş earthquakes and examined the association between pre-hospital fluid resuscitation, admission metabolic parameters, and return of spontaneous circulation (ROSC).

METHODS: This single-center retrospective study was conducted in the emergency department of a tertiary hospital in Mersin, Türkiye. Adult earthquake victims admitted within the first 24 h who developed cardiac arrest before or after emergency department arrival were included. Patients with fatal head, thoracic, or abdominal injuries or missing data were excluded. Initial admission blood gas values were analyzed. The primary outcome was ROSC.

RESULTS: Thirty-seven patients were included. The mean age was 49.30±18.63 years, and 20 patients (54.1%) were female. Pre-hospital fluid resuscitation was administered to 25 patients (67.6%), with a mean volume of 1540±611 mL. Patients receiving fluids had higher pH and lower lactate, potassium, and base excess values. ROSC occurred in 10 patients (27.0%), all of whom had received fluids (p=0.010).

CONCLUSION: Pre-hospital fluid resuscitation was associated with a more favorable metabolic profile and higher ROSC rates in earthquake-related cardiac arrest. These findings support field-based fluid resuscitation and hyperkalemia management in disaster response planning; however, causality cannot be inferred.

Keywords: Cardiac arrest; crush syndrome; disaster risk management; earthquake; emergency medical services; fluid resuscitation; pre-hospital care; return of spontaneous circulation.

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INTRODUCTION

Türkiye is one of the most earthquake-prone countries because of its active tectonic structure. On February 6, 2023, two major earthquakes (Mw 7.7 and Mw 7.6) centered in Kahramanmaraş affected 11 provinces, causing tens of thousands of deaths and injuries and creating one of the largest disasters in the country's recent history.[1,2]

Among survivors rescued from collapsed buildings, crush syndrome is a major cause of early morbidity and mortality. Prolonged muscle compression followed by reperfusion results in rhabdomyolysis, leading to hyperkalemia, metabolic acidosis, hypovolemia, acute kidney injury, and circulatory failure. These metabolic disturbances are recognized causes of sudden cardiac arrest after extrication, often referred to as "rescue death."[3-7]

Current disaster medicine guidelines recommend establishing intravenous access and initiating isotonic fluid resuscitation as early as possible, preferably before or during extrication, to reduce the severity of crush syndrome and its complications.[7,8] However, clinical evidence evaluating the association between pre-hospital fluid resuscitation and resuscitation outcomes in earthquake victims remains limited.

Following the 2023 Kahramanmaraş earthquakes, many critically injured patients were transported to tertiary hospitals, including victims who experienced cardiac arrest before or shortly after hospital arrival. The present study aimed to evaluate adult earthquake victims who developed cardiac arrest within the first 24 h after the earthquakes and to investigate the association between pre-hospital fluid resuscitation, admission metabolic parameters, and return of spontaneous circulation (ROSC). The findings may also contribute to disaster medical response planning by providing evidence on the potential role of early field-based interventions in reducing preventable deaths after major earthquakes.

MATERIALS AND METHODS

Study Design and Setting

This was a single-center, retrospective observational study conducted in the emergency department of a tertiary training and research hospital. The hospital is the largest healthcare center in Mersin, with a capacity of 1440 beds, and actively provided care for earthquake victims after the February 6, 2023 earthquakes that affected 11 provinces.

The study was conducted in accordance with the principles for retrospective chart review studies in emergency medicine described by Kaji et al.[9]

Patient Selection

Between February 6 and February 17, 2023, a total of 7670 earthquake victims were admitted to the emergency department of our hospital. Of these patients, 7575 were transported by road, 74 by sea, and 21 by air. A total of 1983 patients were hospitalized, 389 were transferred to other hospitals, 874 underwent surgical procedures, and 148 died.

This study included adult earthquake victims aged 18 years or older who were admitted to the emergency department within the first 24 h after the earthquakes and who developed cardiac arrest either in the pre-hospital setting or after emergency department arrival. Patients without major fatal head, thoracic, or abdominal injuries were included. Patients brought by emergency medical services with ongoing cardiopulmonary resuscitation (CPR) and patients who developed cardiac arrest after arrival at the emergency department were evaluated.

Patients younger than 18 years, pregnant patients, patients with obvious severe head trauma, patients with pneumothorax or massive hemothorax detected by lung auscultation or radiological evaluation after ROSC, patients with free fluid on Focused Assessment with Sonography for Trauma, patients with fatal arterial injury, patients brought in cardiac arrest without documented emergency medical service intervention, patients who were already in cardiac arrest on arrival by private means, and patients with missing data were excluded.

Data Sources

Patients were identified by reviewing the hospital information system, emergency medical service case forms, and patient files. During the database search, the ICD code "X34" was used for earthquake victims, and the codes "I46," "I46.0," "I46.9," and "R09.2" were used for cardiac arrest.

Data Collection and Definitions

A standardized study data form was created to ensure systematic data collection and to identify cases with missing information. The following variables were recorded: Age, sex, pre-hospital cardiac arrest status, pre-hospital CPR history, pre-hospital resuscitation duration, pre-hospital fluid resuscitation status and amount, emergency department resuscitation status, emergency department resuscitation duration, emergency department fluid resuscitation status, and initial blood gas parameters.

The blood gas values used in the analysis were the first blood gas measurements obtained at the time of emergency department admission. The evaluated laboratory parameters included potassium, pH, base excess, and lactate.

Outcome Measures

The primary outcome of the study was ROSC, defined as ROSC after CPR. ROSC was accepted when spontaneous circulation was achieved either before emergency department arrival or during resuscitation in the emergency department.

Secondary outcomes included the relationship between pre-hospital fluid resuscitation and admission metabolic parameters, including pH, lactate, potassium, and base excess.

Statistical Analysis

Data were analyzed using Statistical Package for the Social

Table 1. Association between pre-hospital fluid resuscitation and in-hospital mortality among patients who underwent CPR

Parameter	In-hospital outcome		p
	Death	Survived	
No pre-hospital fluid resuscitation+CPR	12 (100.0)	0 (0.0)	0.036
Pre-hospital fluid resuscitation+CPR	17 (68.0)	8 (32.0)	

CPR: Cardiopulmonary resuscitation.

Sciences version 26.0. Descriptive data were presented as numbers, percentage, mean±standard deviation, median, minimum, and maximum values, as appropriate. The distribution of continuous variables was evaluated using the Kolmogorov–Smirnov test. Normally distributed continuous variables were expressed as mean±standard deviation and compared using the independent samples t-test. Categorical variables were analyzed using the Pearson Chi-square test or Fisher's exact test when expected cell counts were low. A $p<0.05$ was considered statistically significant.

Ethical Considerations

Ethics committee approval was obtained from the Toros University Scientific Research and Publication Ethics Committee before the study was conducted (decision no. 70; date: June 5, 2023). Because of the retrospective design of the study, the requirement for informed consent was waived. This study was conducted in accordance with the principles of the Declaration of Helsinki.

RESULTS

A total of 37 patients were included in the study. Of these, 20 patients were female (54.1%), and the mean age was 49.30±18.63 years. Twenty-five patients (67.6%) were transported to the emergency department by emergency medical services, whereas 12 patients (32.4%) presented by private means.

Cardiac arrest occurred in the pre-hospital setting in 14 patients (37.8%), all of whom received pre-hospital CPR by emergency medical service teams. CPR was initiated or continued in the emergency department in 34 patients (91.9%). Among the 14 patients who received pre-hospital CPR, resuscitation was continued in the emergency department in 11 patients, whereas 3 patients were delivered to the emergency department after ROSC in the pre-hospital.

The mean duration of pre-hospital CPR was 17.50±7.00 min, whereas the mean duration of in-hospital CPR was 22.71±10.41 min. When the total duration of pre-hospital and in-hospital CPR was considered, the overall mean CPR duration was 27.49±10.55 min.

The in-hospital mortality rate was 78.4% (n=29), whereas 21.6% of the patients (n=8) survived to hospital discharge (Table 1).

Initial blood gas values obtained at emergency department admission showed a mean pH of 6.96±0.16, mean lactate level of 10.55±2.75 mmol/L, mean base excess of −15.22±3.47, and mean potassium level of 6.56±0.69 mEq/L. Pre-hospital fluid resuscitation was administered to 25 patients (67.6%). The mean amount of fluid administered was 1540±611 mL (Table 2).

When laboratory values were compared according to pre-hospital fluid resuscitation status, patients who received fluid resuscitation had significantly higher pH values and significantly lower potassium, lactate, and base excess values than those who did not receive fluid resuscitation. The pH was higher in the fluid resuscitation group than in the non-fluid group (7.02±0.11 vs. 6.83±0.15, $p<0.001$). Lactate levels were lower in the fluid resuscitation group (9.84±2.62 vs. 12.04±2.48,

Table 2. Demographic, clinical, and laboratory characteristics of the study population

Parameter	Value
Age, years	49.30±18.63
Female sex	20 (54.1)
Mode of admission: EMS	25 (67.6)
Mode of admission: private means	12 (32.4)
Cardiac arrest location: pre-hospital	14 (37.8)
Cardiac arrest location: emergency department	23 (62.2)
Pre-hospital CPR	14 (37.8)
Pre-hospital CPR duration, min	18.46±6.25
Emergency department CPR	34 (91.9)
Emergency department CPR duration, min	22.71±10.41
Pre-hospital fluid resuscitation	25 (67.6)
Pre-hospital fluid volume, mL	1540±611
pH	6.96±0.16
Lactate, mmol/L	10.55±2.75
Potassium, mEq/L	6.56±0.69
Base excess	−15.22±3.47
ROSC achieved	10 (27.0)

Values are presented as mean±standard deviation or n (%). CPR: Cardiopulmonary resuscitation; EMS: Emergency medical services; ROSC: Return of spontaneous circulation.

Table 3. Admission laboratory parameters according to pre-hospital fluid resuscitation status

Laboratory parameter	Fluid resuscitation (n=25)	No fluid resuscitation (n=12)	p
pH	7.02±0.11	6.83±0.15	<0.001
Lactate, mmol/L	9.84±2.62	12.04±2.48	0.023
Potassium, mEq/L	6.39±0.44	6.93±0.97	0.020
Base excess	−13.72±2.31	−18.35±3.46	<0.001

Values are presented as mean±standard deviation. Independent samples t-test was used.

Table 4. Admission laboratory parameters according to return of spontaneous circulation

Laboratory parameter	ROSC achieved (n=10)	ROSC not achieved (n=27)	p
pH	7.09±0.12	6.91±0.14	0.001
Lactate, mmol/L	8.91±3.46	11.16±2.21	0.025
Potassium, mEq/L	6.32±0.58	6.66±0.72	0.196
Base excess	−13.03±2.61	−16.03±3.44	0.017

Values are presented as mean±standard deviation. Independent samples t-test was used. ROSC: Return of spontaneous circulation.

Table 5. Association between pre-hospital fluid resuscitation and return of spontaneous circulation

Pre-hospital fluid resuscitation	ROSC achieved	ROSC not achieved	p
Yes (n=25)	10 (40.0)	15 (60.0)	0.010
No (n=12)	0 (0.0)	12 (100.0)	

Values are presented as n (%). Fisher's exact test was used. ROSC: Return of spontaneous circulation.

p=0.023). Potassium levels were also lower in the fluid resuscitation group (6.39±0.44 vs. 6.93±0.97, p=0.020). Base excess values were lower negative in the fluid resuscitation group (−13.72±2.31 vs. −18.35±3.46, p<0.001) (Table 3).

ROSC was achieved in 10 patients. Patients with ROSC had significantly higher pH values than those without ROSC (7.09±0.12 vs. 6.91±0.14, p=0.001). Lactate levels were significantly lower in patients with ROSC (8.91±3.46 vs. 11.16±2.21, p=0.025). Base excess values were also lower negative in patients with ROSC (−13.03±2.61 vs. −16.03±3.44, p=0.017). Potassium levels did not differ significantly between patients with and without ROSC (6.32±0.58 vs. 6.66±0.72, p=0.196) (Table 4).

Among patients who received pre-hospital fluid resuscitation, ROSC was achieved in 10 patients (40.0%). In contrast, ROSC was not achieved in any patient who did not receive pre-hospital fluid resuscitation (p=0.010) (Table 5).

DISCUSSION

In this study, we evaluated earthquake victims who developed cardiac arrest during the first 24 h after the February 6, 2023 Kahramanmaraş earthquakes, one of the most destructive recent disasters in Türkiye.[1,2] The main finding was that pre-hospital fluid resuscitation was associated with a more favorable metabolic profile at emergency department admission and a higher rate of ROSC. Patients who received pre-hospital fluid resuscitation had higher pH values and lower lactate, potassium, and base excess values. In addition, ROSC was achieved only among patients who had received pre-hospital fluid resuscitation.

Deaths after earthquakes are generally evaluated in two phases. In the first phase, traumatic injuries caused by building collapse are the leading cause of death. In the second phase, particularly after extrication, crush syndrome becomes a major contributor to morbidity and mortality. Prolonged muscle compression followed by reperfusion may cause potassium, myoglobin, phosphate, and other intracellular contents to enter the systemic circulation, resulting in hyperkalemia, severe metabolic acidosis, hypovolemia, acute kidney injury, circulatory failure, and sudden cardiac arrest.[3,6,7]

Our findings support the clinical importance of early fluid re-

suscitation in earthquake victims at risk of crush syndrome. International recommendations for mass-disaster crush injury management emphasize that intravenous isotonic fluid administration should be initiated as early as possible, preferably before or during extrication, and continued during transport when feasible.[7] In the present study, patients who received pre-hospital fluid resuscitation had lower potassium levels and lower severity of metabolic acidosis at emergency department admission. Although the retrospective design does not allow a causal conclusion, these findings suggest that early volume replacement may be associated with attenuation of severe metabolic disturbances after extrication and reperfusion.

The relationship between metabolic parameters and resuscitation outcomes was also clinically meaningful. Patients with ROSC had higher pH values and lower lactate and base excess values than patients without ROSC. This finding suggests that the severity of tissue hypoperfusion and metabolic acidosis may be closely related to resuscitation success in earthquake-related cardiac arrest. ROSC is widely used as an immediate outcome measure in standardized cardiac arrest reporting, supporting its use as the primary endpoint in the present disaster cohort.[10] In contrast, potassium levels did not differ significantly between patients with and without ROSC. This may be explained by the limited sample size, the presence of advanced hyperkalemia in both groups, or the multifactorial pathophysiology of cardiac arrest in earthquake victims.

One of the most notable findings of the present study was that ROSC was not achieved in any patient who did not receive pre-hospital fluid resuscitation. This result should be interpreted cautiously because patients who received fluids may have had earlier access to emergency medical services, more complete pre-hospital care, shorter untreated intervals, or a more favorable injury profile. Such sources of selection bias and incomplete documentation are particularly relevant in retrospective emergency medicine chart-review studies.[9] Nevertheless, the finding highlights the potential importance of initiating treatment as early as possible in the disaster field.

The present findings are consistent with previous reports from major earthquakes, particularly the 1999 Marmara earthquake, where crush syndrome and hyperkalemia were identified as leading causes of preventable early deaths after extrication. Sever and colleagues demonstrated that early intravenous fluid administration was one of the most effective interventions to reduce the severity of crush syndrome and acute kidney injury in earthquake victims. These observations established the basis for current recommendations advocating fluid resuscitation before or immediately after extrication whenever possible.[11]

Similar observations were reported following the 2020 İzmir earthquake, where early recognition of crush-related metabolic disturbances and prompt supportive treatment were emphasized to improve patient outcomes. Although the number of patients with cardiac arrest in our study was limited, the association between pre-hospital fluid resuscitation, improved admission metabolic parameters, and successful ROSC supports these previous clinical observations.[12]

Rescue death remains one of the most critical and potentially preventable complications following prolonged entrapment. The sudden release of potassium, acids, and other intracellular contents after extrication may precipitate fatal arrhythmias and circulatory collapse. Our findings reinforce the concept that early pre-hospital fluid resuscitation may mitigate these metabolic disturbances and improve the likelihood of successful resuscitation. While causality cannot be inferred from this retrospective study, the results provide additional clinical evidence supporting early field-based fluid administration as an essential component of crush syndrome management.

Limitations

This study has several limitations. First, it was a single-center retrospective study with a limited sample size. Therefore, selection bias could not be fully excluded, and the statistical power of the study was limited. The small number of patients also prevented robust multivariable analysis to adjust for potential confounders.

Second, the study was conducted under extraordinary disaster conditions. During the 1st h after the earthquakes, the emergency department received a very high number of earthquake victims, and healthcare teams were working under mass-casualty conditions. As a result, some pre-hospital and emergency department records may have been incomplete, non-standardized, or less detailed than records obtained under routine clinical conditions. This limitation is inherent to retrospective studies conducted after large-scale disasters.

Third, several clinically important variables could not be evaluated reliably because of incomplete documentation. These included the exact duration of entrapment under rubble, the time from extrication to emergency department admission, the time from cardiac arrest to initiation of CPR, initial cardiac rhythm, transport duration, the exact timing of fluid initiation, fluid type and infusion rate, total pre-hospital medication use, and the severity and anatomical extent of crush injury. These factors may have influenced both metabolic parameters and resuscitation outcomes.

Fourth, although the blood gas values analyzed in this study were the first measurements obtained at emergency department admission, the exact relationship between blood gas sampling, ongoing CPR, and ROSC could not be standardized in all cases. Therefore, the laboratory parameters should be interpreted as admission metabolic status rather than as strictly pre-treatment values.

Fifth, patients who received pre-hospital fluid resuscitation may have differed systematically from those who did not receive fluids. For example, these patients may have had earlier

contact with emergency medical services, better vascular access, shorter transport times, or less severe traumatic injuries. Therefore, the observed association between fluid resuscitation and ROSC should not be interpreted as definitive evidence of causality.

Finally, long-term outcomes such as survival to hospital discharge, neurological status, renal replacement therapy requirement, and late mortality could not be evaluated within the scope of the available dataset. Future multicenter studies with standardized pre-hospital data collection and longer follow-up are needed to confirm these findings and define optimal field treatment protocols.

In our study, data regarding the interval between the onset of pre-hospital cardiac arrest and the initiation of CPR were not available. In addition, information on amputations and the anatomical distribution of injuries was not consistently documented in the medical records because of the extraordinary conditions during the disaster response and, therefore, could not be analyzed.

Despite these limitations, this study has several important strengths. It presents original clinical data from earthquake victims with cardiac arrest during the first 24 h after one of the largest disasters in recent history, a patient population for which published evidence remains extremely limited. The study integrates pre-hospital interventions, admission metabolic parameters, and resuscitation outcomes, providing clinically relevant insights into the management of crush syndrome under real-world disaster conditions. Furthermore, the observed association between pre-hospital fluid resuscitation and successful ROSC highlights the potential value of early field-based interventions and offers practical information for disaster preparedness, emergency medical services, and future disaster response planning.

CONCLUSION

Pre-hospital fluid resuscitation was associated with more favorable metabolic status on emergency department admission and a higher likelihood of ROSC among adult earthquake victims with cardiac arrest during the first 24 h after the 2023 Kahramanmaraş earthquakes. Although causality cannot be established because of the retrospective design and limited sample size, these findings reinforce the importance of early recognition and treatment of crush syndrome in the pre-hospital setting.

Disaster preparedness and response protocols should prioritize rapid intravenous access, early isotonic fluid resuscitation, timely management of hyperkalemia, and field-based stabilization before transport whenever feasible. Strengthening the capacity of emergency medical services, mobile advanced treatment units, and forward medical posts to provide these interventions may reduce preventable deaths following major earthquakes. Future prospective multicenter studies with standardized pre-hospital data collection are needed to validate these findings and define evidence-based protocols for the management of earthquake-related cardiac arrest.

Ethics Committee Approval: This study was approved by the Toros University Scientific Research and Publication Ethics Committee (Date: 05.06.2023, Decision No: 70).

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ORİJİNAL ÇALIŞMA - *ÖZ*

2023 Kahramanmaraş depremlerinden sonraki ilk 24 saatte kardiyak arrest gelişen depremzedelerde hastane öncesi sıvı resüsitasyonu ile spontan dolaşımın geri dönüşü arasındaki ilişki

AMAÇ: Depremler, ezilme yaralanmalarına ve enkazdan çıkarılma sonrası erken ölümlere neden olabilir. Hiperpotasemi, metabolik asidoz, hipovolemi ve dolaşım yetmezliği, crush sendromu riski taşıyan depremzedelerde kardiyak arrestin temel mekanizmalarıdır. Afet bakımı kapsamında intravenöz sıvı resüsitasyonu önerilmesine rağmen, bunun resüsitasyon sonuçlarıyla ilişkisine dair klinik kanıtlar sınırlıdır. Bu çalışmada, 2023 Kahramanmaraş depremlerinden sonraki ilk 24 saat içinde kardiyak arrest gelişen depremzedeler değerlendirildi ve hastane öncesi sıvı resüsitasyonu, başvuru anındaki metabolik parametreler ve spontan dolaşımın geri dönüşü arasındaki ilişki incelendi.

GEREÇ VE YÖNTEM: Bu tek merkezli retrospektif çalışma, Türkiye'nin Mersin ilindeki üçüncü basamak bir hastanenin acil servisinde yürütüldü. Depremlerden sonraki ilk 24 saat içinde başvuran ve hastane öncesinde veya acil servis başvurusu sonrasında kardiyak arrest gelişen erişkin depremzedeler çalışmaya dahil edildi. Ölümcül kafa, toraks veya batın yaralanması olan hastalar ile verileri eksik olan hastalar çalışma dışı bırakıldı. Başvuru anında alınan ilk kan gazı değerleri analiz edildi. Primer sonlanım spontan dolaşımın geri dönüşü olarak belirlendi.

BULGULAR: Çalışmaya 37 hasta dahil edildi. Ortalama yaş 49.30±18.63 yıl olup, 20 hasta (%54.1) kadındı. Hastane öncesi sıvı resüsitasyonu 25 hastaya (%67.6) uygulanmıştı ve ortalama verilen sıvı miktarı 1540±611 mL idi. Sıvı uygulanan hastalarda pH daha yüksek; laktat, potasyum ve baz açığı değerleri daha düşüktü. Spontan dolaşımın geri dönüşü 10 hastada (%27.0) sağlandı ve bu hastaların tamamına hastane öncesi sıvı verilmişti (p=0.010).

SONUÇ: Depreme bağlı kardiyak arrest olgularında hastane öncesi sıvı resüsitasyonu, daha olumlu bir metabolik profil ve daha yüksek spontan dolaşımın geri dönüşü oranları ile ilişkiliydi. Bu bulgular, afet yanıt planlamasında sahada sıvı resüsitasyonu ve hiperpotasemi yönetiminin önemini desteklemektedir; ancak nedensellik çıkarımı yapılamaz.

Anahtar sözcükler: Acil sağlık hizmetleri; afet risk yönetimi; deprem; ezilme sendromu; hastane öncesi bakım; kardiyak arrest; sıvı resüsitasyonu; spontan dolaşımın geri dönmesi.

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ORIGINAL ARTICLE

Forensic analysis of medical malpractice claims in major joint dislocations: retrospective analysis of 64 cases

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ABSTRACT

BACKGROUND: The objective of this study was to examine the characteristics of medical malpractice claims related to major joint dislocation cases.

METHODS: Our database was used in the study to analyze major dislocation cases involving medical malpractice that were closed between 2018 and 2024. A complete and detailed dataset was collected for each case. This included information such as patients' demographics (age and sex), the specific anatomical location of the dislocation (ankle, knee, hip, wrist, elbow, shoulder, and acromioclavicular joint), the underlying cause of the dislocation, rationales for the claim, complications, and unique characteristics of each case.

RESULTS: This retrospective study analyzed 64 cases of major joint dislocation referred to the Council of Forensic Medicine between 2018 and 2024. The mean age of patients was 30.21±15.3 years, with 60.9% being male and 39.1% being female. Upper extremity dislocations accounted for 78.1% of cases, with the elbow being the most common site. Patients were treated at university hospitals (12.5%), education and research hospitals (57.8%), and private hospitals (29.7%). Complications were observed in 46 patients (71.8%), with restricted joint mobility being the most common complication. The most prevalent complaint was delayed diagnosis (37.5%), followed by inappropriate postoperative management and negligence. The board deemed 35.9% of cases as malpractice, with a significant association between conservative treatment and malpractice. In 22 cases with malpractice rulings, the physician was deemed culpable, whereas in one case, malpractice was assigned to a healthcare worker.

CONCLUSION: The primary causes of malpractice claims in major joint dislocation cases were delayed diagnosis and inadequate postoperative care. Conservative treatment was associated with high rates of medical malpractice. To reduce the risk of medical malpractice, it is necessary to standardize early diagnosis methods and ensure comprehensive postoperative follow-up.

Keywords: Emergency orthopedics; joint dislocation; malpractice; shoulder; upper extremity.

INTRODUCTION

Large joint dislocations frequently occur in emergency orthopaedics, often arising in conjunction with other injuries.[1] In cases of significant joint dislocation, early intervention is paramount, as there is potential for concomitant damage to blood vessels and nerves.[2] Although their frequency varies according to joint type, age group, and mechanism of trauma, major joint dislocations (of the shoulder, elbow, hip, and knee) are relatively common among orthopaedic emergen-

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cies. Major joint dislocations are most prevalent in the shoulder joint among adults, constituting approximately 50–60% of all such dislocations, with an annual incidence ranging from 17 to 25 cases per 100,000 individuals.[3] However, other major joint dislocations are also frequently observed in orthopaedic emergencies and may result in significant morbidity and mortality.[4]

Trauma surgery is widely regarded as a specialized field that is susceptible to a high incidence of legal action, largely attributable to the potential for complications arising from both the diagnostic process and therapeutic interventions.[5] Emergency orthopaedic procedures represent a clinical area in which the risk of malpractice is high.[6] This is due to the need for rapid decision-making and the critical importance of time. Conditions such as traumatic fractures, major joint dislocations, open wounds, and compartment syndrome can result in permanent disability or death if diagnosis is delayed or intervention is inadequate.[7] Previous studies have reported cases of malpractice in orthopaedic procedures involving bone fractures.[8] However, research in this area remains limited, and no studies have examined malpractice cases involving major joint dislocations, which are considered orthopaedic emergencies.

The present study examined malpractice cases involving major joint dislocations in emergency orthopaedics based on the following factors: case characteristics, hospital type (public or private), affected anatomical region, clinical outcomes, and final forensic medical decisions (confirmation or denial of malpractice).

MATERIALS AND METHODS

This study utilized a retrospective analysis to examine cases of patients referred to the 7th Specialized Board of Forensic Medicine for the assessment of malpractice claims between 2018 and 2024 following a diagnosis of major joint dislocation in the orthopaedic emergency department. In order to accomplish this objective, the National Judicial Network Information System (UYAP) was utilized. This is the data entry platform of the Institute of Forensic Medicine and a resource employed by all entities within the justice system and the courts. Through its use, a thorough analysis of all medical malpractice cases involving closed traumatic dislocations of major joints was performed. As the data utilized in this study were entirely anonymized, no further agreement was necessary from either the defendant or the claimant. The study was approved by the Ethics Committee of İstanbul University, İstanbul Faculty of Medicine (Date: 24.04.2026, Decision No: 2026/861).

A database was utilized as a repository for a vast array of court records on cases submitted to courts or arbitration by judges and attorneys. To facilitate further in-depth investigation, each case in our database incorporated detailed summaries, court documents (including expert witness reports), and details about the plaintiffs and defendants. In most cases, radiological images were available as references. Following approval by the Scientific Board of the Council of Forensic Medicine (Date: 18.02.2025, Decision No: 2025/158), the malpractice specialization committee in our country utilized our database to investigate medical malpractice cases.

The inclusion criteria were major joint dislocation, traumatic origin, age >12 months, and complete available data. The exclusion criteria included open fracture–traumatic dislocation and missing data. Within the UYAP system, joint dislocation-related inquiries were conducted, and the resulting data were subsequently filtered using the joint dislocation criteria. A subsequent search was performed using the following keywords: "fracture-dislocation of large joint," "joint dislocation," "shoulder dislocation," "knee joint dislocation," "hip dislocation," "ankle joint dislocation," "elbow joint dislocation," "wrist dislocation," "acromioclavicular joint dislocation," and "acute large joint dislocation."

Following the legal proceedings, the relevant section of the Institute of Forensic Medicine was required to undertake a detailed examination of each case. This included information such as patient demographics (age and sex), the specific anatomical location of the dislocation (ankle, knee, hip, wrist, elbow, shoulder, and acromioclavicular), the underlying cause of the dislocation, rationales for the claim, complications, and the unique characteristics of each case. The cases examined for major joint dislocation injuries were categorized as follows: joint dislocation alone, dislocation with fracture, soft tissue injury, vascular injury, and nerve injury.

Healthcare services in this country are predominantly provided by two sectors: public and private hospitals. Patients receiving treatment at state hospitals are not subject to financial responsibilities; however, those receiving treatment at private hospitals must pay the associated expenses themselves. Public hospitals can be further classified as institutions dedicated to research and education or those affiliated with universities. The duration of hospital stay, need for surgical intervention, and interval between trauma and surgery were determined through a review of medical records.

The mechanisms of major joint dislocations were categorized into four groups: traffic accidents, work accidents, falls, and spontaneous dislocations. Traffic accidents were further categorized into three groups: accidents occurring outside the vehicle, accidents occurring inside the vehicle, and motor vehicle accidents. In cases involving injuries sustained during traffic accidents inside a vehicle, patients were categorized as drivers, front passengers, or rear passengers.

Treatment was classified as either conservative or surgical. The specialties subject to malpractice claims included orthopaedic surgeons, nurses, and healthcare personnel. The professional seniority of physicians facing allegations of medical malpractice was categorized as follows: professor/associate professor, attending surgeon, senior resident, and junior resident. In this study, additional injuries sustained by the patient

Table 1. Demographic data of patients with joint dislocation

n=64	Patients with Joint Dislocation	
	Mean±SD	Min-Max
Age, years	30.21±15.3	16 months-65 years
Gender, Female/Male	25 / 39	
Dislocation joint		
Acromioclavicular, n	2	
Shoulder, n	21	
Elbow, n	24	
Wrist, n	3	
Hip, n	4	
Knee, n	6	
Ankle, n	4	
Additional injury		
Isolated dislocation	25 (39.1%)	
Fracture dislocation	28 (43.8%)	
Soft tissue injury	5 (7.8%)	
Nerve injury	3 (4.7%)	
Vascular injury	3 (4.7%)	
Mechanism of dislocation		
Traffic accident	9 (14.1%)	
Work accident	2 (3.1%)	
Fall	47 (73.4%)	
Spontaneous	6 (9.4%)	
Malpractice litigation against		
Medical Doctor	62 (96.9%)	
Healthcare professional	2 (3.1%)	
Treatment		
Conservative	27 (42.2%)	
Surgery	37 (57.8%)	
Degree of seniority of doctors		
Professor-Associate professor	8 (12.5%)	
Attending surgeon	53 (82.8%)	
Senior resident doctor	3 /4.7%)	
Junior resident doctor	-	
Hospital		
University Hospital	8 (12.5%)	
Education-Research Hospital	37 (57.8%)	
Private Hospital	19 (29.7%)	
Complication, Yes/No	46/18	

cohort were also evaluated. The following types of complications were examined: delayed or failed diagnosis, negligence, surgical error, excessive or inappropriate surgery, inadequate surgery, postoperative management errors, and healthcare system errors.

Statistical Analyses

Statistical analysis was conducted using the IBM Statistical Package for Social Sciences Statistics for Windows version 29.0 (IBM Corp., Armonk, NY, USA). Dispersion parameters (mean or median, standard deviation, minimum, and maximum) were used for quantitative data in descriptive analyses, whereas percentages were used for qualitative data. For quantitative data with a normal distribution, the Student's t-test was used for comparisons. Qualitative variables were compared using Pearson's chi-square test, Fisher's exact test, and the Fisher–Freeman–Halton test. The threshold for statistical significance was set at $p<0.05$.

RESULTS

A total of 64 medical malpractice claims pertaining to cases of large joint dislocations were documented. The mean age was 30.21±15.3 years (range, 16 months–65 years), with 39 (60.9%) subjects identified as male and 25 (39.1%) as female. The analysis revealed that 78.1% of joint dislocations occurred in the upper extremities. The distribution of acromioclavicular, shoulder, elbow, and wrist joint dislocations was as follows: 2, 21, 24, and 3 cases, respectively. In the lower extremities, four cases were identified in the hip joint, six in the knee joint, and four in the ankle joint (Fig. 1). The demographic data of the patients are presented in Table 1.

Of the patients, 12.5% received treatment at a university hospital, 57.8% at an education and research hospital, and 29.7% at private hospitals. Complications were observed in 46 patients (71.8%), most of whom had restricted joint mobility. The most prevalent complaint was delayed diagnosis, accounting for 37.5% of cases. This was followed by inappropriate postoperative management and negligence. The distribution of the complaints is shown in Table 2.

A total of 23 cases (35.9%) were deemed instances of mal-

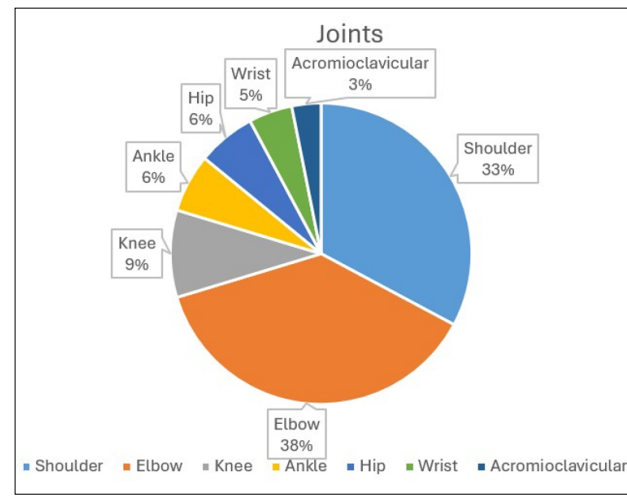


Figure 1. The visual representation of the data illustrates the location of the major joint dislocation.

Table 2. The main reasons for medical malpractice claims that come about after a joint dislocation

Reason for litigation	Total defendant (n=64)
Delay in diagnosis/Failure to diagnosis	24 (37.5%)
Negligence	12 (18.8%)
Surgical error	11 (17.2%)
Excessive or inappropriate treatment	2 (3.1%)
Inadequate surgery	2 (3.1%)
Inappropriate postoperative management	13 (20.3%)

practice by the board. Patients with and without malpractice were compared in Table 3. A detailed examination of the data revealed no statistically significant differences between the parameters examined in cases where malpractice was detected and those where it was not, with the exception of the treatment method. Cases in which malpractice was detected were treated conservatively. Among the 23 malpractice cases, 13 involved delayed diagnosis, four involved negligence, one involved surgical error, and five involved inappropriate postoperative management. Following a thorough examination of the 23 malpractice cases, it was determined that 22 involved medical doctors and one involved a healthcare professional.

Table 3. Comparison of clinical characteristics between cases with malpractice and without malpractice

	Cases with no malpractice (n: 41)		Cases with identified malpractice (n: 23)		
	Mean±SD	Min–Max	Mean±SD	Min–Max	p
Age, years	29.3±14.2	16 months – 54	31.6±17.3	4–65	0.597
Gender, Male/Female	25/16		14/9		0.993
Joints					
Acromioclavicular	2		0		0.927
Shoulder	14		7		
Elbow	15		9		
Wrist	2		1		
Hip	2		2		
Knee	4		2		
Ankle	2		2		
Hospital					
University	5		3		0.987
Education-research	24		13		
Private	12		7		
Trauma					
Traffic accident	7		2		
Work accident	2		0		0.291
Fall	27		20		
Spontaneous	5		1		
Degree of seniority of doctors					
Professor-Associate professor	5		3		
Attending surgeon	35		18		0.515
Senior resident doctor	1		2		
Junior resident doctor	-				
Treatment, Conservative/Surgery	12/29		15/8		0.005*
Complication Yes/No	27/14		19/4		0.153

DISCUSSION

In orthopaedic traumatology, a subspecialty of trauma, incidences of medical negligence are frequently documented, typically arising from patients sustaining high-energy injuries, technical inadequacies in emergency departments, or inadequate emergency care. A considerable body of research has been conducted on this subject, revealing that allegations of medical malpractice in trauma surgery predominantly pertain to diagnostic errors, inadequate surgical planning, and insufficient postoperative care.[8] Of the 10,900 claims received by the NHS in 2023–2024, orthopaedic surgery accounted for 10.8%, establishing it as one of the most frequently involved specialties. This figure represents a 12% decline compared with the rate recorded during 2019–2020.[9,10] However, trauma departments remain among the settings where malpractice cases are most likely to occur due to the high workload and fatigue among healthcare workers. The severity of damage is not directly correlated with the probability of litigation in the emergency department. It is evident that cases involving relatively mild permanent and partial disabilities are more likely to result in legal action. Agout et al.[11] reported that, following a 10-year archive review, 51,582 surgical procedures were performed, of which only 71 resulted in malpractice lawsuits. Of the 71 cases reported in that study, 52.1% were categorized as trauma surgery cases. Over a period of seven years, an evaluation of trauma cases within the Council of Forensic Medicine was conducted, resulting in the identification of 64 instances that led to malpractice lawsuits attributable to joint dislocation.

The most frequent allegations in malpractice cases pertaining to orthopaedic trauma are reported to originate from delayed diagnosis, surgical technique errors, and inadequate management of postoperative complications. Gathen et al.[12] conducted an extensive review of 230 cases in a study performed between 2000 and 2017. The researchers meticulously examined the legal database in their country to collect the data necessary for the study. Furthermore, a significant proportion of the plaintiffs in these 230 cases were female, constituting 56.8% of the total. The mean age of the plaintiffs was 44.6 years, with a standard deviation of±20.1 years. The complaints alleged that misdiagnosis (22.6%), inadequate nursing care (8.3%), and improper management (46.1%) were the primary causes. Ahmed et al.[8] evaluated 201 cases of fractures. The mean age of participants was 41 years. The study revealed that 64 cases (31.8%) involved diagnostic errors and 57 cases (28.4%) exhibited delays. Furthermore, an alleged treatment error was identified in 177 cases (88.1%). Cichos et al.[13] conducted a retrospective study on medical malpractice litigation involving orthopaedic surgeons between 1988 and 2013. In that study, over the course of 26 years, orthopaedic surgeons were the subject of 1,562 malpractice cases, 462 of which were reported to have been successful for plaintiffs. The most commonly litigated procedures were fracture fixation (363 cases), arthroplasty (290 cases), and spine surgery (231 cases); plaintiffs had the highest success rates with fasciotomy (48%), infection therapy (43%), and carpal tunnel release (37%). As demonstrated in that study, the highest average compensation amounts granted to plaintiffs were observed in the fields of paediatrics, spine surgery, and oncology. In our study, the most prevalent complaint was delayed diagnosis, accounting for 37.5% of cases. This was followed by inappropriate postoperative management and negligence.

The proportion of medical malpractice claims that result in favorable outcomes for defendants varies significantly.[14-16] Gidwani et al.[15] obtained data on 97 of 130 cases of alleged medical malpractice brought before the court system between 2004 and 2006. Interestingly, none of these patients proceeded to trial. A total of 55% of cases were withdrawn by the plaintiffs' attorneys, while the remaining 45% were settled out of court. This indicates that no cases were decided in favor of the defendant. Arif et al.[17] evaluated orthopaedic surgeons and non-orthopaedic practitioners involved in medical negligence lawsuits in 358 cases of acute compartment syndrome. In that study, settlements were reached in 67 cases (19%), the defendant was found to be at fault in 203 cases (57%), and the plaintiff was found to be at fault in 88 cases (25%). Furthermore, orthopaedic doctors were substantially more likely than non-orthopaedic physicians to be involved in cases where ACS resulted from fractures or surgery, as well as when the claim was based on alleged incorrect bracing or casting. In our study, malpractice was confirmed by the board in 35.9% of cases.

The length of a physician's professional tenure substantially affects the probability of facing malpractice claims. Empirical evidence suggests that cumulative risk increases with the duration of a physician's career, indicating that the likelihood of a doctor encountering litigation by the age of 65 increases to 75% in low-risk specialties and may approach 99% in high-risk specialties. In high-risk specialties, the probability of incurring damages rises from 33% at age 45 to 71% at age 65. This trend also applies to the risk of incurring damages.[18] The association between the duration of physicians' practice and malpractice claims is evaluated within the framework of defensive medical practices and the determination of legal liability, rather than merely the frequency of claims. Research suggests that physicians with less experience are more inclined to engage in defensive practices, such as ordering unnecessary tests or avoiding high-risk patients, to mitigate liability risks.[19] Conversely, this tendency diminishes as physicians gain greater expertise. When evaluating a physician's negligence in a malpractice claim, subjective factors such as experience, education, and skill level are considered. This suggests that the expected standards of care for more experienced physicians may differ from those applicable to newly qualified physicians. In our cohort of 64 cases, an analysis comparing instances of identified malpractice (n=23) with those without malpractice (n=41) in relation to physician seniority revealed

no statistically significant difference in malpractice incidence among professors/associate professors, specialist doctors, and junior doctors (p=0.515). This finding suggests that physician seniority does not independently influence the risk of medical malpractice.

Our study had several limitations. A notable limitation of this study is its retrospective nature, as it was based on the examination of existing case files. The absence of the ratio of malpractice cases related to joint dislocations to all emergency malpractice cases represents a significant limitation. A further limitation is the heterogeneity of the treatment modalities used for patients.

CONCLUSION

The present study evaluated major joint dislocations, which are common in orthopaedic emergencies and associated with a high risk of malpractice claims. The data indicate that upper-extremity dislocations accounted for 78.1% of cases, with the elbow being the most common site of dislocation. The most prevalent complaint was delayed diagnosis, followed by inappropriate postoperative management. In 35.9% of cases, malpractice was confirmed, and conservative treatment was associated with a higher risk.

Ethics Committee Approval: This study was approved by Forensic Medicine Institution Scientific Board (Date: 18.02.2025, Decision No: 2025/158).

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Informed Consent: Retrospective study.

Conflict of Interest: None declared.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Büyük eklem çıkıklarında tıbbi malpraktis davalarının adli analizi: 64 olgunun geriye dönük analizi

AMAÇ: Bu çalışmanın amacı, büyük eklem çıkığı olgularıyla ilgili tıbbi malpraktis davalarının özelliklerini incelemektir.
GEREÇ VE YÖNTEM: Çalışmada, 2018 ile 2024 yılları arasında sonuçlanan tıbbi malpraktis içeren büyük eklem çıkığı olgularını analiz etmek üzere veri tabanımız kullanılmıştır. Her olgu için eksiksiz ve ayrıntılı bir veri seti toplanmıştır. Bu veriler arasında hastaların demografik bilgileri (yaş ve cinsiyet), çıkığın anatomik konumu (ayak bileği, diz, kalça, el bileği, dirsek, omuz ve akromiyoklavikular eklem), çıkığın altta yatan nedeni, talebin gerekçeleri, olası komplikasyonlar ve her olgunun kendine özgü özellikleri yer almaktadır.
BULGULAR: Bu retrospektif çalışmada, 2018 ile 2024 yılları arasında Adli Tıp Kurumu'na sevk edilen 64 büyük eklem çıkığı olgusu analiz edildi. Hastaların ortalama yaşı 30.21±15.3 yıl idi ve %60.9'u erkek, %39.1'i kadın idi. Üst ekstremite çıkıkları olguların %78.1'ini oluşturuyordu ve en sık görülen bölge dirsek idi. Hastalar üniversite hastanelerinde (%12.5), eğitim ve araştırma hastanelerinde (%57.8) ve özel hastanelerde (%29.7) tedavi görmüştü. Kırkaltı hastada (%71.8) komplikasyon gözlendi ve en sık görülen komplikasyon eklem hareket kısıtlılığıydı. En yaygın şikayet gecikmiş tanı (%37.5) idi; bunu uygun olmayan postoperatif yönetim ve ihmal izledi. Kurul, olguların %35.9'unu malpraktis olarak değerlendirdi ve konservatif tedavi ile malpraktis arasında anlamlı bir ilişki olduğunu belirledi. Yirmi iki olguda tıbbi malpraktis kararında hekim suçlu bulunurken, bir olguda ise malpraktis bir sağlık çalışanına atfedildi.
SONUÇ: Büyük eklem çıkığı olgularında malpraktis davalarının başlıca nedenleri geç teşhis ve yetersiz ameliyat sonrası bakımdı. Konservatif tedavi, yüksek malpraktis oranlarıyla ilişkilendirildi. Tıbbi malpraktis riskini azaltmak için erken teşhis yöntemlerinin standartlaştırılması ve kapsamlı bir ameliyat sonrası takip yapılması gerekmektedir.

Anahtar sözcükler: Acil ortopedi; eklem çıkığı; malpraktis; omuz; üst ekstremite.

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ORIGINAL ARTICLE

Factors associated with radiographic and clinical outcomes after posterior long-segment instrumentation for neurologically intact thoracolumbar fractures: a single-center retrospective study

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ABSTRACT

BACKGROUND: This study aimed to quantify radiographic correction and long-term maintenance, assess pain and health-related quality of life, and identify factors associated with outcomes after standardized posterior long-segment fixation for neurologically intact traumatic thoracolumbar junction fractures.

METHODS: This single-center retrospective cohort study included consecutive adults with acute traumatic T11–L2 fractures treated between March 2014 and February 2023 with posterior long-segment pedicle screw instrumentation (two levels above and two levels below, including fracture-level screws) without decompression. Patients required at least 24 months of radiographic follow-up, available pre-operative sagittal computed tomography images, and early post-operative and final lateral radiographs. Imaging parameters were vertebral compression angle (VCA) and anterior/posterior vertebral corpus height. Clinical outcomes were final Visual Analog Scale (VAS) and 36-item short form health survey (SF-36) scores, which were assessed cross-sectionally at final follow-up and therefore reflect final health status rather than change from pre-operative levels. Paired comparisons were used for longitudinal imaging changes, and multivariable linear regression with robust standard errors was used to evaluate factors associated with final outcomes.

RESULTS: Seventy-eight patients were included (mean age 40.2±13.9 years; 65.4% male), with a median follow-up of 48 months. VCA changed from 11.75° (7.83–16.48) preoperatively to 4.30° (2.55–6.65) early postoperatively and was 6.00° (4.00–8.80) at final follow-up, indicating limited correction loss over time. Restoration of both anterior and posterior vertebral body heights was observed, with partial loss at final follow-up. Final pain levels were low (VAS 1 [interquartile range=1–1]). In adjusted analyses, AO fracture type was associated with greater VCA loss and poorer SF-36 scores across several domains, particularly for AO type C fractures. However, the number of type C fractures was limited (n=9). Superficial wound infection occurred in 5 patients (6.4%) and resolved with local care and antibiotics; no deep infection, implant failure, revision surgery, or junctional complications were observed.

CONCLUSION: Posterior long-segment fixation for neurologically intact T11–L2 fractures provided substantial early radiographic correction with generally limited long-term loss of alignment and low final pain levels. Nevertheless, radiographic correction did not necessarily translate into complete functional recovery, as reflected by persistent variability in SF-36 domains. Among the variables analyzed, AO fracture type showed the most consistent association with correction loss and patient-reported outcomes. These hypothesis-generating findings suggest that fracture morphology may be associated with outcomes and may help frame post-operative expectations and follow-up discussions in similar patient populations. However, confirmation in larger, prospective, and comparative studies is required.

Keywords: 36-Item short form health survey; AO spine classification; long-segment posterior instrumentation; radiographic correction loss; thoracolumbar fracture; vertebral compression angle.

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INTRODUCTION

Most traumatic thoracolumbar fractures occur at the thoracolumbar junction (T11–L2), a transitional zone where the relatively rigid thoracic spine meets the more mobile lumbar spine.[1] Maintaining sagittal alignment in this region is clinically important, as post-traumatic kyphosis may lead to persistent pain, functional impairment, and reduced health-related quality of life.[2,3] Despite the frequency of these injuries, the optimal surgical strategy remains controversial, particularly regarding the number of motion segments that should be included to balance construct stability with preservation of spinal mobility.[4-6]

The debate between short-segment and long-segment posterior instrumentation has persisted for decades. Meta-analytic evidence suggests that long-segment constructs may provide better maintenance of post-operative correction and lower implant failure rates, although at the expense of greater operative time and blood loss, while disability outcomes may remain similar between approaches.[7] To improve the mechanical performance of shorter constructs while preserving motion segments, the inclusion of intermediate pedicle screws at the fracture level has been proposed. A systematic review and meta-analysis comparing 4-screw and 6-screw constructs found that fracture-level screw augmentation was associated with less correction loss, better radiographic outcomes, and fewer implant failures, despite slightly increased operative time and blood loss.[8] Nevertheless, failure after posterior short-segment instrumentation remains clinically relevant, and greater pre-operative structural severity, particularly higher load-sharing burden, has been consistently associated with an increased risk of such failure. A recent systematic review and meta-analysis confirmed that load-sharing classification (LSC) scores >7, higher pre-operative Cobb angle, and greater vertebral wedge angle are associated with short-segment instrumentation failure.[2] In addition, age ≥65 years and posterior ligamentous complex (PLC) injury have been identified as independent predictors of instrumentation failure in both short- and long-segment constructs.[9] Recent comparative studies have confirmed that long-segment posterior fixation provides similar clinical outcomes to short-segment fixation, albeit with longer operative time and greater blood loss.[10] Furthermore, intermediate (fracture-level) screws have been shown to significantly reduce pedicle screw loosening and instrumentation failure.[11]

Beyond construct selection, fracture morphology itself may play an important role in long-term outcome. The AO spine thoracolumbar injury classification categorizes fractures according to increasing instability, from type A compression injuries to type B distraction injuries and type C translational or rotational injuries.[12] The World Federation of Neurosurgical Societies (WFNS) Spine Committee has recommended that anterior vertebral body height loss >50%, PLC injury, and post-operative Cobb angle >10.5° should be considered when counseling patients about expected outcomes.[13] However, the extent to which AO fracture severity is associated with longer-term radiographic maintenance and patient-reported outcomes after a standardized posterior fixation strategy has not been fully established. In particular, it remains unclear whether more unstable AO type B and C injuries continue to influence outcomes even after stabilization with a uniform long-segment construct.

Therefore, in this retrospective cohort study, we evaluated a standardized posterior long-segment fixation strategy (two levels above and two levels below) with routine fracture-level screw inclusion in a homogeneous cohort of neurologically intact T11–L2 fractures. The aims of this study were to quantify radiographic correction and its long-term maintenance, assess pain and health-related quality of life using the Visual Analog Scale (VAS) and 36-Item Short Form Health Survey (SF-36), and identify factors associated with final radiographic and clinical outcomes, with particular emphasis on AO fracture severity. Given the retrospective design and limited sample size for certain fracture types, these analyses are considered exploratory and hypothesis-generating.

MATERIALS AND METHODS

Study Design and Setting

This single-center retrospective cohort study was conducted at a Level 1 trauma center. Consecutive adult patients who underwent surgical treatment for traumatic thoracolumbar junction fractures between March 2014 and February 2023 were identified and screened for eligibility. Ethical approval was granted by the Ege University Medical Research Ethics Committee (Approval No. 26-3T/1, Date: 05.03.2026), and the requirement for written informed consent was waived due to the retrospective study design. Clinical trial registration was not applicable. All procedures were performed in accordance with the Declaration of Helsinki and applicable institutional regulations.

Participants and Eligibility Criteria

Patients were identified from institutional surgical logs and electronic medical records. Eligible patients were adults (≥18 years) with an acute traumatic fracture at T11, T12, L1, or L2 who were treated with posterior long-segment pedicle screw instrumentation and had at least 24 months of radiographic follow-up, including available pre-operative sagittal computed tomography (CT) images and early post-operative and final lateral radiographs.

Because the present study was designed to evaluate outcomes in a relatively homogeneous cohort treated without neural decompression, only neurologically intact patients were included. Accordingly, all included patients had no documented motor or sensory deficit at presentation (ASIA grade E). Patients with any neurological impairment related to the index injury were excluded.

Additional exclusion criteria were: any decompressive proce-

dure performed at the index surgery (including laminectomy or foraminotomy); pathological or insufficiency fractures (e.g., tumor, infection, or severe metabolic bone disease); prior thoracolumbar surgery that could affect sagittal alignment measurements; multilevel fractures without a clearly definable index vertebra for standardized radiographic assessment; incomplete clinical or imaging records, and follow-up shorter than 24 months. A detailed flow diagram of patient selection is summarized in Figure 1.

A subset of patients included in the present single-center cohort was also included in a previously published multicenter comparative study evaluating fracture-level screw placement. The present study addresses a distinct research question by examining fracture morphology and factors associated with long-term radiographic and patient-reported outcomes in an extended single-center cohort. The previous study is cited to transparently disclose the partial overlap between the study populations.[14]

Surgical Technique and Post-operative Management

All operations were performed under general anesthesia by the same surgical team with the patient in the prone position on a radiolucent table. The surgical indication for neurologically intact patients was based on fracture instability assessed by the treating spine team, including loss of vertebral body height >50%, kyphotic deformity >20°, or canal compromise, in accordance with institutional practice. For the purposes of this study, long-segment fixation was defined as instrumentation spanning two vertebrae above and two vertebrae below the fractured level.

Pedicle screw–rod constructs were applied under fluoroscopic guidance, and indirect reduction maneuvers were used to restore vertebral body height and sagittal alignment. Fracture-level pedicle screws were routinely inserted at the index vertebra as part of the standardized construct in all included patients. No posterior decompression was performed in any patient included in this analysis.

Titanium polyaxial pedicle screw–rod systems (Instinct® Java® Spinal Fixation System, Zimmer) were used. Screw diameter and length were selected according to pre-operative CT-based pedicle anatomy. Patients were mobilized on the 1st or 2nd post-operative day with a thoracolumbosacral orthosis for 8–12 weeks, depending on surgeon preference and fracture characteristics. Weight-bearing was allowed as tolerated, with avoidance of excessive bending, lifting, and twisting during the early post-operative period.

Data Collection and Variables

Demographic and injury-related variables were extracted from the medical records, including age, sex, trauma mechanism, fracture level (T11, T12, L1, or L2), and fracture morphology according to the AO spine thoracolumbar injury classification. AO classification was performed independently by two spine surgeons blinded to clinical outcomes, based on pre-operative CT and radiographs. Disagreements were resolved by consensus. Trauma mechanism was categorized as fall from height or traffic accident. Pedicle screw diameter (5.5 mm vs. 6.5 mm) was also recorded for each patient. Complications were recorded from inpatient charts and follow-up records.

The following definitions were used:

(a). Superficial surgical site infection: Erythema or discharge involving only skin/subcutaneous tissue, requiring oral antibiotics or local wound care

(b). Deep surgical site infection: Infection involving fascia or muscle, requiring surgical debridement or intravenous antibiotics

(c). Implant failure: Visible breakage of rods or screws, or screw loosening defined as a radiolucent halo >1 mm on final radiograph

(d). Revision surgery: Any unplanned return to the operating room for implant-related issues, including removal, replacement, or extension of instrumentation

(e). Proximal junctional kyphosis (PJK): Sagittal Cobb angle >10° between the upper instrumented vertebra and the vertebra two levels above, measured on final lateral radiograph

(f). Adjacent segment disease: New degenerative changes or stenosis at an adjacent level requiring treatment.

Outcomes

The primary outcome was radiographic loss of correction, defined as the change in vertebral compression angle (VCA) from the early post-operative period to final follow-up. This endpoint was selected because maintenance of sagittal alignment is a principal aim of posterior stabilization.

Secondary outcomes were final VCA, final anterior vertebral corpus height (VCH-A), final posterior vertebral corpus height (VCH-P), loss of anterior vertebral height, loss of posterior vertebral height, pain intensity at final follow-up assessed with the VAS, and health-related quality of life at final follow-up assessed with the SF-36. All clinical outcomes were assessed cross-sectionally at final follow-up; therefore, they represent final health status rather than change from pre-operative status.

Clinical Outcome Assessment

Pain intensity was assessed at final follow-up using a 10-point VAS ranging from 0 (no pain) to 10 (worst imaginable pain). Health-related quality of life was assessed at final follow-up using the validated Turkish version of the SF-36 (version 1).[15,16] Eight domain scores were calculated and transformed to a 0–100 scale, with higher scores indicating better perceived health status. The health transition item was not included in domain scoring.

Radiographic Outcome Assessment

Imaging evaluation was performed using pre-operative sagittal CT images and standard lateral thoracolumbar radio-

graphs obtained in the early post-operative period and at final follow-up. The early post-operative radiograph was defined as the first post-operative radiograph obtained during routine clinical care, typically within 3–5 days after surgery. Final follow-up radiographs were those obtained at or beyond 24 months.

Pre-operative VCA, VCH-A, and VCH-P measurements were obtained on sagittal CT images, whereas early post-operative and final follow-up measurements were performed on lateral radiographs. The use of different imaging modalities across time points (CT vs. radiograph) represents a methodological limitation; to assess the potential impact, we performed a sensitivity analysis (described below). All measurements were performed using institutional PACS tools by two independent observers blinded to clinical outcomes. The following parameters were recorded:

A. VCA: Measured on the lateral view as the angle formed by the superior and inferior endplates of the fractured vertebral body

B. VCH-A: Measured as the distance between the superior and inferior endplates along the anterior vertebral cortex

C. VCH-P: Measured as the distance between the superior and inferior endplates along the posterior vertebral cortex.

To characterize post-operative restoration and maintenance over time, we calculated the following derived parameters:

I. VCA correction=VCA~pre~−VCA~early~

II. Loss of correction=VCA~final~−VCA~early~

III. Anterior height restoration=VCH-A~early~−VCH-A~pre~

IV. Anterior height loss=VCH-A~early~−VCH-A~final~

V. Posterior height restoration=VCH-P~early~−VCH-P~pre~

VI. Posterior height loss=VCH-P~early~−VCH-P~final~

Statistical Analysis

Continuous variables were summarized as mean±standard deviation (SD) when normally distributed and as median (Q1–Q3) when non-normally distributed. Categorical variables are presented as number and percentage. Normality was assessed using the Shapiro–Wilk test together with visual inspection of distribution plots.

Within-patient comparisons between pre-operative and early post-operative values and between early post-operative and final follow-up values were performed using paired t-tests or Wilcoxon signed-rank tests, as appropriate. Associations between radiographic correction-loss parameters and patient-reported outcomes were explored using Spearman rank correlation coefficients.

To evaluate factors associated with final radiographic and clinical outcomes, multivariable linear regression models with HC3 robust standard errors were constructed. Candidate variables were selected a priori based on clinical relevance and included AO fracture type, age, sex, trauma mechanism, fracture level, and pedicle screw diameter (5.5 mm vs. 6.5 mm). Regression results are presented as beta coefficients with 95% confidence intervals (CI).

Given the retrospective design, no formal sample size calculation was performed. Because multiple secondary and domain-specific analyses (including eight SF-36 domains) were conducted, these analyses were considered exploratory and hypothesis-generating. We did not apply a formal multiplicity correction (e.g., Bonferroni) to avoid an overly conservative increase in Type II error; however, findings with p-values between 0.01 and 0.05 should be interpreted cautiously as hypothesis-generating rather than definitive. No formal imputation was required because no missing data were present for the primary radiographic outcome measures or for the final VAS and SF-36 assessments among the included patients.

Subgroup analysis

To further explore the association between fracture morphology and outcomes within a more homogeneous group, we performed a post hoc subgroup analysis limited to patients with AO type A fractures (n=42). Multivariable regression models were repeated within this subgroup using the same candidate variables.

Sensitivity analysis for imaging modality

Because pre-operative measurements were obtained from sagittal CT while post-operative and final measurements were obtained from lateral radiographs, we conducted a sensitivity analysis to assess modality-related measurement consistency. In a randomly selected subset of 20 patients, VCA was measured on both pre-operative sagittal CT and available pre-operative lateral radiographs. The mean difference between the two modalities was calculated using a paired t-test.

Additional analysis for screw properties

In addition to screw diameter, we attempted to collect data on screw length and distance from screw tip to anterior vertebral cortex. However, these measurements were not reliably available or standardized across all 78 patients due to variability in imaging quality and the retrospective nature of the study. This limitation is acknowledged in the discussion.

Interobserver reliability for continuous radiographic measurements was assessed using intraclass correlation coefficients based on a two-way random-effects model for absolute agreement. Inter-rater reliability for AO classification was assessed using weighted kappa statistics. A two-sided $p<0.05$ was considered statistically significant. Statistical analyses were performed using IBM Statistical Package for the Social Sciences Statistics version 26.0 (IBM Corp., Armonk, NY, USA).

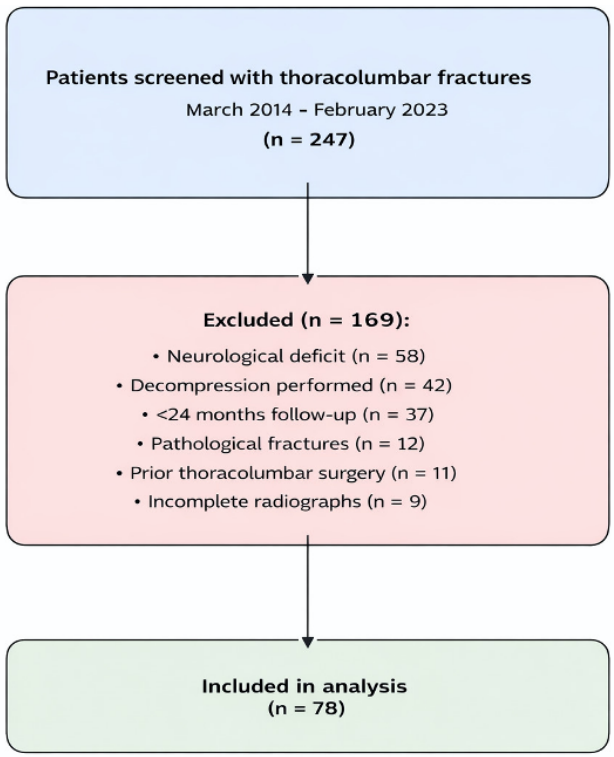


Figure 1. Flow diagram of patient selection for the final study cohort.

RESULTS

Study Population

A total of 78 patients with thoracolumbar junction fractures (T11–L2) treated with posterior long-segment instrumentation met the eligibility criteria and were included in the analysis (Fig. 1). The mean age was 40.2±13.9 years (range, 18–65), and 27 patients (34.6%) were female. The most common trauma mechanism was a fall from height (56/78, 71.8%), followed by traffic accidents (22/78, 28.2%). Fracture levels were L1 in 30 patients (38.5%), T12 in 24 (30.8%), L2 in 17 (21.8%), and T11 in 7 (9.0%). According to the AO classification, 42 fractures were type A (53.8%), 27 were type B (34.6%), and 9 were type C (11.5%). Median follow-up was 48.0 months (Q1–Q3: 36.0–67.8). Pedicle screw diameter was 5.5 mm in 52 patients (66.7%) and 6.5 mm in 26 patients (33.3%) (Table 1A).

Baseline Characteristics Stratified by AO Type

Baseline characteristics stratified by AO type are shown in Table 1B. Pre-operative imaging-based severity differed across fracture types. Median pre-operative VCA was 10.2° (6.8–14.5) in AO type A, 12.8° (8.9–17.2) in type B, and 16.4° (12.1–21.3) in type C (p=0.008). Pre-operative anterior vertebral height was also lower in more severe fracture patterns (p=0.04). Age, sex, and trauma mechanism did not differ significantly across AO groups (all p>0.05).

Sagittal Alignment and Vertebral Height Measurements Over Time

Imaging measurements over time are summarized in Table 2. Pre-operative measurements were obtained from sagittal CT images, whereas early post-operative and final follow-up measurements were obtained from lateral radiographs. The median VCA was 11.75° (7.83–16.48) preoperatively, 4.30°

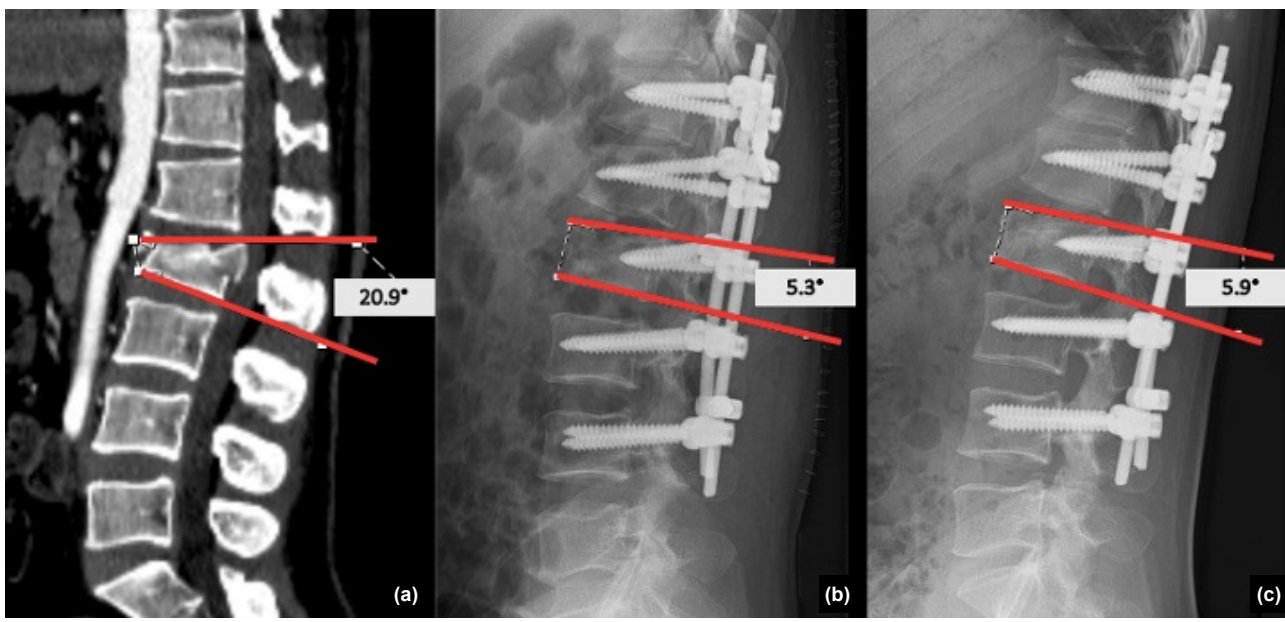


Figure 2. Representative sagittal images of a 34-year-old male patient with an AO type B2 fracture of the L2 vertebra. **(a)** Pre-operative computed tomography image showing measurement of the vertebral compression angle (VCA). **(b)** Early post-operative lateral radiograph showing VCA measurement. **(c)** Lateral radiograph at 32-month follow-up showing VCA measurement at final follow-up.

Table 1A. Baseline characteristics

Variable	Overall (n=78)
Patients, n	78
Age (years), mean±SD	40.2±13.9
Female sex, n (%)	27 (34.6)
Follow-up (months), median (Q1–Q3)	48.0 (36.0–67.8)
Final VAS, median (Q1–Q3)	1 (1–1)
Screw diameter, n (%)	
5.5 mm	52 (66.7)
6.5 mm	26 (33.3)
Mechanism, n (%)	
Fall from height	56 (71.8)
Traffic accident	22 (28.2)
Fracture level, n (%)	
T11	7 (9.0)
T12	24 (30.8)
L1	30 (38.5)
L2	17 (21.8)
AO fracture type, n (%)	
A	42 (53.8)
B	27 (34.6)
C	9 (11.5)

SD: Standard devaition; VAS: Visual Analog Scale. Screw diameter refers to the pedicle screw diameter used at all instrumented levels (including fracture level).

(2.55–6.65) early postoperatively, and 6.00° (4.00–8.80) at final follow-up. The mean absolute correction between the pre-operative and early post-operative assessments was 7.61±4.65°. At final follow-up, the median loss of correction from the early post-operative period was 1.00° (0.40–2.57) (p<0.001).

VCH-A was 15.81±3.61 mm preoperatively, 25.71±3.30 mm early postoperatively (mean change 9.90±4.25 mm, p<0.001), and 22.56±3.61 mm at final follow-up (median loss 2.15 mm [1.00–4.50] from early post-operative, p<0.001). VCH-P was 22.96±3.68 mm preoperatively, 29.72±2.77 mm early postoperatively (mean change 6.76±3.31 mm, p<0.001), and 28.14±2.66 mm at final follow-up (mean loss 1.58±1.04 mm, p<0.001).

When changes over time were examined according to AO fracture type, more severe fracture patterns showed greater early correction but also greater loss over time. In particular, AO type C fractures appeared to show the largest early VCA correction and the greatest subsequent correction loss (Fig. 2). However, these observations regarding AO type C fractures should be interpreted with caution given the small number of such injuries (n=9).

Interobserver Reliability

Interobserver reliability was excellent for imaging measurements. Intraclass correlation coefficient (ICC) values were 0.94 (95% CI, 0.90–0.97) for VCA, 0.91 (95% CI, 0.86–0.95) for anterior vertebral height, and 0.89 (95% CI, 0.83–0.94) for posterior vertebral height. Agreement for AO classification was substantial (weighted κ=0.84, 95% CI, 0.76–0.91).

Table 1B. Baseline characteristics stratified by AO type

Characteristic	AO type A (n=42)	AO type B (n=27)	AO type C (n=9)	p
Age (years)	39.8±14.2	41.1±13.5	39.6±14.8	0.89
Female sex, n (%)	15 (35.7)	9 (33.3)	3 (33.3)	0.97
Fall from height, n (%)	30 (71.4)	19 (70.4)	7 (77.8)	0.91
Preop VCA (°)	10.2 (6.8–14.5)	12.8 (8.9–17.2)	16.4 (12.1–21.3)	0.008
Preop VCH-A (mm)	16.8±3.4	15.2± 3.7	13.9± 3.9	0.04

VCA: Vertebral compression angle; VCH-A: Anterior vertebral corpus height.

Table 2. Radiographic outcomes over time

Measure	Preopera-tive	Early post-operative	Final	Δ Pre→Early	Δ Ear-ly→Final
VCA (°)	11.75 (7.83–16.48)	4.30 (2.55–6.65)	6.00 (4.00–8.80)	7.61±4.65a	1.00 (0.40–2.57)b
Anterior VCH (mm)	15.81±3.61	25.71±3.30	22.56±3.61	9.90±4.25a	2.15 (1.00–4.50)b
Posterior VCH (mm)	22.96±3.68	29.72±2.77	28.14±2.66	6.76±3.31a	1.58±1.04b

Δ Pre→Early represents correction/restoration; Δ Early→Final represents loss from early post-operative to final follow-up. Values are mean±SD or median (Q1–Q3) as appropriate. a p<0.001 for Pre-operative versus Early post-operative (paired test). b p<0.001 for early versus final (paired test). VCA: Vertebral compression angle; VCH: Vertebral corpus height.

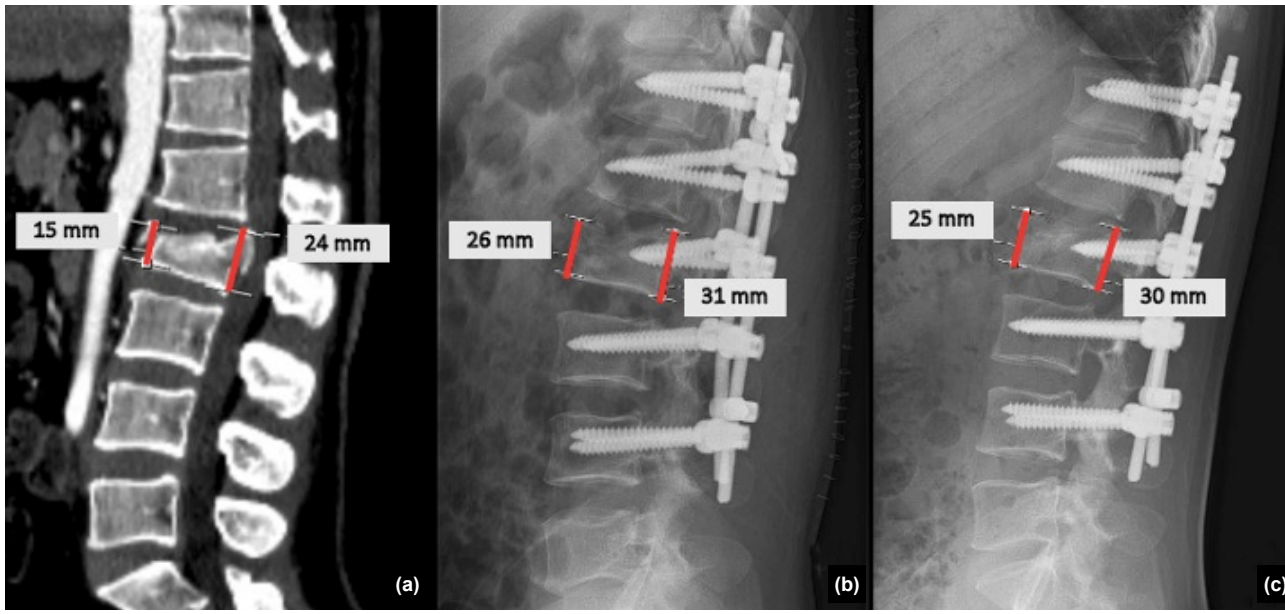


Figure 3. Representative sagittal images of the same patient shown in Figure 2. **(a)** Pre-operative computed tomography image showing measurement of anterior and posterior vertebral corpus heights (VCH-A and VCH-P). **(b)** Early post-operative lateral radiograph showing VCH-A and VCH-P measurements. **(c)** Lateral radiograph at 32-month follow-up showing VCH-A and VCH-P measurements at final follow-up.

Table 4A. Factors associated with final VAS, final VCA, and VCA loss

Predictor	Final VAS	Final VCA (°)	VCA Loss (°)
Age (per year)	−0.01 (−0.02–0.00) p=0.077	0.00 (−0.05–0.06) p=0.862	0.01 (−0.02–0.04) p=0.504
Sex (female vs. male)	0.01 (−0.23–0.25) p=0.939	−0.66 (−2.21–0.89) p=0.403	0.45 (−0.38–1.28) p=0.290
Mechanism (traffic vs. fall)	0.05 (−0.22–0.32) p=0.732	0.32 (−1.62–2.25) p=0.749	0.00 (−0.91–0.92) p=0.995
Fracture level			
T11 versus L1	0.62 (0.14–1.11) p=0.012	0.80 (−2.16–3.77) p=0.596	−0.14 (−1.21–0.94) p=0.804
T12 versus L1	0.23 (−0.03–0.49) p=0.077	1.29 (−0.52–3.11) p=0.163	0.85 (−0.19–1.88) p=0.108
L2 versus L1	0.50 (0.14–0.87) p=0.007	−0.70 (−2.63–1.24) p=0.482	0.36 (−0.47–1.20) p=0.394
AO type			
B versus A	0.01 (−0.26–0.27) p=0.970	−1.13 (−2.62–0.37) p=0.141	1.85 (0.98–2.72) p<0.001
C versus A	0.03 (−0.33–0.39) p=0.874	3.58 (1.03–6.13) p=0.006	4.75 (3.02–6.49) p<0.001
Screw diameter (6.5 mm vs. 5.5 mm)	0.02 (−0.24–0.28) p=0.882	−0.42 (−1.98–1.14) p=0.603	0.31 (−0.52–1.14) p=0.468

VAS: Visual Analog Scale; VCA: Vertebral compression angle. Multivariable linear regression with robust standard errors (HC3). Reference categories: male, fall from height, L1 fracture level, AO type A, screw diameter 5.5 mm. Values are β coefficients (95% confidence intervals). Bold indicates statistical significance (p<0.05). All models adjusted for age, sex, mechanism, fracture level, AO type, and screw diameter

Clinical Outcomes

At final follow-up, pain levels were low overall. Median VAS was 1 (interquartile range: 1–1); 55 patients (70.5%) reported a VAS score of 1, 18 (23.1%) reported 2, and 5 (6.4%) reported 0. No patient reported VAS >2. These represent cross-sectional final pain status, not change from pre-operative levels.

SF-36 domain scores at final follow-up are summarized in Table 3. Median scores were highest for role physical and role emotional, both reaching 100 in the upper range, whereas lower values were observed for vitality and mental health.

Factors Associated with Final Pain and Radiographic Outcomes

Multivariable regression results for final VAS, final VCA, and VCA loss are presented in Table 4A. Final VAS was higher in L2 fractures (β 0.50, 95% CI 0.14 to 0.87; p=0.007) and T11

Table 4B. Factors associated with vertebral height outcomes

Predictor	Final VCH−A (mm)	VCH−A Loss (mm)	Final VCH−P (mm)	VCH−P Loss (mm)
Age (per year)	0.01 (-0.04–0.06) p=0.719	0.02 (-0.01–0.06) p=0.196	0.01 (-0.04–0.07) p=0.587	0.01 (-0.01–0.02) p=0.375
Sex				
(female vs. male)	0.28 (-1.11–1.67) p=0.693	−0.49 (-1.46–0.47) p=0.318	-1.10 (-2.34–0.14) p=0.083	-0.35 (-0.84–0.15) p=0.174
Mechanism				
(traf-fic vs. fall)	-0.36 (-1.74-1.03) p=0.615	−0.24 (-1.26–0.77) p=0.636	-0.09 (-1.35–1.17) p=0.890	0.39 (−0.17–0.94) p=0.172
Fracture level				
T11 versus L1	-1.69 (-4.55–1.17) p=0.246	−0.54 (-2.09–1.01) p=0.491	-0.96 (-3.93–2.01) p=0.527	-0.73 (-1.35–-0.11) p=0.022
T12 versus L1	-2.38 (-4.04–-0.71) p=0.005	0.40 (-0.60–1.39) p=0.434	-1.45 (-2.79–−0.12) p=0.033	-0.64 (-1.27–-0.01) p=0.048
L2 versus L1	0.90 (-0.74–2.54) p=0.281	0.78 (-0.61–2.18) p=0.270	0.14 (-1.63–1.92) p=0.877	-0.33 (-0.98–0.33) p=0.327
AO type				
B versus A	-3.67 (-5.16–-2.19) p<0.001	3.16 (2.12–4.20) p<0.001	-0.76 (-2.11–0.59) p=0.270	0.39 (-0.10–0.87) p=0.117
C versus A	-3.95 (-6.26–-1.64) p<0.001	6.16 (4.16–8.16) p<0.001	-1.31 (-3.79–1.17) p=0.300	0.84 (0.05–1.64) p=0.038
Screw diameter	0.58 (-1.02–2.18) p=0.478	-0.22 (-1.18–0.74) p=0.651	-0.15 (-1.58–1.28) p=0.837	0.08 (-0.42–0.58) p=0.752
(6.5 mm vs. 5.5 mm)				

Multivariable linear regression with robust standard errors (HC3). Reference categories: male, fall from height, L1 fracture level, AO type A, screw diameter 5.5 mm. Values are β coefficients (95% confidence interval). Bold indicates statistical significance (p<0.05). All models adjusted for age, sex, mechanism, fracture level, AO type, and screw diameter. VCH-A: Anterior vertebral corpus height; VCH-P: Posterior vertebral corpus height.

Table 4C. Subgroup analysis: AO Type A fractures only (n=42)

Outcome	β coefficient (95% CI)	p
Final VCA (°)		
L2 versus L1	1.82 (−0.45–4.09)	0.116
Age (per year)	0.02 (−0.06–0.10)	0.612
Screw diameter (6.5 vs. 5.5 mm)	−0.38 (−2.22–1.46)	0.683
VCA loss (°)		
L2 versus L1	1.45 (0.32–2.58)	0.012
Age (per year)	0.01 (−0.03–0.05)	0.581
Screw diameter (6.5 vs. 5.5 mm)	0.22 (−0.69–1.13)	0.633
Final physical functioning (SF 36)		
L2 versus L1	−6.32 (−18.44–5.80)	0.304
Age (per year)	−0.15 (−0.52–0.22)	0.422
Screw diameter (6.5 vs. 5.5 mm)	3.15 (−7.88–14.18)	0.573

CI: Confidence interval; VCA: Vertebral compression angle. Multivariable linear regression with robust standard errors (HC3). Analysis limited to patients with AO type A fractures (n=42). Reference category for fracture level: L1. Reference category for screw diameter: 5.5 mm. Bold indicates statistical significance (p<0.05).

fractures (β 0.62, 95% CI 0.14 to 1.11; p=0.012) compared with L1 fractures. Age, sex, trauma mechanism, AO type and screw diameter were not significantly associated with final VAS.

For sagittal alignment outcomes, AO fracture type was the main variable associated with final deformity and correction loss. Compared with AO type A, AO type C was associated with a higher final VCA (β 3.58°, 95% CI 1.03 to 6.13; p=0.006). VCA loss from the early post-operative period to final follow-up was greater in AO type B (β 1.85°, 95% CI 0.98–2.72; p<0.001) and AO type C (β 4.75°, 95% CI 3.02 to 6.49; p<0.001) than in AO type A.

Regression models for vertebral height outcomes are shown in Table 4B. Final anterior vertebral height was lower in AO type B (β −3.67 mm, 95% CI −5.16–−2.19; p<0.001) and AO type C (β −3.95 mm, 95% CI −6.26–−1.64; p<0.001) compared with AO type A. T12 level was also associated with lower final anterior height (β −2.38 mm, 95% CI −4.04–−0.71; p=0.005). Anterior height loss was greater in AO type B (β 3.16 mm, 95% CI 2.12–4.20; p<0.001) and AO type C (β 6.16 mm, 95% CI 4.16–8.16; p<0.001).

For posterior height outcomes, T12 was associated with lower final posterior vertebral height (β −1.45 mm, 95% CI −2.79–−0.12; p=0.033). AO type C was associated with greater posterior height loss (β 0.84 mm, 95% CI 0.05–1.64; p=0.038), whereas T11 and T12 fractures showed less posterior height loss than L1 fractures.

Subgroup Analysis: AO Type A Fractures Only

To further examine factors associated with outcomes within a more homogeneous fracture group, we performed a post hoc subgroup analysis limited to the 42 patients with AO type A fractures. In this subgroup, the median VCA loss from early post-operative to final follow-up was 0.80° (0.30–1.90). On multivariable analysis, L2 fracture level (compared with L1) was associated with greater VCA loss (β 1.45°, 95% CI 0.32–2.58; p=0.012). No other variables (age, sex, mechanism, and screw diameter) were significantly associated with VCA loss or final SF-36 scores within this subgroup (all p>0.05). These results are presented in Table 4C.

Sensitivity Analysis for Imaging Modality

To assess potential measurement variability due to different imaging modalities (pre-operative CT vs. follow-up radiographs), we compared VCA measurements on pre-operative sagittal CT and available pre-operative lateral radiographs in a randomly selected subset of 20 patients. The mean difference between the two modalities was 0.8° (95% CI −1.2° to 2.8°; p=0.42), indicating acceptable agreement with no systematic bias (Table 5).

Screw Diameter

Pedicle screw diameter (6.5 mm vs. 5.5 mm) was included as a covariate in all multivariable regression models. Screw diameter was not significantly associated with final VCA (β −0.42°, 95% CI −1.98–1.14; p=0.60), VCA loss (β 0.31°, 95% CI −0.52–1.14; p=0.47), final anterior height (β 0.58 mm, 95% CI −1.02–2.18; p=0.48) (Table 4A and B), or any SF-36 domain (all p>0.05; see footnote to Table 6).

Correlation between Radiographic and Clinical Outcomes

Correlations between radiographic correction-loss parameters and SF-36 domains are presented in Table 7. Greater VCA loss was modestly associated with lower physical functioning (ρ=−0.28, p=0.013) and vitality (ρ=−0.24, p=−0.036), whereas no significant association was observed with bodily pain (ρ=−0.11, p=0.34). VCH-A loss showed a non-significant trend toward lower physical functioning (ρ=−0.21, p=0.06) and was not significantly associated with the other SF-36 domains.

Factors Associated with Health-Related Quality of Life

Multivariable regression models for SF-36 domains are shown in Table 6. Adjusted R2 values ranged from 0.309 to 0.482 for most domains, whereas the model for general health explained little variance (adjusted R2=0.036).

AO fracture type showed the most consistent associations across SF-36 domains. Compared with AO type A, AO type B was associated with lower scores in physical functioning (β −13.75, p=0.007), role physical (β −21.54, p<0.001), role emotional (β −27.65, p<0.001), social functioning (β −15.09, p<0.001), vitality (β −14.56, p<0.001), and mental health (β −10.53, p=0.002). AO type C showed larger reductions across multiple domains, including physical functioning (β −34.28, p<0.001), role physical (β −50.42, p<0.001), role emotional (β −45.39, p<0.001), bodily pain (β −27.29, p<0.001), social functioning (β −31.41, p<0.001), vitality (β −29.13, p<0.001), and mental health (β −24.00, p<0.001).

Traffic accidents were associated with lower role emotional scores than falls (β −16.63, 95% CI −32.90 to −0.36; p=0.045). Fracture level also showed domain-specific associations: L2 fractures were associated with lower social functioning (β −9.49, p=0.006) and lower vitality (β −8.09, p=0.038), whereas T11 fractures were associated with lower vitality (β −8.81, p=0.019). No independent predictors were identified for general health. Screw diameter was not significantly associated with any SF-36 domain (all p>0.05).

Complications

Overall, complications were limited. Five patients (6.4%) developed superficial wound infection, all of which resolved with dressing changes and antibiotic treatment. No patient

Table 5. Sensitivity analysis: VCA measured on pre-operative CT versus lateral radiograph (n=20)

Imaging modality	Mean VCA (°)±SD	Mean difference (95% CI)	p*
Pre-operative sagittal CT	12.4°±4.2°	0.8° (−1.2°–2.8°)	0.42
Pre-operative lateral radio-graph	11.6°±4.5°		

Paired t-test. No statistically significant difference between modalities (p=0.42). CT: Computed tomography; VCA: Vertebral compression angle; SD: Standard deviation; CI: Confidence interval.

Table 6. Multivariable linear regression models for SF-36 domains at final follow-up

Predictor	Physical functioning	Role physical	Role emotional	Bodily pain	Social functioning	Vitality	Mental health	General health
AO type B versus A	−13.75	−21.54	−27.65	−7.60	−15.09	−14.56	−10.53	−4.07
	(−23.82–−3.68)	(−33.22–−9.86)	(−41.07–−14.24)	(−16.10–0.91)	(−21.08–−9.10)	(−21.00–−8.12)	(−17.31–−3.75)	(−9.68–1.53)
	p=0.007	p<0.001	p<0.001	p=0.080	p<0.001	p<0.001	p=0.002	p=0.154
AO type C versus A	−34.28	−50.42	−45.39	−27.29	−31.41	−29.13	−24.00	−8.19
	(−42.19–−26.38)	(−74.27–−26.57)	(−62.91–−27.87)	(−43.22–−11.35)	(−41.05–−21.78)	(−36.69–−21.56)	(−33.38–−14.62)	(−16.77–0.39)
	p<0.001	p<0.001	p<0.001	p<0.001	p<0.001	p<0.001	p<0.001	p=0.061
Age (per year)	−0.21	−0.20	0.09	0.16	−0.07	−0.04	−0.09	−0.05
	(−0.50–0.08)	(−0.59–0.20)	(−0.33–0.51)	(−0.16–0.47)	(−0.24–0.10)	(−0.24–0.16)	(−0.32–0.13)	(−0.27–0.17)
	p=0.153	p=0.329	p=0.675	p=0.327	p=0.418	p=0.710	p=0.408	p=0.655
Female versus male	5.04	3.54	2.85	−2.77	−1.50	1.43	1.08	−0.33
	(−3.94–14.03)	(−7.31–14.40)	(−10.89–16.59)	(−11.62–6.08)	(−6.76–3.76)	(−4.70–7.57)	(−5.31–7.48)	(−5.51–4.85)
	p=0.271	p=0.522	p=0.684	p=0.540	p=0.576	p=0.647	p=0.740	p=0.900
Traffic versus fall	4.71	−7.19	−16.63	−2.66	3.43	0.41	2.64	2.41
	(−4.63–14.05)	(−19.89–5.51)	(−32.90–−0.36)	(−12.53–7.22)	(−2.57–9.42)	(−5.38–6.20)	(−4.02–9.31)	(−3.32–8.14)
	p=0.323	p=0.267	p=0.045	p=0.598	p=0.263	p=0.889	p=0.437	p=0.410
T11 versus L1	9.96	9.63	−7.81	7.52	−3.07	−8.81	−7.41	0.90
	(−0.96–20.89)	(−11.37–30.63)	(−31.01–15.39)	(−6.88–21.91)	(−15.13–8.99)	(−16.17–−1.44)	(−19.30–4.48)	(−6.94–8.73)
	p=0.074	p=0.369	p=0.509	p=0.306	p=0.618	p=0.019	p=0.222	p=0.823
T12 versus L1	5.80	−4.30	9.49	4.43	−4.49	−5.42	−6.65	3.49
	(−5.31–16.92)	(−14.14–5.53)	(−2.56–21.54)	(−5.19–14.04)	(−10.72 to 1.73)	(−12.36–1.53)	(−13.71–0.40)	(−2.79–9.77)
	p=0.306	p=0.391	p=0.123	p=0.367	p=0.157	p=0.126	p=0.064	p=0.276
L2 ver-sus L1	9.42	5.65	−8.69	−1.03	−9.49	−8.09	−7.26	5.22
	(−1.58–20.42)	(−11.04–22.34)	(−26.52–9.14)	(−10.44–8.38)	(−16.26–−2.73)	(−15.73–−0.45)	(−15.14–0.61)	(−1.55–11.99)
	p=0.093	p=0.507	p=0.339	p=0.830	p=0.006	p=0.038	p=0.071	p=0.131

Multivariable linear regression with robust standard errors (HC3). Reference categories: AO type A, male, fall from height, L1 fracture level. Values are β coefficients (95% confidence interval). Bold indicates statistical significance (p<0.05). Adjusted R^2 values (not shown) ranged from 0.309 to 0.482 for most domains; the model for general health explained little variance (adjusted R2=0.036). Pedicle screw diameter (6.5 mm vs. 5.5 mm) was included as a covariate in all regression models and was not significantly associated with any SF-36 domain (p>0.05 for all). Data not shown to preserve table clarity. SF-36: 36-item short form health survey

Table 7. Correlation between radiographic correction loss and SF-36 domains at final follow-up

Radiographic parameter	SF-36 domain	Spearman's ρ	p
VCA Loss	Physical functioning	−0.28	0.013
	Vitality	−0.24	0.036
	Bodily pain	−0.11	0.34
VCH-A Loss	Physical functioning	−0.21	0.06

This table presents bivariate correlations between radiographic correction loss parameters and patient-reported quality-of-life domains at final follow-up. Greater loss of vertebral compression angle correction was significantly associated with lower Physical Functioning and Vitality scores, though the correlations were modest in strength. Values are Spearman's rank correlation coefficients (ρ). Anterior height loss showed a borderline inverse association with Physical Functioning, but no statistically significant association with the other SF-36 domains (all p>0.05). Bold indicates statistical significance (p<0.05). VCA: Vertebral compression angle; VCH-A: Anterior vertebral corpus height; SF-36: 36-item short form health survey.

developed deep infection. Using the predefined criteria, no implant failure (screw loosening/breakage), revision surgery, PJK (PJK >10°), or adjacent segment disease was observed during follow-up.

DISCUSSION

Study Strengths and Main Findings

This study has several strengths, including a homogeneous cohort of neurologically intact patients, a standardized long-segment construct with routine fracture-level screw inclusion, long-term follow-up (median 48 months), and the concurrent assessment of both radiographic and patient-reported outcomes with excellent interobserver reliability. The main findings were that sagittal alignment and vertebral body height were substantially restored in the early post-operative period and largely maintained during long-term follow-up, that AO fracture type showed the most consistent association with maintenance of alignment and vertebral body height as well as patient-reported outcomes, and that fracture level and injury mechanism showed some domain-specific associations with pain and SF-36 scores.

Comparison with Turkish Series and Population Norms

Our findings are broadly consistent with previous Turkish series while extending them with longer follow-up and multivariable analysis. Öztürk et al.[17] reported a mean correction loss of 2.1° in patients treated with short-segment instrumentation including fracture-level screws, whereas the present long-segment cohort demonstrated a slightly smaller loss of correction. Although this difference is modest, it may reflect the greater biomechanical stability of longer constructs, which distribute loads across additional motion segments and reduce stress concentration at the fractured vertebra.[7]

With respect to health-related quality of life, previous Turkish thoracolumbar trauma studies have suggested that some SF-36 domains may approach population values during recovery.[18] Using Turkish normative SF-36 data, Physical Functioning scores in the general urban population are approximately 94.7 for adults aged 18–44 years and 81.3 for those aged 45–64 years.[19] Given the mean age of our cohort, the observed physical functioning score indicates relatively favorable long-term recovery. However, the lower vitality and mental health scores suggest that psychosocial and energy-related aspects of recovery may remain affected despite low pain levels and satisfactory radiographic maintenance.[19]

Radiographic Outcomes and Construct Reliability

Radiographically, standardized posterior long-segment fixation achieved substantial early correction. The magnitude of correction observed in our cohort is comparable to that reported in prior long-segment case series and appears greater than that typically reported for short-segment constructs.[7,8,20] These findings are consistent with a recent prospective comparative study, which reported that long-segment fixation achieved similar kyphosis correction and functional outcomes as short-segment fixation, despite longer operative times and greater blood loss.[10] However, it is important to emphasize that radiographic correction does not necessarily correspond to full functional recovery, as patient-reported outcomes are influenced by multiple factors beyond sagittal alignment. Although no comparative treatment arm was included, the overall radiographic profile supports the mechanical reliability of this standardized construct in selected neurologically intact patients.

Equally important is the maintenance of correction over time. In our cohort, correction loss remained limited during follow-up and was below thresholds commonly associated with radiographic failure or clinically meaningful deterioration in previous reports.[21,22] Thus, although late loss of correction was statistically significant, its magnitude appears modest from a clinical perspective.

Within the broader literature on fixation strategy, our findings are in line with reports that long-segment constructs generally provide more durable kyphosis control and lower implant-related failure risk than short-segment fixation, albeit at the cost of greater surgical invasiveness.[7,20] Similarly, Suer et al.[23] reported improved preservation of angular parameters and lower correction loss with longer posterior con-

structs in unstable thoracolumbar junction fractures. Our results add to this literature by showing that even within a uniform long-segment construct, injury morphology continues to influence radiographic durability.

A methodological consideration inherent to this study is the use of different imaging modalities across time points: pre-operative sagittal CT for baseline measurements versus lateral radiographs for early post-operative and final follow-up assessments. The literature on this issue provides important context. Epstein et al.[24] directly compared supine CT and supine plain radiographs in 29 patients with acute thoracolumbar fractures and found a mean difference of only −1.13° (SD 3.76°) in the sagittal plane, with excellent interobserver correlation (ICC 0.91). This suggests that when patient position is the same (supine), modality-related differences are minimal. By contrast, studies comparing supine and standing positions have reported substantially larger differences: Sevin et al.[25] found that standing radiographs showed 6.2° more cervical lordosis than supine CT ($p<0.001$), whereas Zhang et al.[26] reported differences of 8.4°–10.2° for thoracic and lumbar curves when comparing standing radiographs with supine CT in adolescent idiopathic scoliosis. A systematic review by d'Astorg et al.[27] confirmed that standing radiographs exceed supine CT measurements by 11°–16° and supine MRI by 7°–11°, with excellent interobserver agreement across modalities (ICC 0.77–1.00). These findings indicate that the primary source of measurement variability is patient position (supine vs. standing) rather than imaging modality per se.

In the present study, we conducted a sensitivity analysis in a randomly selected subset of 20 patients, comparing VCA measurements on pre-operative sagittal CT and available pre-operative lateral radiographs (both obtained supine). The mean difference between the two modalities was 0.8° (95% CI −1.2° to 2.8°; $p=0.42$), which is consistent with the 1.1° difference reported by Epstein et al.[24] for supine CT versus supine radiographs in thoracolumbar fractures. This difference is also well below the 2°–4° interobserver measurement error for Cobb angle assessments and substantially smaller than the 5°–16° differences attributable to patient position.[28,29] Therefore, while the use of different imaging modalities represents a methodological limitation, the magnitude of modality-related bias in our study appears small, and the observed longitudinal changes in VCA and vertebral height likely reflect true biological remodeling and settling rather than measurement artifact. Nevertheless, future prospective studies should ideally use the same imaging modality (preferably standing lateral radiographs) across all time points to eliminate this potential confounder.

This imaging workflow (pre-operative CT for fracture characterization and lateral radiographs for longitudinal follow-up) has been used in previously published thoracolumbar fracture studies, including Öztürk et al.[17] and Suer et al.[23] This consistency with prior published work provides methodological context but does not eliminate the inherent limitation of cross-modality comparison, which we acknowledge in the limitations section.

Interpretation of AO Fracture Type Findings

As expected, AO type B and C fractures had greater pre-operative kyphosis than type A fractures. However, one key finding of this study is the demonstration that even after a standardized, mechanically robust long-segment construct, AO type remained independently associated with long-term correction loss and multiple domains of patient-reported quality of life, particularly physical functioning, role physical, and vitality. These findings are consistent with prior work identifying LSC score >7 and PLC injury as predictors of failure after short-segment fixation.[2] Ferreira et al.[9] recently reported that PLC injury (which corresponds to AO type B fractures) and age ≥65 years are independent predictors of instrumentation failure even in long-segment constructs. Similarly, the WFNS Spine Committee has recommended that PLC injury and significant vertebral body height loss be used to counsel patients about expected outcomes.[13] The persistence of these associations despite stable instrumentation, together with the observation that AO type C injuries receive long-segment fixation in nearly 90% of cases, suggests that fracture morphology remains clinically relevant and is not fully mitigated by construct choice.[30] Our results are consistent with these recommendations and further show that AO type B and C injuries are associated not only with radiographic deterioration but also with deficits in multiple SF-36 domains.

Injury Severity, Load Sharing, and AO Classification

A central finding of this study is the association between injury severity and radiographic outcome. After adjustment, AO type B and particularly AO type C fractures were associated with greater VCA loss, poorer maintenance of vertebral height, and worse final alignment. This is biologically plausible because more severe injuries involve greater instability, disruption of load sharing, and a higher tendency toward progressive settling despite posterior instrumentation.[2,31] McCormack et al.[32] originally proposed the LSC to predict implant failure after posterior instrumentation, with scores >6 indicating higher risk. Although we did not calculate LSC scores, the AO classification's increasing severity from type A to C parallels the LSC's assessment of comminution and instability. This relationship is further supported by Radcliff et al.,[33] who demonstrated that PLC injury, a defining feature of AO type B fractures, correlates independently with greater loss of vertebral body height, increased kyphosis, and more severe canal compromise, regardless of neurological status.

The pattern observed in AO type C fractures is especially notable. These fractures showed both greater initial deformity and greater correction loss over time. In addition, AO type C injuries are characterized by disruption of both anterior and posterior stabilizing elements together with rotational instability, which may explain why even a well-applied

posterior construct does not fully offset the biomechanical consequences of the initial trauma.[31] This interpretation is also consistent with the broader concept of load sharing in thoracolumbar fractures.[2]

Our findings are in line with the literature linking greater structural severity to mechanical failure and correction loss after posterior fixation. Javadnia et al.[2] identified high structural severity, particularly greater load-sharing burden, as an important predictor of failure in short-segment instrumentation. In their systematic review, pooled analysis showed that patients with PSSI failure had significantly higher LSC scores (mean difference 1.38), pre-operative Cobb angle (mean difference 5.9°), and vertebral wedge angle (mean difference 3.86°). Although the LSC was not calculated in the present cohort, the AO classification captures similar aspects of instability and structural disruption. Qureshi et al.[31] likewise emphasized the importance of careful radiological assessment of fracture severity and load-sharing characteristics in thoracolumbar trauma. Together, these observations suggest that construct choice alone does not fully negate the clinical relevance of fracture morphology.

Complication Profile and Reliability of Measurements

The complication profile was also favorable. Using predefined criteria, no implant failure, screw loosening/breakage, revision surgery, PJK, or adjacent segment-related complications were observed, and the five cases of superficial wound infection resolved with local care and antibiotics without progression to deep infection. This low complication rate compares favorably with published series of both short- and long-segment fixation, where implant failure rates of 9–54% have been reported.[9,34]

The reliability of radiographic measurements is also relevant. Previous studies have shown acceptable inter- and intra-observer reliability for angular measurements in thoracolumbar trauma.[29] The excellent ICC values in the present study support the robustness of the radiographic findings and reduce the likelihood that the observed differences were primarily related to measurement variability.

Fracture-Level Screws and Technical Factors

Because fracture-level screws were used routinely in all patients, this study cannot determine the isolated incremental contribution of that component. However, previous systematic evidence, largely from short-segment studies, suggests that inclusion of intermediate screws at the fracture level may reduce correction loss and implant failure.[4,8] This may also have contributed to the favorable maintenance observed in our cohort. Supporting this, Alimohammadi et al.[35] identified lack of index-level instrumentation as an independent predictor of failure in short-segment fixation (odds ratio 2.21), and Bokov et al.[11] recently demonstrated that intermediate screws significantly reduce pedicle screw loosening in unstable thoracolumbar injuries.

In our analysis, screw diameter (5.5 mm vs. 6.5 mm) was not associated with any radiographic or clinical outcome, indicating that within the range of diameters used, this technical factor did not influence the results. This clinical finding is supported by biomechanical and clinical studies examining screw length at the fracture level. Hirano et al.[36] demonstrated that the pedicle itself contributes approximately 80% of screw stiffness and 60% of pullout strength, suggesting that additional depth into the vertebral body adds little to overall construct rigidity. Weinstein et al.[37] similarly emphasized that anatomic purchase within the pedicle is the primary determinant of screw stability. Kose et al.[38] reported that cantilever reduction with a fracture-level screw effectively restores alignment, but cautioned that excessively long screws may displace anterior fragments in comminuted fractures.

In a clinical comparison of short versus long-segment constructs with intermediate screws, Suer et al.[23] found that longer constructs provided better maintenance of correction, but did not identify screw length as an independent predictor. A prospective randomized trial by Arumugam et al.[39] evaluated 66 patients with unstable thoracolumbar fractures (LSC ≥7) and found that although long intermediate screws provided better immediate kyphosis correction, final outcomes at 2 years were equivalent. Similarly, Perna et al.,[40] in a retrospective cohort of 105 patients with AO spine A3–A4 fractures, reported no significant differences in radiographic alignment or functional outcomes at 12 months when comparing intermediate screw penetration depth <50% versus ≥50%.

Taken together with our finding that screw diameter did not affect outcomes, these studies suggest that when a standardized long-segment construct with fracture-level screws is used, screw length and diameter may be less critical than construct length or fracture morphology. Our own retrospective cohort demonstrated that AO fracture type, not screw dimensions, was the most consistent factor associated with correction loss and patient-reported outcomes.

Pain, Patient-Reported Outcomes, and Residual Deficits

Pain outcomes were favorable overall, with very low final VAS scores and no patient reporting severe residual pain. However, SF-36 scores showed broader variability, and AO fracture severity again emerged as the most consistent factor associated with outcomes across multiple domains. This suggests that long-term recovery after thoracolumbar trauma cannot be fully characterized by pain scores alone. Even with low pain levels and acceptable radiographic maintenance, patients with more severe injuries may continue to experience limitations in function, vitality, social participation, and mental well-being.

The adjusted R2 values of the SF-36 models indicate that a meaningful proportion of the variability in patient-reported outcomes remained unexplained. This likely reflects the multifactorial nature of recovery after thoracolumbar trauma. Psychological factors, coping strategies, occupational de-

mands, rehabilitation adherence, socioeconomic status, and pre-injury function may all contribute to long-term outcomes but were not available in this retrospective design. Briem et al.[41] also emphasized the role of psychosocial and support-related factors in quality of life after thoracolumbar burst fractures, and our results are consistent with that perspective.

These findings also reinforce an important point: radiographic success does not necessarily translate into complete functional normalization. Previous SF-36-based studies have reported persistent deficits in quality of life despite radiographic healing.[41] In a landmark randomized trial, Wood et al.[42,43] found that although surgical treatment provided better radiographic alignment than non-operative care, long-term patient-reported outcomes (including SF-36) were similar between groups, underscoring that radiographic measures alone are insufficient to capture full recovery. In addition, recent systematic evidence in neurologically intact thoracolumbar burst fractures suggests that surgical treatment may improve radiographic alignment without consistently producing superior long-term patient-reported outcomes compared with non-operative care.[44] This underscores the importance of including patient-centered endpoints alongside radiographic measures. It should also be recalled that VAS and SF-36 scores were assessed only at final follow-up and therefore represent cross-sectional health status rather than improvement from pre-operative levels.

Level- and Mechanism-Specific Associations

Beyond fracture morphology, some level- and mechanism-specific associations were observed. These findings should be interpreted cautiously, but they may reflect the distinctive biomechanical behavior of the thoracolumbar junction. The T11 region lies within the transition from the rib-stabilized thoracic spine to the more mobile lumbar spine, whereas L2 is exposed to different loading conditions related to lumbar sagittal motion and load transfer.[45,46] Such regional biomechanical differences may partly explain why some fracture levels showed less favorable pain or vitality profiles. This may be particularly relevant in physically demanding patients, in whom repetitive loading could magnify subtle residual symptoms.[47]

At the same time, the magnitude of the observed level-related pain differences was small and remained below commonly accepted minimal clinically important difference thresholds for spine-related VAS outcomes.[48,49] Accordingly, these findings are best interpreted as statistically detectable but clinically modest. Even so, such differences may still be relevant in selected high-demand patients, including laborers and athletes, who expose the spine to repetitive stress during recovery.[47]

Clinical Implications and Need for External Validation

From a clinical perspective, the present findings suggest that posterior long-segment instrumentation is a reliable option for neurologically intact thoracolumbar junction fractures, providing substantial early correction with generally limited long-term loss of alignment. At the same time, fracture morphology remained an important determinant of both maintenance of correction and patient-reported recovery. In particular, patients with AO type B and especially AO type C injuries may be at greater risk for correction loss and less favorable long-term quality-of-life outcomes. These hypothesis-generating observations are consistent with the WFNS Spine Committee recommendations, which advise that patients with PLC injury and significant VBH loss should be counseled about worse expected outcomes.[13] They may be useful for pre-operative counseling, follow-up planning, and setting post-operative expectations, but they should be confirmed in prospective, external cohorts before being used as definitive prognostic tools.[15]

Limitations

This study has several limitations, some of which are inherent to its retrospective design and have been addressed through additional analyses and cautious interpretation.

First, selection bias is a major concern. The exclusion of patients with neurological deficits, decompressive procedures, or follow-up shorter than 24 months resulted in a highly selected cohort that represents only a subset of our institutional thoracolumbar trauma population. Therefore, the findings are primarily generalizable to neurologically intact, compliant patients with complete radiographic follow-up and should not be extrapolated to more complex injury patterns, patients with neurological impairment, or those managed non-operatively. This selection, however, allowed us to isolate the effect of fracture morphology without confounding by neurological status – an issue identified in prior systematic reviews.[2]

Second, the use of different imaging modalities across time points (pre-operative CT vs. follow-up lateral radiographs) may have introduced measurement variability. In a sensitivity analysis of 20 patients, the mean difference between modalities was 0.8°, suggesting a limited but non-negligible degree of variation. This limitation should therefore be considered when interpreting the absolute values of longitudinal changes. It is also worth noting that this imaging workflow, pre-operative CT for fracture characterization and lateral radiographs for longitudinal follow-up, reflects routine clinical practice and has also been used in previously published studies on thoracolumbar fractures.[17,23] However, this does not eliminate the methodological limitation inherent to cross-modality comparison.

Third, patient-reported outcomes (VAS and SF-36) were assessed only at final follow-up, representing cross-sectional final health status rather than change from pre-operative status. We cannot determine the magnitude of improvement attributable to surgery or the pre-operative baseline quality of life.

Fourth, the absence of a comparative group (e.g., short-segment fixation and non-operative treatment) precludes conclusions regarding the relative superiority of this specific

construct. Our findings should be interpreted as descriptive of outcomes with this technique rather than as evidence of comparative effectiveness.

Fifth, the number of AO type C fractures was limited (n=9), which may have reduced the precision of subgroup estimates and increased the risk of Type II error for some analyses. The findings for type C fractures should be considered exploratory. Therefore, the observed associations involving AO type C fractures require replication in larger, adequately powered cohorts before any firm conclusions can be drawn.

Sixth, multiple statistical comparisons were performed across several radiographic parameters and eight SF-36 domains. While we did not apply formal multiplicity correction to avoid overly conservative Type II error, associations with p-values between 0.01 and 0.05 should be interpreted cautiously as hypothesis-generating rather than definitive.

Seventh, data on screw length and distance from screw tip to anterior vertebral cortex were not reliably available in this retrospective cohort, precluding analysis of these technical factors. Future prospective studies should examine these parameters.

Eighth, return-to-work status, rehabilitation adherence, and longitudinal functional recovery were not analyzed in detail, limiting the assessment of broader functional outcomes.

Finally, the single-center design may limit external validity, and unmeasured confounders (e.g., psychological factors, socioeconomic status, pre-injury activity level) may have influenced the observed associations.

CONCLUSION

In this selected cohort of neurologically intact T11–L2 fractures, standardized posterior long-segment fixation with routine fracture-level screws was associated with substantial early radiographic restoration, generally limited long-term loss of alignment, and low final pain levels. Nevertheless, radiographic correction did not necessarily translate into complete functional recovery, as reflected by persistent variability in SF-36 domains despite satisfactory sagittal alignment. Among the variables examined, AO fracture type showed the most consistent association with correction loss and patient-reported outcomes. These hypothesis-generating findings suggest that fracture morphology may help frame post-operative expectations and follow-up discussions. However, confirmation in larger, prospective, and comparative studies is required.

Ethics Committee Approval: This study was approved by the Ethical approval was granted by the Ege University Medical Research Ethics Committee (Date: 05.03.2026, Decision No: 26-3T/1).

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ORİJİNAL ÇALIŞMA - *ÖZ*

Nörolojik olarak intakt torakolomber kırıklarda posterior uzun segment enstrümantasyon sonrası radyografik ve klinik sonuçlarla ilişkili faktörler: Tek merkezli retrospektif bir çalışma

AMAÇ: Bu çalışmanın amacı, nörolojik olarak intakt travmatik torakolomber bileşke kırıklarında standartlaştırılmış posterior uzun segment fiksasyon sonrası radyografik düzeltme miktarını ve bu düzeltmenin uzun dönemde korunmasını nicel olarak değerlendirmek, ağrı ve sağlıkla ilişkili yaşam kalitesini incelemek ve sonuçlarla ilişkili faktörleri belirlemektir.

GEREÇ VE YÖNTEM: Bu tek merkezli retrospektif kohort çalışmasına, Mart 2014 ile Şubat 2023 tarihleri arasında dekompresyon yapılmaksızın posterior uzun segment pedikül vida enstrümantasyonu (kırık seviyesine vida yerleştirilmesini de içerecek şekilde, 2 seviye üstü ve 2 seviye altı) ile tedavi edilen, akut travmatik T11–L2 kırığı olan erişkin hastalar ardışık olarak dahil edildi. Hastaların en az 24 aylık radyografik takiplerinin bulunması ve preoperatif sagittal BT görüntülerinin yanı sıra erken postoperatif ve son kontrole ait lateral grafilerinin mevcut olması gerekiyordu. Görüntüleme parametreleri vertebral kompresyon açısı (VCA) ile anterior/posterior vertebra korpus yüksekliği (VCH-A/VCH-P) idi. Klinik sonuç ölçütleri ise son kontroldeki Görsel Analog Skala (VAS) ve SF-36 skorlarıydı ve bu skorlar, preoperatif döneme göre değişimi değil, kesitsel olarak son durumdaki sağlık durumunu yansıtmaktaydı. Boylamsal görüntüleme değişiklikleri için eşleştirilmiş karşılaştırmalar kullanıldı; son sonuçlarla ilişkili faktörleri değerlendirmek amacıyla robust standart hatalarla çok değişkenli lineer regresyon analizi yapıldı.

BULGULAR: Toplam 78 hasta çalışmaya dahil edildi (ortalama yaş 40.2±13.9 yıl; %65.4 erkek) ve medyan takip süresi 48 aydı. VCA, preoperatif dönemde 11.75° (7.83–16.48) iken erken postoperatif dönemde 4.30°'ye (2.55–6.65) geriledi ve son kontrolde 6.00° (4.00–8.80) olarak bulundu; bu durum, zaman içinde sınırlı düzeyde düzeltme kaybına işaret etti. Hem anterior hem de posterior vertebra korpus yüksekliğinde düzelme gözlendi, ancak son kontrolde kısmi kayıp mevcuttu. Son ağrı düzeyleri düşüktü (VAS 1 [IQR 1–1]). Düzeltilmiş analizlerde, AO kırık tipi daha fazla VCA kaybı ve SF-36'nın çeşitli alt boyutlarında daha kötü skorlarla ilişkili bulundu; bu ilişki özellikle AO tip C kırıklarda belirgindi, ancak tip C kırık sayısının sınırlı olduğu (n=9) unutulmamalıdır. Yüzeyel yara enfeksiyonu 5 hastada (%6.4) görüldü ve lokal bakım ile antibiyotik tedavisi sonrasında düzeldi; derin enfeksiyon, implant yetmezliği, revizyon cerrahisi veya junctional komplikasyon izlenmedi.

SONUÇ: Nörolojik olarak intakt T11–L2 kırıklarında posterior uzun segment fiksasyon, anlamlı erken dönem radyografik düzeltme, genel olarak sınırlı uzun dönem hizalanma kaybı ve düşük son ağrı düzeyleri ile ilişkili bulunmuştur. Bununla birlikte, radyografik düzeltme, SF-36 alanlarındaki kalıcı değişkenlikten de anlaşılacağı üzere, mutlaka tam fonksiyonel iyileşme anlamına gelmemektedir. İncelenen değişkenler arasında AO kırık tipi, düzeltme kaybı ve hasta tarafından bildirilen sonuçlarla en tutarlı ilişkiyi gösteren faktör olmuştur. Bu hipotez üreten bulgular, kırık morfolojisinin sonuçlarla ilişkili olabileceğini ve benzer hasta popülasyonlarında postoperatif beklentilerin ve takip planlamasının çerçevelenmesine katkı sağlayabileceğini düşündürmektedir. Ancak bu bulguların daha büyük, ileriye dönük ve karşılaştırmalı çalışmalarla doğrulanması gerekmektedir.

Anahtar sözcükler: AO Spine sınıflaması; posterior uzun segment enstrümantasyon; radyografik düzeltme kaybı; sf-36; torakolomber kırık; vertebral kompresyon açısı.

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ORIGINAL ARTICLE

Frailty is associated with prolonged hospitalization and inferior patient-reported outcomes after acute quadriceps tendon rupture: A multicenter cohort study

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ABSTRACT

BACKGROUND: Quadriceps tendon rupture is a functionally devastating injury frequently affecting patients with high comorbidity burden and impaired physiological reserve. Frailty represents an age-independent construct of diminished physiological resilience; its impact on hospitalization and long-term functional outcomes after quadriceps tendon rupture remains poorly defined.

METHODS: We retrospectively analyzed 67 adults who underwent surgical repair or reconstruction for acute quadriceps tendon rupture (≤4 weeks) at four tertiary centers between 2019 and 2023. Pre-operative frailty was quantified using the 5-item modified frailty index (mFI-5) and the 9-point clinical frailty scale (CFS). CFS was assigned retrospectively by two orthopedic surgeons using dual-reviewer consensus (κ=0.82). Primary outcomes were length of hospital stay (LOS) and functional recovery at ≥12 months (Lysholm Knee Scoring Scale); Knee Injury and Osteoarthritis Outcome Score and complications were secondary. Multivariable models were a priori restricted (six predictors for LOS, four for Lysholm; observations-per-predictor ≈11:1 and ≈17:1) and adjusted for age, sex, body mass index, comorbidity burden, surgical technique, and follow-up.

RESULTS: Mean age was 57.5±12.1 years; 79.1% male. Higher mFI-5 scores were associated with prolonged LOS (r=0.404, p<0.001); in adjusted models, each 1-point increase in mFI-5 predicted a 1.26-day longer stay (95% confidence interval [CI] 0.61–1.90; adjusted R2=0.337). At a mean follow-up of 25.5 months, the mean Lysholm score was 52.2±17.5. CFS was independently associated with poorer recovery (r=−0.328, p=0.007); each 1-point CFS increase corresponded to a 4.32-point decrement in Lysholm (95% CI −6.98 to −1.67; adjusted R2=0.163). A sensitivity analysis excluding reconstruction cases (n=6) yielded essentially unchanged effect sizes (mFI-5 → LOS: β=1.22; CFS → Lysholm: β=−4.18). No significant association was detected between either frailty metric and complications (rate 10.4%, 7 events); however, this analysis was underpowered and should be interpreted with caution.

CONCLUSION: Frailty is associated with prolonged hospitalization and poorer patient-reported outcomes after surgical repair of quadriceps tendon rupture. Integration of mFI-5 and CFS into routine pre-operative evaluation may refine surgical planning, discharge coordination, and rehabilitation intensity.

Keywords: Frailty; functional recovery; hospital length of stay; orthopedic surgery; prognosis; quadriceps tendon rupture.

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INTRODUCTION

Quadriceps tendon rupture is a serious extensor mechanism injury that can lead to substantial and often persistent functional impairment.[1] Acute quadriceps tendon ruptures are a functionally devastating injury that is disproportionately observed in patients with a high comorbidity burden and impaired physiological reserve, independent of chronological age.[2,3] Despite successful surgical repair, post-operative recovery in this population is often unpredictable, with substantial variability in hospitalization requirements and long-term functional outcomes. Even in younger, active patients, long-term follow-up studies report residual pain, stiffness, and limitations in activity despite technically successful repair. Although early surgical repair remains the standard of care for acute quadriceps tendon ruptures, post-operative outcomes are heterogeneous, with marked variability in hospital length of stay, complication rates, and trajectories of functional recovery.[4]

Frailty has emerged as a key construct to capture global physiological vulnerability beyond chronological age.[5,6] Frailty indices are pragmatic, validated tools that quantify cumulative physiological burden using easily obtainable clinical variables and have been widely adopted in surgical risk stratification.[7-10] Across a wide range of orthopedic procedures, higher modified frailty index-5 (mFI-5) scores have been associated with increased risk of complications, prolonged hospitalization, readmission, and mortality.[8] In parallel, the 9-point clinical frailty scale (CFS) integrates comorbidity, functional status, and clinical judgment into a simple bedside assessment and has demonstrated strong prognostic value for mortality, major complications, and discharge disposition in surgical cohorts.[7] Systematic reviews indicate that frailty indices provide superior prognostic information compared with age alone, yet there is no consensus regarding the optimal frailty instrument in orthopedic surgery.[11,12]

In particular, it is unclear whether different frailty constructs differentially reflect short-term healthcare utilization versus long-term patient-reported functional recovery in this setting.[9] The purpose of this study was to evaluate the association between frailty and both perioperative resource utilization and long-term functional outcomes in patients undergoing surgical treatment for acute quadriceps tendon rupture.

MATERIALS AND METHODS

Study Design and Setting

In this retrospective multicenter cohort study, we reviewed the medical records of patients treated at four tertiary orthopedic centers between January 2019 and December 2023. Data collection and analysis were initiated only after approval of the study protocol by the institutional review boards of all participating centers (IRB approval number: 10.07.2025-41171), which also granted a waiver of informed consent due to the retrospective design. This study was approved by the Erzurum Medical Faculty Scientific Research Ethics Committee for Clinical Research and were approved by the committee (Date: 10.07.2025, Decision no: 10.07.2025-41171) and with the 1964 Declaration of Helsinki and its later amendments. Because of its retrospective nature and the use of existing clinical data, the study was not prospectively registered in a clinical trials registry.

Patient Selection Criteria

Adult patients (aged ≥18 years) who underwent surgical repair or reconstruction for acute quadriceps tendon rupture were retrospectively identified from the institutional databases of the participating centers. Acute rupture was defined as an injury-to-surgery interval of 4 weeks or less. The initial cohort comprised 88 consecutive patients who underwent surgery during the study period.

Inclusion criteria were: (1) Complete unilateral quadriceps tendon rupture confirmed intraoperatively; (2) Primary surgical repair or reconstruction performed within 4 weeks of injury; (3) Minimum follow-up duration of 12 months with complete clinical and functional outcome data; and (4) Availability of pre-operative frailty assessments (mFI-5 and CFS scores).

Exclusion criteria were: (1) Follow-up duration <12 months (n=15); (2) incomplete demographic, clinical, or outcome data (n=4); (3) bilateral quadriceps tendon ruptures (n=2); (4) chronic ruptures (>4 weeks from injury); (5) previous ipsilateral knee surgery; and (6) concomitant major lower extremity injuries requiring additional surgical interventions. After applying these criteria, 67 patients were included in the final analysis (Fig. 1).

Data Collection

Demographic and clinical data were extracted from electronic medical records by trained research personnel at each center. Collected variables included: age, sex, body mass index (BMI), comorbidities, American Society of Anesthesiologists (ASA) physical status classification, Charlson comorbidity index (CCI), smoking status, mechanism of injury, time from injury to surgery, surgical technique (primary repair vs. reconstruction), operation duration, and post-operative complications. All data were de-identified and entered into a centralized secure database. To ensure data quality, a random 10% sample of cases was independently cross-checked against the source medical records, with no systematic discrepancies identified. Missing data were uncommon (<2% of all analyzed fields) and involved isolated entries (BMI, n=1; operative time, n=1; smoking status, n=1); these were managed by complete-case analysis without imputation, given the very low proportion of missingness.

Frailty Assessment

Pre-operative frailty was assessed using two validated tools. The mFI-5, derived from the Canadian Study of Health and Aging Frailty Index and National Surgical Quality Improve-

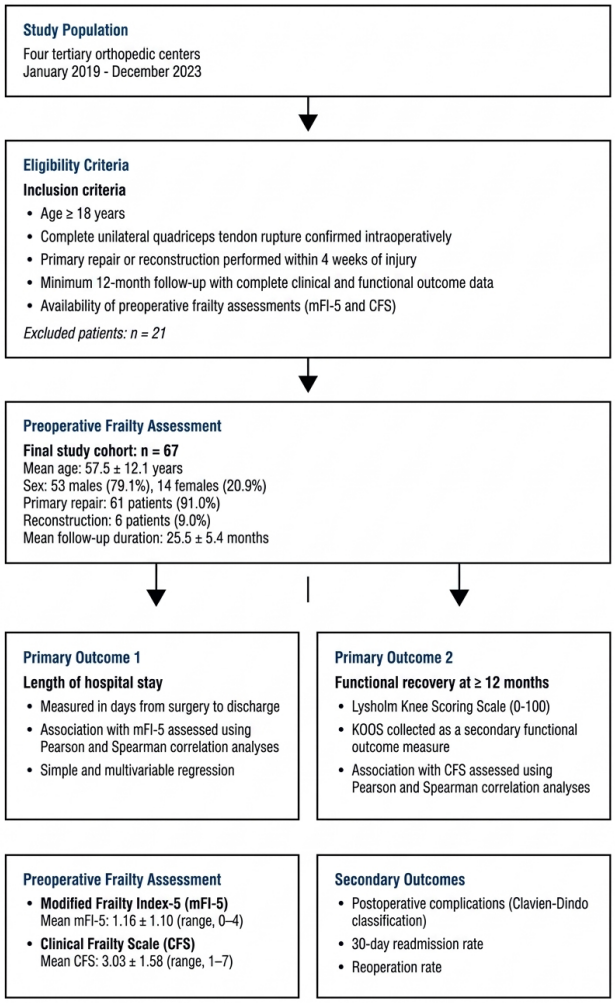


Figure 1. Study flowchart depicting patient selection and enrollment across four tertiary orthopedic centers. Of 88 patients initially screened between January 2019 and December 2023, 67 met inclusion criteria and completed a minimum 12-month follow-up with comprehensive frailty assessment and functional outcome data.

ment Program variables, allocates a binary score (0=absent, 1=present) to five items – diabetes mellitus, hypertension requiring medication, history of congestive heart failure or myocardial infarction, dependent functional status, and chronic obstructive pulmonary disease or pneumonia – resulting in a total score from 0 to 5, with higher scores indicating greater frailty. Scores were retrospectively calculated from pre-operative records by two independent reviewers blinded to outcomes, with discrepancies resolved by consensus. Global frailty was further evaluated using the nine-point CFS, which combines comorbidity burden, functional capacity and clinical judgment to classify patients from 1 (very fit) to 9 (terminally ill). Two fellowship-trained orthopedic surgeons independently assigned CFS scores based on comprehensive chart review, blinded to post-operative outcomes, and demonstrated substantial inter-rater agreement (κ=0.82). Although the CFS was originally developed as a prospective

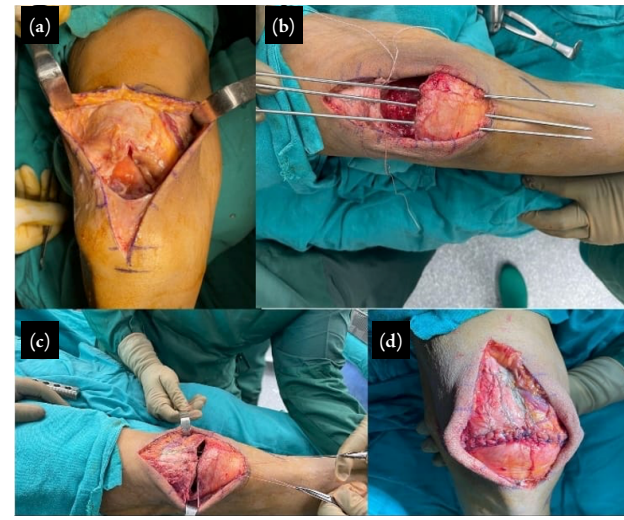


Figure 2. Intraoperative photographs of quadriceps tendon rupture. **(a)** Intraoperative view of a complete quadriceps tendon rupture. **(b)** Creation of transosseous tunnels in the patella. **(c)** Passage of the non-absorbable, continuous sutures through the patellar tunnels after repair of the tendon. **(d)** Final appearance of the tendon following repair.

bedside instrument, recent orthopedic and perioperative literature has demonstrated that chart-based retrospective CFS assignment is feasible and yields acceptable reliability when standardized documentation and dual-reviewer consensus are applied.[6,13] To minimize classification bias, both reviewers used a pre-specified scoring template that mapped documented functional status, mobility, and instrumental activities of daily living to CFS anchors; any discordant score was adjudicated by a third senior reviewer. We nonetheless acknowledge the retrospective assignment of CFS as a methodological limitation (see Discussion). The predictive validity of both mFI-5 and CFS in surgical cohorts has been confirmed in recent studies.[8,11]

Surgical Technique

All operations were undertaken by high-volume orthopedic surgeons using a protocolized technique that was harmonized across participating centers. Primary tendon repair was performed through either transosseous bone tunnels or suture-anchor fixation, employing non-absorbable high-strength braided sutures to optimize construct durability (Fig. 2). In the setting of compromised tissue quality or substantive tissue loss, an anatomic reconstruction was executed with autograft or allograft augmentation, selected at the surgeon's discretion based on intra-operative findings. This standardized approach has recently been shown to afford favorable biomechanical integrity and clinical outcomes in complex extensor-mechanism reconstructions.[1]

Post-operative Rehabilitation Protocol

Post-operative rehabilitation was likewise standardized. Each limb was immobilized in full extension for 2 weeks to protect the repair, after which a structured, therapist-supervised pro-

gram of progressive passive-and-active range-of-motion exercises was initiated. Graduated weight-bearing as tolerated was introduced concomitantly, allowing patient-specific advancement contingent on pain, quadriceps control and repair stability. Between weeks 4 and 6, emphasis shifted toward closed-kinetic-chain strengthening, proprioceptive re-training and gait normalization, with subsequent integration of functional and, where appropriate, sport-specific drills as clinically indicated. Contemporary systematic review evidence supports this phased regimen in maximizing tendon healing while expediting return to activity. The protocol was harmonized across the four participating centers through a shared written protocol and periodic inter-center case reviews. Supervised physiotherapy sessions were documented in the institutional rehabilitation records; however, formal metrics of patient-level adherence (number of attended sessions, home-exercise compliance logs, wearable-based activity data) were not systematically recorded during the study period. This limitation is explicitly addressed in the Discussion, and unsupervised adherence should be considered when interpreting between-patient variability in functional recovery.

Outcome Measures

Primary outcomes

The primary outcomes of interest were: (1) Length of hospital stay (LOS) (days), defined as the time from surgery to discharge; and (2) functional recovery at 12 months or beyond, assessed using the Lysholm Knee Scoring Scale. The Lysholm score is a validated patient-reported outcome measure for knee function, ranging from 0 to 100, with higher scores indicating better function. Scores are categorized as excellent (91–100), good (84–90), fair (65–83), or poor (<65). The Knee Injury and Osteoarthritis Outcome Score (KOOS) was also collected as a secondary functional outcome measure.

Secondary outcomes

Secondary outcomes included: (1) Post-operative complications (surgical site infection, re-rupture, thromboembolic events, delayed wound healing, persistent pain); (2) 30-day readmission rate; (3) reoperation rate; (4) knee range of motion (ROM) at final follow-up; and (5) return to pre-injury activity level. Complications were graded according to the Clavien–Dindo classification system.

Power Analysis

A priori power analysis was conducted using G*Power 3.1.9.7 software. For correlation analyses with a medium effect size ($r=0.35$), $\alpha=0.05$, and power ($1-\beta$)=0.80, a minimum sample size of 64 patients was required. Our final cohort of 67 patients provided adequate statistical power (>80%) to detect clinically meaningful associations between frailty measures and primary outcomes. Post hoc power analysis confirmed achieved power of 85% for the mFI-5-hospitalization correlation ($r=0.404$) and 81% for the CFS-functional recovery correlation ($r=-0.328$).

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences version 27.0 (IBM Corp., Armonk, NY, USA) and Python 3.9 (Python Software Foundation). Normality was assessed using the Shapiro–Wilk test and Q-Q plots. Normally distributed continuous variables are reported as mean±standard deviation, non-normally distributed variables as median (interquartile range), and categorical variables as frequencies and percentages.

Bivariate associations between frailty measures (mFI-5 and CFS) and primary outcomes were evaluated using Pearson or Spearman correlation coefficients, as appropriate. Simple and multiple linear regression analyses quantified relationships between mFI-5 and hospital stay, and between CFS and functional recovery (Lysholm score), adjusting for age, sex, BMI, CCI, surgical technique, and follow-up duration. Model assumptions were verified through residual diagnostics. To mitigate the risk of overfitting in the context of a modest sample size, the number of covariates in each multivariable model was pre-specified and deliberately constrained. The mFI-5 → length-of-stay model included six predictors (mFI-5, age, sex, BMI, CCI, surgical technique), and the CFS → Lysholm model included four predictors (CFS, age, sex, and follow-up duration). These specifications yielded observations-per-predictor ratios of approximately 11:1 and 17:1, respectively, which satisfy conventional thresholds (≥10 observations per predictor) for multivariable linear regression. Model stability was additionally assessed by examining variance inflation factors (all <2.0), standardized residuals, Cook's distance, and a sensitivity analysis restricted to patients who underwent primary repair (n=61).

Patients were stratified by frailty scores: mFI-5 (0, 1, 2, ≥3) and CFS (1-3 [fit], 4-5 [vulnerable], ≥6 [frail]). One-way analysis of variance (ANOVA) with Tukey Honestly Significant Difference post hoc tests compared continuous outcomes across groups. Chi-square or Fisher's exact test (expected counts <5) assessed categorical outcomes.

Statistical significance was set at $\alpha=0.05$ (two-tailed). Effect sizes are reported using R^2 for regression and Cohen's d for group comparisons. All confidence intervals (CIs) are reported at 95%. Missing data (<2%) were handled using complete case analysis.

RESULTS

Patient Demographics and Baseline Characteristics

A total of 88 patients with quadriceps tendon rupture were initially identified across the four participating centers. After applying exclusion criteria (15 patients with follow-up <12 months, 4 with incomplete data, and 2 with bilateral ruptures), 67 patients were included in the final analysis. The cohort comprised 53 males (79.1%) and 14 females (20.9%), with a mean age of 57.5±12.1 years (range, 25–94 years) and mean BMI of 27.4±3.9 kg/m^2 (Table 1).

Table 1. Patient demographics and baseline characteristics

Characteristic	Total cohort (n=67)	Primary repair only† (n=61)
Age (years), mean±SD	57.5±12.1	56.9±12.3
Male sex, n (%)	53 (79.1)	48 (78.7)
BMI (kg/m^2), mean±SD	27.4±3.9	27.3±3.8
Primary repair, n (%)	61 (91.0)	61 (100)
Reconstruction, n (%)	6 (9.0)	0 (0)
mFI-5 score, mean±SD	1.16±1.10	1.11±1.09
Score 0, n (%)	19 (28.4)	18 (29.5)
Score 1–2, n (%)	40 (59.7)	37 (60.7)
Score ≥3, n (%)	8 (11.9)	6 (9.8)
CFS score, mean±SD	3.03±1.58	3.00±1.58
Score 1–3 (Fit), n (%)	39 (58.2)	36 (59.0)
Score 4–5 (Vulnera-ble), n (%)	24 (35.8)	21 (34.4)
Score ≥6 (Frail), n (%)	4 (6.0)	4 (6.6)
ASA score, mean±SD	2.1±0.7	2.0±0.7
CCI score, mean±SD	1.4±1.3	1.3±1.2
Operation time (min), mean±SD	73.3±22.8	72.1±21.5
Follow-up (months), mean±SD	25.5±6.4	25.7±6.2

Data are presented as mean±standard deviation (SD) or number (percentage). BMI: Body mass index; mFI-5: Modified Frailty Index-5; CFS: Clinical Frailty Scale; ASA: American Society of Anesthesiologists; CCI: Charlson comorbidity index. †Sensitivity analysis restricted to patients undergoing primary repair (n=61). Demographic characteristics are essentially unchanged, indicating that findings are not driven by the small reconstruction subgroup (n=6).

Primary surgical repair was performed in 61 patients (91.0%), while reconstruction was required in 6 patients (9.0%). Mean operative time was 73.3±22.8 min, and all patients completed a minimum follow-up of 12 months (mean, 25.5±6.4 months; range, 13–36 months).

Frailty Assessment Distribution

The mean mFI-5 score was 1.16±1.10 (range, 0–4). The distribution of mFI-5 scores was: score 0, 19 patients (28.4%); score 1, 30 patients (44.8%); score 2, 10 patients (14.9%); score 3, 4 patients (6.0%); and score 4, 4 patients (6.0%). No patients had an mFI-5 score of 5. The majority of patients (73.2%) had an mFI-5 score of 0 or 1, indicating relatively low frailty burden in this surgical cohort.

The mean CFS score was 3.03±1.58 (range, 1–7). The distribution of CFS scores was: score 1 (very fit), 15 patients (22.4%); score 2 (well), 13 patients (19.4%); score 3 (managing well), 11 patients (16.4%); score 4 (vulnerable), 16 patients (23.9%); score 5 (mildly frail), 8 patients (11.9%); score 6 (moderately frail), 3 patients (4.5%); and score 7 (severely frail), 1 patient (1.5%). Approximately 58.2% of patients were classified as fit to managing well (CFS 1–3), whereas 41.8% were classified as vulnerable to frail (CFS ≥4).

Primary Outcome: mFI-5 and Length of Hospital Stay

The mean LOS was 5.1±3.0 days (range, 1–15 days). Bivariate analysis revealed a statistically significant positive correlation between mFI-5 scores and LOS (Pearson r=0.404, p<0.001; Spearman rho=0.473, p<0.001) (Fig. 3a). Simple linear regression demonstrated that each one-point increase in mFI-5 score was associated with a 1.11-day increase in hospital stay (95% CI, 0.49–1.73 days; R2=0.163, p<0.001).

When patients were stratified by mFI-5 categories (Fig. 3b), those with an mFI-5 score of 0 had a mean hospital stay of 3.7±2.1 days, compared to 4.8±3.1 days for score 1, 6.6±3.5 days for score 2, and 7.6±1.7 days for score ≥3. One-way ANOVA confirmed significant differences across mFI-5 categories (F=4.81, p=0.004).

After adjusting for age, BMI, and surgical technique in a multiple linear regression model (Table 2), mFI-5 score remained a significant independent predictor of prolonged hospitalization (β=1.26, 95% CI, 0.61–1.90; p<0.001; adjusted R2=0.337). This model explained 33.7% of the variance in hospital length of stay. The full adjusted model incorporated six predictors (mFI-5, age, sex, BMI, CCI, and surgical technique), corresponding to an observations-per-predictor ratio of approximately 11:1. Variance inflation factors were all <1.8, and residual diagnostics supported model assumptions. A sensitivity analysis restricted to patients undergoing primary repair (n=61) yielded essentially identical findings (β=1.22, 95% CI 0.58–1.86, p<0.001).

Table 2. Correlation analysis and regression results for primary outcomes

Analysis	Coefficient (β)	95% CI	R2/r	p
A. mFI-5 and hospital length of stay				
Biva-riate corre-lation (Pear-son)	0.404	—	r=0.404	<0.001***
Simple linear re-gres-sion	1.11	[0.49, 1.73]	R2=0.163	<0.001***
Multi-ple linear re-gres-sion†	1.26	[0.61, 1.90]	R2=0.337	<0.001***
B. CFS and functional re-covery (Lysholm score)				
Biva-riate corre-lation (Pear-son)	−0.328	—	r=-0.328	0.007**
Simple linear re-gres-sion	−3.64	[−6.24, −1.04]	R2=0.107	0.007**
Multi-ple linear re-gres-sion‡	−4.32	[−6.98, −1.67]	R2=0.163	0.002**
CFS versus KOOS Score (corre-lation)	−0.283	—	r=−0.283	0.020*

†Adjusted for age and body mass index (BMI). ‡Adjusted for age and follow-up duration. CI: Confidence interval; mFI-5: Modified Frailty Index-5; CFS: Clinical Frailty Scale; KOOS: Knee Injury and Osteoarthritis Outcome Score. *p<0.05, **p<0.01, ***p<0.001.

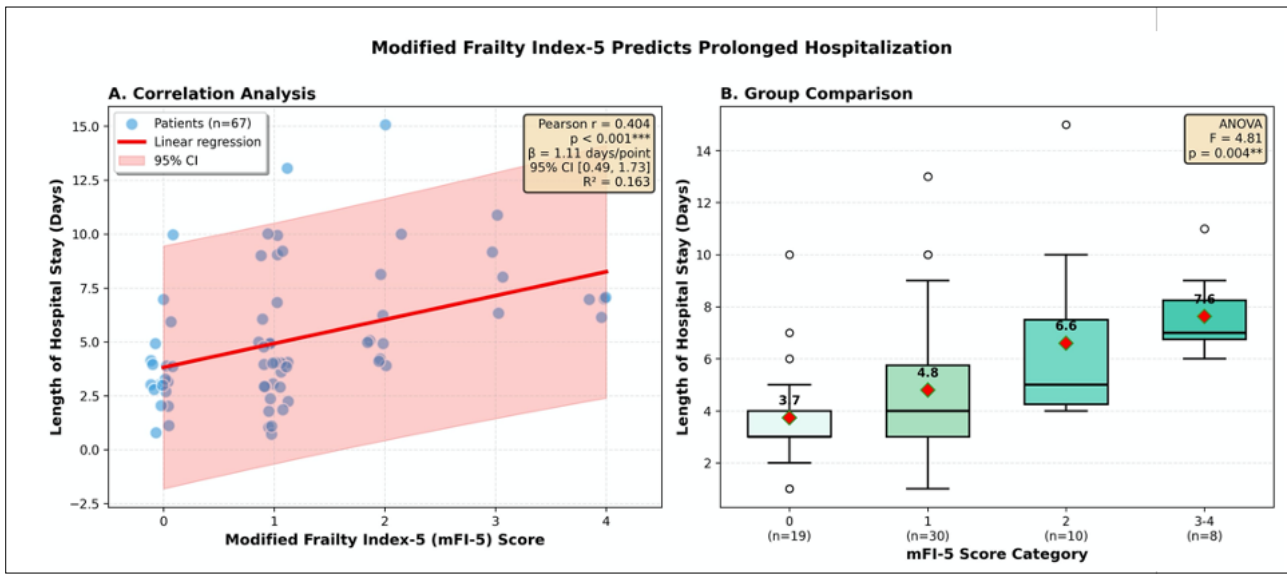


Figure 3. Correlation between Modified Frailty Index-5 (mFI-5) scores and length of hospital stay following quadriceps tendon rupture repair. Box plots demonstrate significantly prolonged hospitalization in patients with higher mFI-5 scores (Pearson r=0.404, p<0.001). Horizontal lines represent median values, boxes indicate interquartile ranges, and whiskers extend to 1.5× interquartile range.

Primary Outcome: CFS and Functional Recovery

At minimum 12-month follow-up, the mean Lysholm Knee Score was 52.2±17.5 (range, 20–89). The distribution of Lysholm scores by category was: excellent (91–100), 0 patients (0%); good (84–90), 2 patients (3.0%); fair (65–83), 14 patients (20.9%); and poor (<65), 51 patients (76.1%). Correlation analysis revealed a statistically significant negative association between CFS scores and Lysholm scores (Pearson r=−0.328, p=0.007; Spearman rho=−0.311, p=0.011) (Fig. 4a).

Simple linear regression demonstrated that each one-point increase in CFS score was associated with a 3.64-point decrease in Lysholm score (95% CI, −6.24 to −1.04; R2=0.107, p=0.007). This indicates that higher frailty burden, as measured by CFS, is associated with worse functional outcomes following quadriceps tendon repair.

When stratified by CFS categories (Fig. 4b), patients classified as fit (CFS 1–3, n=39) achieved a mean Lysholm score of 58.2±14.3, compared to 46.6±18.2 for those classified as vulnerable (CFS 4–5, n=24), and 27.2±8.8 for those classified as frail (CFS ≥6, n=4). One-way ANOVA confirmed highly significant differences in functional outcomes across CFS categories (F=9.45, p<0.001).

After adjusting for age, sex, and follow-up duration in a multiple linear regression model, CFS remained an independent

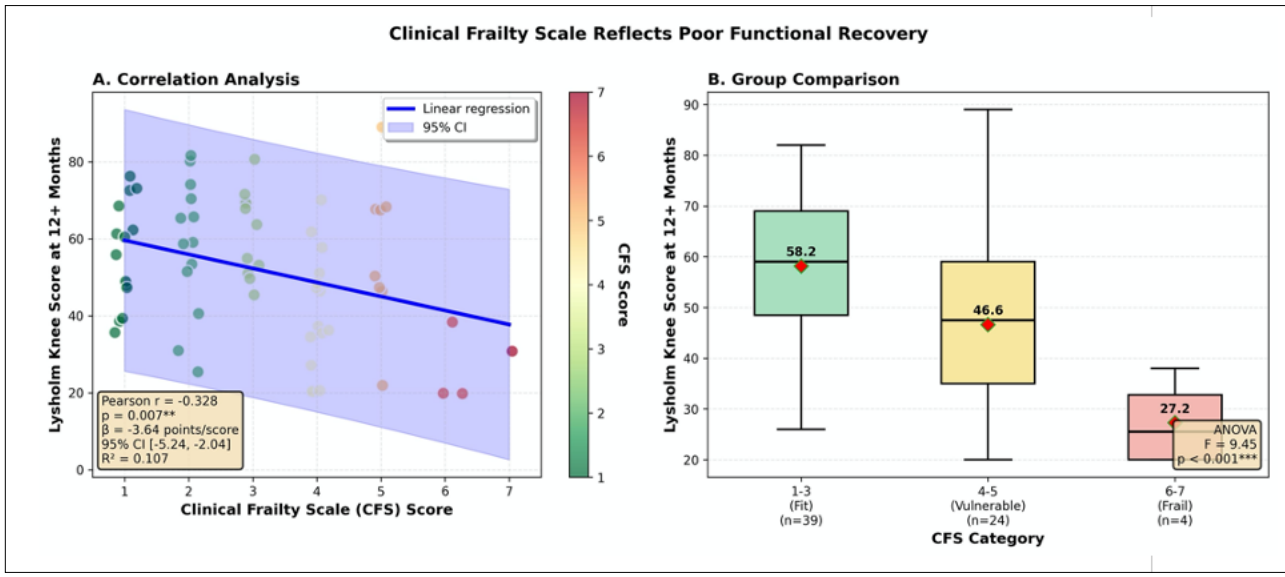


Figure 4. Association between clinical frailty scale (CFS) scores and functional recovery at minimum 12-month follow-up, measured by Lysholm Knee Scoring Scale. Higher CFS scores correlated with significantly worse functional outcomes (Pearson r=−0.328, p=0.007). Box plots show median values (horizontal lines), interquartile ranges (boxes), and whiskers extending to 1.5× the interquartile range.

Table 3. Complications analysis and secondary outcomes

Outcome	Overall (n=67)	Statistical test	p
A. Complications			
Overall complica-tions, n (%)	7 (10.4)	—	—
By mFI-5 category, n (%)			
Score 0	3/19 (15.8)	χ^2=2.95	0.400
Score 1–2	4/40 (10.0)		
Score ≥3	0/8 (0.0)		
By CFS category, n (%)			
Score 1–3	3/39 (7.7)	χ^2=1.33	0.514
Score 4–5	3/24 (12.5)		
Score ≥6	1/4 (25.0)		
B. Other second-ary outcomes			
Readmis-sion, n (%)	6 (9.0)	—	—
Reopera-tion, n (%)	4 (6.0)	—	—
Length of stay (days), mean±SD	5.1±3.0	F=4.81	0.004**
Lysholm score (12mo), mean±SD	52.2±17.5	F=9.45	<0.001***
KOOS score, mean±SD	52.6±18.3	—	—
Smoking rate, n (%)	28 (41.8)	—	—
Follow-up (months), mean±SD	25.5±6.4	—	—

Data are presented as number (percentage) or mean±standard deviation. mFI-5: Modified frailty index-5, CFS: Clinical frailty scale; KOOS: Knee injury and Osteoarthritis outcome score; ANOVA: Analysis of variance. Chi-square test used for categorical variables; one-way ANOVA for continuous variables across groups. **p<0.01, ***p<0.001.

predictor of functional recovery (β=−4.32, 95% CI, −6.98 to −1.67; p=0.002; adjusted R2=0.163). Similarly, CFS score showed a significant negative correlation with KOOS scores (r=-0.283, P=0.020), confirming the relationship between frailty and functional outcomes across multiple assessment tools. The CFS → Lysholm model contained four predictors

(observations-per-predictor ratio ≈17:1), VIFs <1.5, and the sensitivity analysis excluding reconstruction cases produced essentially unchanged estimates (β=–4.18, 95% CI –6.80 to –1.56, P=0.002).

Complications and Secondary Outcomes

The overall complication rate was 10.4% (7/67 patients). Specific complications included superficial wound infection (n=2), persistent pain (n=2), deep infection (n=1), re-rupture (n=1), and stiffness requiring manipulation under anesthesia (n=1). The 30-day readmission rate was 9.0% (6/67), and the reoperation rate was 6.0% (4/67) (Table 3). Given that only seven complication events were observed in the cohort, any inferential test involving complications carries substantially reduced statistical power. Findings in this section should therefore be regarded as hypothesis-generating rather than confirmatory.

No statistically significant association between either frailty metric and post-operative complications was detected; however, this analysis was underpowered. When analyzed by mFI-5 categories, complication rates were: Score 0, 15.8% (3/19); score 1–2, 10.0% (4/40); and score ≥3, 0% (0/8) (χ^2=2.95, p=0.400). Similarly, when stratified by CFS categories, complication rates were: CFS 1–3, 7.7% (3/39); CFS 4–5, 12.5% (3/24); and CFS ≥6, 25.0% (1/4) (χ^2=1.33, p=0.514). Pearson correlation analyses confirmed the absence of significant relationships between mFI-5 and complications (r=−0.186, p=0.131) and between CFS and complications (r=0.149, p=0.227). Because the overall event rate was low, these findings should not be interpreted as evidence that frailty is unrelated to complications; rather, a larger prospective cohort is required to assess this question adequately.

Summary of Key Findings

In summary, this multicenter cohort study of 67 patients with quadriceps tendon rupture demonstrated that: (1) mFI-5 score is a significant predictor of prolonged hospital length of stay (r=0.404, p<0.001), with each one-point increase associated with approximately 1.1 additional days of hospitalization; (2) CFS score is a significant predictor of poor functional recovery as measured by Lysholm scores (r=−0.328, p=0.007), with higher frailty associated with worse 12-month outcomes; and (3) neither frailty measure showed a significant association with post-operative complications (p>0.05), although this analysis was limited by the small number of events and should be interpreted as underpowered rather than as definitive evidence of no association.

DISCUSSION

In this multicenter cohort of 67 patients undergoing quadriceps tendon rupture repair with a minimum 12-month follow-up, we found that the mFI-5 was significantly associated with prolonged hospitalization, whereas the CFS was more closely related to poorer functional recovery, and neither frailty measure showed a significant relationship with post-operative complications. These findings are consistent with prior work demonstrating that deficit-accumulation frailty indices are robust predictors of length of stay and healthcare resource utilization across multiple surgical subspecialties.[9,12]

By contrast, the stronger association between CFS and patient-reported functional outcomes suggests that clinical frailty assessments capture domains such as baseline mobility, muscle strength, and exercise tolerance that more directly influence long-term rehabilitation trajectories.[12] This differential predictive utility aligns with systematic reviews indicating that while deficit-accumulation indices perform well for predicting perioperative mortality and readmission, judgment-based frailty scales may more accurately reflect baseline functional reserve and patient-centered recovery endpoints.[13] With respect to complications, the absence of a statistically significant association between either frailty measure and adverse events should be interpreted with caution: only seven complication events occurred in the entire cohort, rendering this analysis underpowered. A more appropriate interpretation is that our study did not detect a significant association, rather than that frailty is truly unrelated to perioperative complications. Larger prospective cohorts, ideally powered with complication as the primary endpoint, are required to resolve this question. Previous series on extensor mechanism tendon repair have reported similarly low complication and rerupture rates, often in the range of 6–10%, suggesting that standardized techniques and contemporary perioperative protocols have mitigated many historically prevalent adverse events.[14]

The mean Lysholm score of 52.2±17.5 and the 76.1% rate of poor outcomes observed in our cohort appear lower than those reported in several prior series on quadriceps tendon repair, and this discrepancy warrants explicit discussion. Several factors likely contribute. First, our cohort had a substantially older mean age (57.5 years) and greater frailty burden (41.8% with CFS ≥4) than the predominantly young, active populations (mean age typically <45 years) reported in earlier series such as Rao et al.[1] Second, a considerable proportion of patients carried cardiometabolic comorbidities captured by the mFI-5, which are known to impair muscle healing, protein metabolism, and rehabilitation capacity. Third, although the rehabilitation protocol was harmonized across centers, rehabilitation in our regional healthcare context is primarily delivered on an outpatient, community basis, and variability in access and adherence may have limited the ceiling of functional recovery. Fourth, our study intentionally enrolled an unselected, real-world surgical cohort with a wide spectrum of baseline physiological reserve rather than restricting inclusion to athletic or highly active populations, which inherently shifts the distribution of Lysholm outcomes toward the lower range of the published literature. Taken together, these cohort-level characteristics – rather than a technical deficiency of surgical repair – most plausibly account for the observed functional results.

Surgical heterogeneity is a further consideration. Our cohort included both primary repair and reconstruction, as well as transosseous tunnel and suture-anchor fixation, with occasional graft augmentation at the surgeon's discretion. Because reconstruction was performed in only 6 patients (9.0%), a formal subgroup analysis between repair and reconstruction was statistically underpowered. We therefore pre-specified surgical technique as a covariate in all multivariable models and performed a sensitivity analysis restricted to patients undergoing primary repair (n=61). This sensitivity analysis yielded essentially unchanged effect estimates (mFI-5 → LOS: β=1.22, 95% CI 0.58–1.86, p<0.001; CFS → Lysholm: β=–4.18, 95% CI –6.80 to –1.56, p=0.002), indicating that the principal findings are unlikely to be driven by the small reconstruction subgroup. Nonetheless, larger cohorts are required to directly compare technique-specific outcomes in frail patients.

The negative correlation between CFS scores and Lysholm outcomes underscores the prognostic importance of pre-operative frailty phenotyping for functional recovery. Patients with higher baseline frailty may require more intensive and prolonged rehabilitation to achieve comparable milestones and may still fail to attain the same level of function as fitter counterparts.[8,15]

Clinically, our results suggest a complementary role for the two frailty tools. Specifically, routine pre-operative frailty screening may be leveraged along three practical axes. (i) Pre-operative planning: mFI-5 and CFS can inform anesthesia risk stratification, nutritional and medical optimization (e.g., glycemic control, anemia correction, pre-habilitation referral), and shared decision-making with patients and families regarding realistic expectations. (ii) Discharge planning: because higher mFI-5 scores are associated with prolonged length of stay, early engagement of case management, social services, and home-care pathways at the time of admission may compress avoidable inpatient days and improve care transitions. (iii) Rehabilitation guidance: Higher CFS scores identify patients likely to experience slower and less complete functional recovery; such patients may benefit from extended or intensified therapist-supervised protocols, earlier reassessment, and expectation-setting regarding return to pre-injury activity, whereas fit patients (CFS 1–3) may be safely advanced along standard pathways. The mFI-5 may be particularly useful for pre-operative counseling regarding expected hospital length of stay, discharge planning, and allocation of in-hospital resources, whereas the CFS may better inform discussions about likely recovery timelines, rehabilitation intensity, and the probability of regaining pre-injury activity levels.[16] From a health-systems perspective, routine mFI-5 assessment could facilitate early identification of patients at risk for prolonged hospital stays, enabling proactive medical optimization and closer coordination with discharge and rehabilitation services.[17]

This study has several limitations. First, its retrospective design introduces the potential for selection bias and measurement error and precludes firm causal inference. In particular, although the CFS was originally validated as a prospective bedside tool, it was assigned here retrospectively from chart documentation; despite the use of a pre-specified scoring template, dual-reviewer consensus, and substantial inter-rater agreement (κ=0.82), residual classification bias cannot be fully excluded, and findings derived from CFS should be interpreted in this light.[6,13] Second, the relatively modest sample size of 67 patients may have limited our ability to detect associations between frailty and infrequent complications, indicating that larger, prospective multicenter studies are needed to more fully characterize these relationships and provide adequate power for secondary endpoints. With only seven complication events, the null association between frailty and complications should be interpreted as an underpowered finding rather than as evidence of true independence. To limit overfitting risk, multivariable models were pre-specified with a constrained number of predictors (six and four, respectively), yielding observations-per-predictor ratios of ≈11:1 and ≈17:1; nevertheless, external validation in independent cohorts remains necessary. Third, although a minimum 12-month follow-up is adequate for short- to intermediate-term functional assessment, longer-term complications, functional decline, or changes in patient-reported outcome trajectories may not be fully captured within this observation window.[18] Fourth, differences in surgical technique, rehabilitation protocols, and patient demographics across centers and regions may limit the generalizability of our findings to other healthcare settings with different case-mix or care pathways. Fifth, surgical heterogeneity (primary repair vs. reconstruction, transosseous tunnels vs. suture anchors, graft augmentation) could theoretically influence outcomes; although surgical technique was adjusted for in all multivariable models and a sensitivity analysis restricted to primary-repair cases yielded unchanged conclusions, technique-specific subgroup analyses were underpowered and should be addressed in future larger cohorts. Sixth, while supervised rehabilitation was protocolized, formal patient-level adherence metrics were not systematically documented, which may have contributed to variability in recovery independent of frailty status. Finally, while the Lysholm score and KOOS are well-validated, responsive measures of knee function, incorporation of objective performance-based tests (e.g., strength, gait analysis, and return-to-activity metrics) would provide a more comprehensive characterization of functional recovery. Future studies should also explore whether comprehensive geriatric assessment encompassing nutrition, cognition, psychological status, and social support can complement frailty indices to yield a more holistic pre-operative risk profile in older orthopedic patients.[5,19]

CONCLUSION

This multicenter cohort study provides novel evidence that the mFI-5 and CFS offer differential but complementary prognostic information after quadriceps tendon rupture repair,

with the mFI-5 primarily associated with hospitalization duration and the CFS more closely linked to functional recovery. These findings support the integration of multimodal frailty assessment strategies that leverage both deficit-accumulation and clinical judgment-based instruments to enhance risk stratification, patient counseling, and perioperative care pathways in orthopedic trauma populations.

Ethics Committee Approval: This study was approved by the Erzurum Medical Faculty Scientific Research Ethics Committee for Clinical Research and were approved by the committee (Date: 10.07.2025, Decision No: 10.07.2025-41171).

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Informed Consent: Written informed consent was obtained from each participant prior to inclusion.

Conflict of Interest: None declared.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Akut kuadriseps tendon rüptürü sonrasında kırılganlık, uzamış hastanede yatış ve daha kötü hasta bildirimli sonuçlarla ilişkilidir: Çok merkezli kohort çalışması

AMAÇ: Kusadriseps tendon rüptürü, yüksek ek hastalık yükü ve azalmış fizyolojik rezervi olan hastalarda sık görülen, fonksiyonel açıdan yıkıcı bir yaralanmadır. Kırılganlık, yaştan bağımsız fizyolojik dayanıklılık kaybını yansıtır; ancak kuadriseps tendon rüptürü sonrası yatış ve uzun dönem fonksiyonel sonuçlar üzerindeki etkisi yeterince tanımlanmamıştır.

GEREÇ VE YÖNTEM: Bu geriye dönük, çok merkezli kohort çalışmasında, 2019–2023 yılları arasında dört üçüncü basamak merkezde akut kuadriseps tendon rüptürü (≤4 hafta) nedeniyle cerrahi onarım veya rekonstrüksiyon uygulanan 67 erişkin hasta analiz edildi. Ameliyat öncesi kırılganlık, 5 maddelik Modifiye Kırılganlık İndeksi (mFI-5) ve 9 puanlık Klinik Kırılganlık Ölçeği (CFS) ile nicelendirildi. CFS, iki bağımsız ortopedi cerrahı tarafından standart belgelemeye dayalı çift-gözlemci konsensus yöntemiyle (κ=0.82) geriye dönük puanlandı. Birincil sonlanımlar hastanede kalış süresi ve ≥12. ayda Lysholm Diz Skorlama Ölçeği; ikincil sonlanımlar KOOS ve komplikasyonlardı. Çok değişkenli modeller önceden belirlenmiş sınırlı değişken setiyle kuruldu (yatış modeli için 6, Lysholm modeli için 4 ön görücü; ön görücü başına ≈11:1 ve ≈17:1 gözlem) ve yaş, cinsiyet, VKİ, ek hastalık yükü, cerrahi teknik ve takip süresine göre düzeltildi.

BULGULAR: Ortalama yaş 57.5±12.1 yıl; %79.1 erkek. Daha yüksek mFI-5 skorları uzamış yatış ile ilişkiliydi (r=0.404; p<0.001); düzeltilmiş modelde mFI-5'teki her 1 puanlık artış 1,26 günlük uzamayı öngördü (%95 GA: 0.61–1.90; düzeltilmiş R2=0.337). Ortalama takip 25.5 ay; ortalama Lysholm 52.2±17.5. CFS daha kötü fonksiyonel iyileşme ile bağımsız olarak ilişkiliydi (r=−0.328; p=0.007); CFS'deki her 1 puanlık artış Lysholm skorunda 4.32 puanlık azalmaya karşılık geldi (%95 GA: −6.98 ile −1.67; düzeltilmiş R2=0.163). Rekonstrüksiyon olgularını (n=6) dışlayan duyarlılık analizi benzer etki büyüklükleri verdi (mFI-5 → yatış: β=1.22; CFS → Lysholm: β=−4.18). Her iki kırılganlık ölçütünün de komplikasyonlarla (oran %10.4; 7 olay) anlamlı ilişkisi saptanmadı; ancak analiz yetersiz güçtedir ve dikkatle yorumlanmalıdır.

SONUÇ: Kırılganlık, kuadriseps tendon rüptürünün cerrahi onarımı sonrasında uzamış yatış ve daha düşük hasta bildirimli sonuçlarla ilişkilidir. mFI-5 ve CFS'nin rutin preoperatif değerlendirmeye entegrasyonu cerrahi planlama, taburculuk koordinasyonu ve rehabilitasyon yoğunluğunun bireyselleştirilmesinde klinik fayda sağlayabilir.

Anahtar sözcükler: Fonksiyonel iyileşme; hastanede kalış süresi; kırılganlık; kuadriseps tendon rüptürü; ortopedik cerrahi; prognoz.

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ORIGINAL ARTICLE

Clinical course and management of extremity frostbite in populations under forced movement in border regions

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ABSTRACT

BACKGROUND: Frostbite is a serious cold injury that can progress to deep tissue damage and even amputation. The increasing number of cases among refugee and migrant populations who are forcibly mobile in border regions necessitates a detailed evaluation of clinical course and risk factors. This study aimed to assess the demographic characteristics, clinical course, laboratory findings, and treatment outcomes of patients presenting with frostbite-related extremity injuries.

METHODS: This retrospective study included a total of 154 patients who presented with a clinically confirmed diagnosis of frostbite. Patients were analyzed according to three predefined classifications: treatment approach (conservative, medical, advanced/interventional), anatomical distribution of frostbite involvement, and time to hospital presentation (≤12 h, 12–24 h, 24–36 h, 36–48 h, and >48 h). Demographic data, clinical findings, laboratory parameters, treatment modalities, and clinical outcomes were evaluated. Statistical analyses were performed using non-parametric tests and Chi-square analysis.

RESULTS: The median age of the patients was 23 years, and 94.2% were foreign nationals. The most common time to presentation was 12–24 h after cold exposure (61%). As the time to hospital admission increased, frostbite grade, number of affected extremities, frequency of hypotension, white blood cell (WBC) levels, and length of hospital stay increased significantly ($p<0.001$). Amputation was performed in 77.3% of patients, and all amputated cases had fourth-grade frostbite. Amputation was significantly associated with delayed presentation, hypotension, elevated WBC levels, larger frostbite area, and longer hospital stay ($p<0.05$).

CONCLUSION: Delayed presentation and severe systemic involvement are the most important determinants of amputation risk. Early diagnosis, rapid and controlled rewarming, appropriate patient transfer, and timely access to advanced treatment options are critical for reducing amputation rates.

Keywords: Amputation; cold injury; frostbite; public health; refugees.

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INTRODUCTION

Cold injuries are complex yet preventable conditions that result from exposure to extremely low temperatures and can lead to tragic outcomes, ranging from cellular-level damage to multi-organ involvement.[1,2] This process begins with superficial vasoconstriction and local heat loss and may progress through the formation of extracellular ice crystals, endothelial injury, microthrombosis, and reperfusion injury, ultimately resulting in deep tissue necrosis, amputation, and death.[3,4] Therefore, frostbite is not merely a localized tissue injury but a complex clinical condition involving systemic inflammatory responses, coagulation disturbances, and metabolic alterations.[5]

Frostbite is most commonly encountered in harsh environmental conditions such as polar regions, high-altitude mountainous areas, military operation zones, conflict regions, and migration routes.[6,7] In recent years, increasing geopolitical instability and forced migration have dramatically raised the incidence of frostbite. Severe frostbite cases reported among migrant populations at European border crossings, along the Balkan route, and at North American borders indicate that this condition represents a global public health problem.[8-10] Key factors increasing the risk of frostbite among migrants and refugees include long-distance walking, lack of appropriate equipment, exposure to wind and moisture, nighttime travel, hypothermia, malnutrition, and trauma.[11,12] These individuals are more vulnerable to the disease not only because of environmental challenges but also due to adverse social and humanitarian conditions.[13]

The epidemiology of frostbite is closely associated with age, sex, occupation, and socioeconomic status. Young adult males, soldiers, mountaineers, homeless individuals, and irregular migrants have been reported to be at particularly high risk.[14,15] Children, on the other hand, are more prone to severe clinical presentations due to rapid heat loss resulting from a higher surface area-to-mass ratio.[16] Time to hospital presentation is one of the most critical determinants of frostbite prognosis. The literature demonstrates that rapid and controlled rewarming within the first 6–12 h significantly reduces tissue loss, whereas delays substantially increase the risk of amputation.[17,18] However, delayed presentation rates are known to be high among migrant populations because of barriers to healthcare access during migration.[19]

In the diagnosis and management of frostbite, imaging modalities such as planar scintigraphy, magnetic resonance imaging (MRI), and angiography play an important role in determining the extent of necrosis and the amount of viable tissue.[20] Laboratory parameters assist in assessing clinical severity by reflecting the grade of inflammation, coagulation status, oxidative stress, and organ function.[21,22] Amputation rates in advanced frostbite cases have been reported to range between 30% and 70%, imposing substantial individual, functional, and psychosocial burdens.[23,24] The presence of amputation is associated with additional consequences, including physical disability, psychological trauma, and difficulties in accessing healthcare services.[25] Moreover, frostbite-related amputations constitute a significant economic burden.

This study aims to comprehensively evaluate the regional epidemiology, pathophysiology, and clinical outcomes of frostbite by analyzing the demographic, clinical, and laboratory characteristics of patients presenting with frostbite in a border region.

MATERIALS AND METHODS

Study Design and Setting

This retrospective, observational study was conducted at a tertiary-level burn center located in a border region with a high volume of forced migration movements. Medical records of patients hospitalized with a diagnosis of frostbite between September 2020 and September 2025 were reviewed retrospectively. The study was approved by the Van Training and Research Hospital Clinical Research Ethics Committee (approval date: August 08, 2025, approval number: 60KAEK/2025-06-01). The study was designed in accordance with the principles of the Declaration of Helsinki.

Patient Population

A total of 154 patients who were hospitalized and treated with a diagnosis of extremity frostbite were included in the study. All patients had clinically confirmed frostbite affecting at least one extremity at the time of presentation. Demographic data (age, sex), migration and shelter status, environmental exposure history, clinical findings, laboratory parameters, imaging results, treatments administered, and clinical outcomes were recorded.

Initial Clinical Assessment

At the time of hospital admission, all patients underwent an initial evaluation in accordance with standard trauma and burn management protocols. After stabilization of vital signs, core body temperature, presence of systemic hypothermia, level of consciousness, and accompanying traumatic findings were assessed. Local examination included documentation of frostbite grade, depth of involvement, blister formation, color changes, signs of necrosis, and distal circulation status.

Rewarming Protocol

According to the standard frostbite treatment protocol applied at our center, all patients received controlled local rewarming. Local hydrotherapy was performed using water at 42°C for 15 min every 6 h during the first 72 h. The duration of rewarming was terminated based on clinical findings and perfusion status.

Medical Treatment

To support reperfusion of pre-ischemic tissues and prevent microthrombosis, all patients were initiated on standard medical therapy. This protocol included enoxaparin 1 mg/kg/

day subcutaneously (divided into two doses), acetylsalicylic acid 100 mg/day orally, iloprost 0.5–2 ng/kg/min through intravenous infusion (6 h/day), pentoxifylline 400 mg orally 3 times daily, and amlodipine 5–10 mg/day orally for adult patients. Depending on clinical status, a beta-blocker (metoprolol 25–50 mg/day orally) was added in cases of tachycardia or hypertension, while dexamethasone 4–8 mg/day intravenously was included in patients with marked inflammation and edema. For infection prophylaxis, all adult patients were started on ceftriaxone 2 g/day intravenously at the time of hospitalization. Analgesia was provided with paracetamol 1,000 mg orally or intravenously 3–4 times daily and ibuprofen 400–600 mg orally 3 times daily; in cases where adequate pain control was not achieved, tramadol 50–100 mg orally or intravenously 2–3 times daily was added.

Imaging and Surgical Evaluation

The decision for amputation was not based on a single parameter but on a comprehensive multidisciplinary clinical evaluation involving burn surgeons, orthopedic surgeons, vascular surgeons, and infectious disease specialists. The amputation decision was primarily based on clinical criteria rather than imaging findings.

The following criteria were considered collectively: presence of fourth-degree frostbite with irreversible tissue necrosis or gangrene, absence of distal perfusion despite standardized medical therapy and controlled rewarming, progressive tissue necrosis observed in serial physical examinations, clear demarcation of non-viable tissue, and development of severe infection or systemic complications.

Doppler ultrasonography was routinely used to assess vascular flow and tissue perfusion. Advanced imaging modalities, including scintigraphy, MRI, or angiography, were performed in hemodynamically stable patients when available to support the evaluation of tissue viability. However, due to the retrospective nature of the study and the high proportion of patients presenting at advanced stages, these modalities could not be applied uniformly to all cases.

In all patients, the final surgical decision was guided primarily by clinical assessment of tissue viability and disease progression, with imaging findings serving as supportive tools when obtainable (Fig. 1).

Inclusion and Exclusion Criteria

Inclusion criteria were the presence of a clinically confirmed diagnosis of frostbite, complete medical records, and first-time presentation for frostbite injury.

Exclusion criteria included incomplete medical records; non-freezing cold injuries; electrical or chemical burns; trauma-related tissue loss; and patients with comorbidities affecting circulation, such as peripheral vascular disease, Raynaud phenomenon, or connective tissue disorders. In addition, individuals with chronic alcohol dependence or those from whom a reliable medical history could not be obtained were excluded.

Data Collection

All patient data were systematically recorded using a standardized data collection form. In addition to demographic variables (age, sex, smoking status), the clinical characteristics of frostbite injury were evaluated in detail. The number of affected digits in the right and left hands and feet, percentage of tissue involvement, extent of involvement, and frostbite grade (grades 1–4) were recorded separately.

For analytical purposes, patients were categorized according to the anatomical distribution of frostbite involvement into seven predefined groups: Group 1 (both hands and both feet affected), Group 2 (both hands and one foot affected), Group 3 (one hand and both feet affected), Group 4 (both feet affected), Group 5 (both hands affected), Group 6 (one hand affected), and Group 7 (one foot affected).

In addition, time to clinical presentation was stratified into five categories: Group A (≤12 h), Group B (12–24 h), Group C (24–36 h), Group D (36–48 h), and Group E (>48 h).

Laboratory data obtained at admission were retrieved from the hospital's electronic medical record system and transferred to the study dataset. The analyzed laboratory parameters included complete blood count (hemoglobin, g/dL; white blood cell (WBC) count, ×103/μL; platelet count, ×103/μL), renal function tests (urea, mg/dL; creatinine, mg/dL), liver enzymes (aspartate aminotransferase, U/L; alanine aminotransferase, U/L), electrolytes (sodium, mmol/L; potassium, mmol/L; magnesium, mg/dL; calcium, mg/dL), C-reactive protein (mg/L), international normalized ratio, and albumin levels (g/dL).

Statistical Analysis

Statistical analyses were performed using IBM Statistical Package for the Social Sciences Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). The normality of data distribution was assessed using the Shapiro–Wilk test. As the data did not show normal distribution, nonparametric tests were used (Mann–Whitney U test or Kruskal–Wallis test). The Chi-square test was applied for comparisons of categorical variables. A $p<0.05$ was considered statistically significant.

RESULTS

Demographic Characteristics

A total of 154 patients were included in the study. The median age was 23 years (range: 16–52 years), and the majority of the patients were male. Most of the patients were foreign nationals presenting with frostbite injuries during irregular migration routes.

Frostbite-Affected Extremities

Frostbite involvement was identified in four extremities in 16 patients (10.4%), three extremities in 45 patients (29.2%), two extremities in 68 patients (44.2%), and a single extremity in 25 patients (16.2%) (Table 1). According to the anatomical

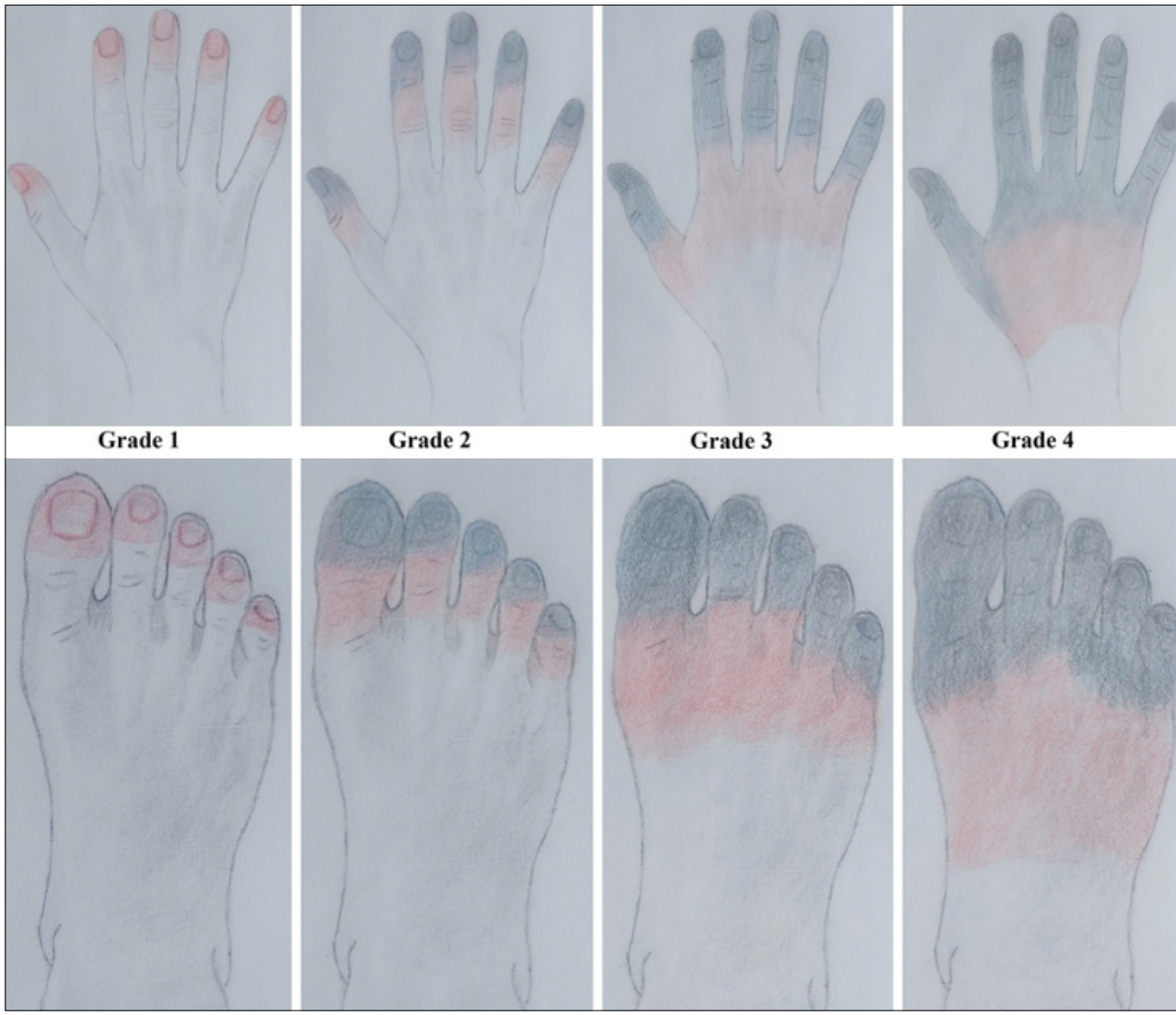


Figure 1. Schematic representation of the clinical grading of frostbite injuries involving the fingers and toes. Grade 1 is characterized by superficial epidermal involvement with erythema and edema. Grade 2 demonstrates deeper dermal injury with blister formation. Grade 3 involves full-thickness skin and subcutaneous tissue damage, often associated with hemorrhagic blisters. Grade 4 represents the most severe form, with involvement of deep structures including muscle, tendon, and bone, resulting in irreversible tissue necrosis and gangrene.

distribution of frostbite involvement, patients were classified into seven groups, the proportional and numerical distributions were as follows: Group 4 (both feet) constituted the largest proportion (31.8%, n=49), followed by Group 2 (both hands and one foot, 16.2%, n=25), Group 3 (one hand and both feet, 13.0%, n=20), Group 5 (both hands, 12.3%, n=19), Group 1 (both hands and both feet, 10.4%, n=16), Group 6 (one hand, 9.2%, n=14), and Group 7 (one foot, 7.1%, n=11) (Table 2).

Time to Clinical Presentation

All patients were transferred to the emergency department within the first 3 days following exposure. Time to clinical presentation was analyzed in five groups. Of the patients, 26.6% (Group A, 41 cases) presented within the first 12 h, 61.0% (Group B, 94 cases) between 12 and 24 h, 9.2% (Group C, 14 cases) between 24 and 36 h, 0.6% (Group D, 1 case) between 36 and 48 h, and 2.6% (Group E, 4 cases) after 48 h. Increasing delay in emergency department presentation was associated with a higher number of affected extremities ($p<0.001$). Prolonged time to presentation was also associated with increased frostbite severity ($p<0.001$) and a higher frequency of hypotensive cases ($p<0.001$) (Table 2). Longer time to presentation was associated with increased length of hospital stay ($p<0.001$) and higher WBC levels ($p=0.042$) (Table 3).

Amputation Frequency

Amputation was performed in 77.3% of patients (119 cases: 115 foreign nationals and 4 Turkish nationals). Neither the

type (hand vs. foot) nor the number of affected extremities was associated with amputation frequency (p>0.05). All patients who underwent amputation had fourth-grade frostbite and presented later to the emergency department (p<0.001). Amputation was more frequently performed in hypotensive patients (p<0.001). While no association was found between

Table 1. Distribution of the number of affected fingers or toes according to the study groups (Kruskal-Wallis Test)

Parameters	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6	Group 7	p
Number of fingers affected on the right hand	2 (2–5)	3 (2–4)	1 (0–4)	0	3 (1–4)	0 (0–4)	0	<0.001
Number of fingers affected on the left hand	3 (1–5)	2 (1–4)	1 (0–4)	0	3 (1–5)	3 (0–4)	0	<0.001
Number of toes affected on the right foot	3 (2–5)	0 (0–4)	3 (2–5)	3 (2–5)	0	0	0 (0–4)	<0.001
Number of toes affected on the left foot	3 (2–5)	3 (0–4)	3 (2–5)	3 (1–5)	0	0	3 (0–4)	<0.001
Total number of fingers/ toes affected	12 (9–19)[a,b,c,d,e,f]	8 (6–11)[c,d,e,f]	9 (7–14)[c,d,e,f]	6 (4–10)[e,f]	6 (3–9)[e,f]	3 (2–4)	4 (3–4)	<0.001
Freezing percentage (%)	9.50 (6–15)[a,b,c,d,e,f]	7 (4–10)[c,d,e,f]	7 (5–12)[c,d,e,f]	5 (3–10)[e,f]	5 (2–8)[e,f]	2.50 (2–3)	3 (2–3)	<0.001

Group 1 (n=16): Patients with 2 hands and 2 feet affected, Group 2 (n=25): Patients with 2 hands and 1 foot affected, Group 3 (n=20): Patients with 1 hand and 2 feet affected, Group 4 (n=49): Patients with 2 feet affected, Group 5 (n=19): Patients with 2 hands affected, Group 6 (n=14): Patients with 1 hand affected, Group 7 (n=11): Patients with 1 foot affected. aComparison to group 2, bComparison to group 3, cComparison to group 4, dComparison to group 5, eComparison to group 6, fComparison to group 7, p<0.05. Bold "p" values indicate statistically significant parameters. Since the parameters did not follow a normal distribution, the data in the table were presented as median (minimum–maximum).

Table 2. Evaluation of the categorical variables according to the hospital access time (Chi-square test)

Parameters	Analysis	Group A (%)	Group B (%)	Group C (%)	Group D (%)	Group E (%)	Total (%)	p
Number of limbs affected	Four limbs	5 (31.3)	6 (37.5)	1 (6.2)	1 (6.2)	3 (18.8)	16 (10.4)	0.001
	Three limbs	11 (24.5)	28 (62.2)	6 (13.3)	0 (0)	0 (0)	45 (29.2)	
	Two limbs	15 (22.1)	46 (67.6	6 (8.8)	0 (0	1 (1.5)	68 (44.2)	
	One limb	10 (40)	14 (56)	1 (4)	0 (0)	0 (0)	25 (16.2)	
Study groups	Group 1	5 (31.3)	6 (37.5)	1 (6.2)	1 (6.2)	3 (18.8)	16 (10.4)	0.020
	Group 2	7 (28)	15 (60)	3 (12)	0 (0)	0 (0)	25 (16.2)	
	Group 3	4 (20)	13 (65)	3 (15)	0 (0)	0 (0)	20 (13	
	Group 4	11 (22.5)	32 (65.3)	5 (10.2)	0 (0)	1 (2)	49 (31.8)	
	Group 5	4 (21.1)	14 (73.6)	1 (5.3)	0 (0)	0 (0)	19 (12.3)	
	Group 6	8 (57.2)	5 (35.7)	1 (7.1)	0 (0)	0 (0)	14 (9.2)	
	Group 7	2 (18.2)	9 (81.8)	0 (0)	0 (0)	0 (0)	11 (7.1)	
Freezing grade	Second-grade	7 (70)	3 (30)	0 (0)	0 (0	0 (0)	10 (6.5)	<0.001
	Third-grade	14 (56)	11 (44)	0 (0)	0 (0)	0 (0)	25 (16.2)	
	Fourth-grade	20 (16.8)	80 (67.2)	14 (11.8)	1 (0.8)	4 (3.4)	119 (77.3)	
Blood pressure	Hypotensive	6 (6.8)	64 (71.9)	14 (15.7)	1 (1.1)	4 (4.5)	89 (57.8)	<0.001
	Normotensive	28 (49.1)	29 (50.9)	0 (0)	0 (0)	0 (0)	57 (37)	
	Hypertensive	7 (87.5)	1 (12.5)	0 (0)	0 (0)	0 (0)	8 (5.2)	

Group 1 (n=16): Patients with 2 hands and 2 feet affected, Group 2 (n=25): Patients with 2 hands and 1 foot affected, Group 3 (n=20): Patients with 1 hand and 2 feet affected, Group 4 (n=49): Patients with 2 feet affected, Group 5 (n=19): Patients with 2 hands affected, Group 6 (n=14): Patients with 1 hand affected, Group 7 (n=11): Patients with 1 foot affected, Group A (n=41): Patients that arrive at the hospital within the first 12 h, Group B (n=94): Patients that arrive at the hospital between 12 and 24 h, Group C (n=14): Patients that arrive at the hospital between 24 and 36 h, Group D (n=1): Patients that arrive at the hospital between 36 and 48 h, Group E (n=4): Patients that arrive at the hospital after 48 h. Bold "p" values indicate statistically significant parameters.

Table 3. Comparison of the parameters according to the hospital access time (Kruskal-Wallis Test)

Parameters	Group A	Group B	Group C	Group D	Group E	p
Total number of fingers/ toes affected	7 (2–16)	6 (3–14)	8 (4–13)	14 (14–14)	12.50 (5–19)	0.058
Freezing per-centage (%)	5 (2–12)	5 (2–12)	6 (3–12)	11 (11–11)	10.50 (4–15)	0.072
Length of hospital stay (day)	11 (4–24)	13 (6–29)	16 (9–27)	40 (40–40)	35.50 (26–43)	<0.001
pH	7.36 (7.29–7.43)	7.35 (7.25–7.43)	7.36 (7.30–7.44)	7.41 (7.41–7.41)	7.37 (7.23–7.39)	0.580
PaO_2 (mmHg)	86 (77–95)	84 (75–96)	84 (76–93)	84 (84–84)	87.50 (83–91)	0.097
$PaCO_2$ (mmHg)	43 (37–47)	42 (30–52)	42 (38–48)	41 (41–41)	41 (40–42)	0.550
Glucose (mg/dL)	91 (75–115)	92.50 (68–132)	96 (75–131)	91 (91–91)	76 (62–81)	0.054
WBC (10^3/uL)	8.90 (4.70–19.80)	9.65 (3.50–19.10)	9.95 (7.20–16.80)	17.20 (17.20–17.20)	16.75 (10–19.10)	0.042
Hgb (g/dL)	13.60 (10.50–16.50)	13.70 (10.30–16.80)	13.30 (10.60–16.80)	15.60 (15.60–15.60)	16.30 (10.80–17)	0.435
INR	1 (0.50–1.40)	1 (0.60–1.50)	0.90 (0.80–1.20)	1 (1–1)	0.80 (0.60–0.80)	0.054
ALT (U/L)	55 (33–78)	59 (35–80)	66.50 (40–80)	67 (67–67)	59 (36–79)	0.757
AST (U/L)	50 (32–70)	53.50 (29–70)	53 (33–68)	59 (59–59)	58.50 (31–82)	0.971
Creatinine (mg/dL)	0.90 (0.50–1.40)	0.90 (0.50–1.60)	0.90 (0.60–1.30)	1.20 (1.20–1.20)	1 (0.90–1.40)	0.509
Na (mEq/L)	139 (132–145)	139 (131–147)	139.50 (135–146)	139 (139–139)	137 (132–141)	0.823
K (mEq/L)	3.90 (3.10–4.90)	4 (3.10–5.30)	3.95 (3.10–5)	4.60 (4.60–4.60)	4 (3.10–4.80)	0.438
Mg (mg/dL)	1.90 (1.50–2.20)	1.90 (1.40–2.30)	1.80 (1.60–2.20)	1.80 (1.80–1.80)	1.85 (1.20–2)	0.977
Ca (mg/dL)	8.50 (7.10–9.90)	8.45 (7.10–9.90)	8.60 (7.30–9.90)	7.10 (7.10–7.10)	8.25 (7.80–9.70)	0.557
Albumin (g/dL)	3.20 (1.80–5.20)	3.50 (1.80–5.20)	4.10 (1.70–5.10)	1.60 (1.60–1.60)	2.30 (1.60–5.10)	0.247

Group A (n=41): Patients that arrive at the hospital within the first 12 h, Group B (n=94): Patients that arrive at the hospital between 12 and 24 h, Group C (n=14): Patients that arrive at the hospital between 24 and 36 h, Group D (n=1): Patients that arrive at the hospital between 36 and 48 h, Group E (n=4): Patients that arrive at the hospital after 48 h. Bold "p" values indicate statistically significant parameters. pH: Blood acidity level; PaO2: Partial arterial oxygen pressure; PaCO2: Partial arterial carbon dioxide pressure; WBC: White blood cell count; Hgb: Hemoglobin; INR: International normalized ratio; ALT: Alanine aminotransferase, AST: Aspartate aminotransferase; Na: sodium; K: Potassium; Mg: Magnesium; Ca: calcium.



Figure 2. Clinical presentation of frostbite injuries involving the hand and fingers at varying degrees of severity.

amputation frequency and smoking status (p=0.488), a significant association was observed with alcohol use (p=0.007), with alcohol consumption associated with a reduced risk of amputation (Table 4). Patients who underwent amputation had a significantly higher percentage of frostbite involvement (p=0.037) and longer hospital stays (p<0.001) (Table 5). In addition, WBC levels were significantly higher in patients who underwent amputation (p=0.009) (Table 5; Figs. 2 and 3).

DISCUSSION

This study evaluated the epidemiological and clinical characteristics of patients hospitalized for frostbite injuries and demonstrated that frostbite is not merely a clinical condition resulting from environmental exposure, but also a significant public health problem closely associated with forced migration, sociopolitical conditions, and delayed access to health-

Table 4. Evaluation of the categorical variables according to the presence or absence of amputation (Chi-square test)

Parameters	Analysis	Absence (n=35) (%)	Presence (n=119) (%)	Total (%)	p
Number of limbs affected	Four limbs	2 (12.5)	14 (87.5)	16 (10.4)	0.259
	Three limbs	7 (15.6)	38 (84.4)	45 (29.2)	
	Two limbs	20 (29.4)	48 (70.6)	68 (44.2)	
	One limb	6 (24)	19 (76)	25 (16.2)	
Study groups	Group 1	2 (12.5)	14 (87.5)	16 (10.4)	0.241
	Group 2	3 (12)	22 (88)	25 (16.2)	
	Group 3	4 (20)	16 (80)	20 (13)	
	Group 4	16 (32.7)	33 (67.3)	49 (31.8)	
	Group 5	4 (21.1)	15 (78.9)	19 (12.3)	
	Group 6	5 (35.7)	9 (64.3)	14 (9.2)	
	Group 7	1 (9.1)	10 (90.9)	11 (7.1)	
Freezing grade	Second-grade	10 (100)	0 (0)	10 (6.5)	<0.001
	Third-grade	25 (100)	0 (0)	25 (16.2)	
	Fourth-grade	0 (0)	119 (100)	119 (77.3)	
Hospital access time	Group A	21 (51.2)	20 (48.8)	41 (26.6)	<0.001
	Group B	14 (14.9)	80 (85.1)	94 (61)	
	Group C	0 (0)	14 (100)	14 (9.2)	
	Group D	0 (0)	1 (100)	1 (0.6)	
	Group E	0 (0)	4 (100)	4 (2.6)	
Blood pressure	Hypotensive	6 (6.7)	83 (93.3)	89 (57.8)	<0.001
	Normotensive	24 (42.1)	33 (57.9)	57 (37)	
	Hypertensive	5 (62.5)	3 (37.5)	8 (5.2)	
Smoking	No	27 (21.6)	98 (78.4)	125 (81.2)	0.488
	Yes	8 (27.6)	21 (72.4)	29 (18.8)	
Alcohol use	No	27 (19.4)	112 (80.6)	139 (90.3)	0.007
	Yes	8 (53.3)	7 (46.7)	15 (9.7)	

Group 1 (n=16): Patients with 2 hands and 2 feet affected, Group 2 (n=25): Patients with 2 hands and 1 foot affected, Group 3 (n=20): Patients with 1 hand and 2 feet affected, Group 4 (n=49): Patients with 2 feet affected, Group 5 (n=19): Patients with 2 hands affected, Group 6 (n=14): Patients with 1 hand affected, Group 7 (n=11): Patients with 1 foot affected, Group A: Patients that arrive at the hospital within the first 12 h, Group B: Patients that arrive at the hospital between 12 and 24 h, Group C: Patients that arrive at the hospital between 24 and 36 h, Group D: Patients that arrive at the hospital between 36 and 48 h, Group E: Patients that arrive at the hospital after 48 h. Bold "p" values indicate statistically significant parameters.



Figure 3. Clinical images demonstrating advanced frostbite injuries (Grade 3–4) affecting the foot and toes.

Table 5. Comparison of the parameters according to the presence or absence of amputation (Mann-Whitney U Test).

Parameters	Analysis	Absence (n=35)	Presence (n=119)	p
Clinical findings	Total number of fingers/toes affected	6 (3–11)	7 (2–19)	0.110
	Freezing percentage (%)	5 (3–8)	6 (2–15)	0.037
	Length of hospital stay (day)	9 (4–15)	14 (8–43)	<0.001
Laboratory findings	pH	7.35 (7.29–7.43)	7.36 (7.23–7.44)	0.807
	PaO_2 (mmHg)	85 (80–95)	84 (75–96)	0.201
	$PaCO_2$ (mmHg)	42 (36–50)	42 (30–52)	0.755
	Glucose (mg/dL)	90 (75–115)	93 (62–132)	0.359
	WBC (10^3/uL)	7.90 (3.50–17.60)	10.10 (3.60–19.80)	0.009
	Hgb (g/dL)	13.30 (10.50–16.80)	13.90 (10.30–17)	0.235
	INR	1 (0.80–1.20)	1 (0.50–1.50)	0.757
	ALT (U/L)	53 (33–80)	61 (35–80)	0.325
	AST (U/L)	53 (31–70)	53 (29–82)	0.458
	Creatinine (mg/dL)	0.90 (0.50–1.60)	0.90 (0.50–1.40)	0.454
	Na (mEq/L)	138 (132–145)	139 (131–147)	0.545
	K (mEq/L)	3.90 (3.10–5)	4 (3.10–5.30)	0.223
	Mg (mg/dL)	1.90 (1.50–2.20)	1.80 (1.20–2.30)	0.119
	Ca (mg/dL)	8.60 (7.10–9.90)	8.40 (7.10–9.90)	0.666
	Albumin (g/dL)	3.30 (1.80–5.20)	3.40 (1.60–5.20)	0.612

Bold "p" values indicate statistically significant parameters. pH: Blood acidity level; PaO2: Partial arterial oxygen pressure; PaCO2: Partial arterial carbon dioxide pressure; WBC: White blood cell count; Hgb: Hemoglobin; INR: İnternational normalized ratio; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; Na: Sodium; K: Potassium; Mg: Magnesium; Ca: Calcium; PaO2: Partial arterial oxygen pressure; PaCO2: Partial arterial carbon dioxide pressure; Glucose: Blood glucose level; Creatinine: Serum creatinine level; Albumin: Serum albumin level; Length of hospital stay: Duration of hospitalization; Freezing percentage: Percentage of body surface affected by freezing.

care services.[3,8,10] The predominance of refugee and migrant individuals in the study population is consistent with trends reported in previous studies,[14,15] indicating that, in border regions, the primary determinant of frostbite severity is not cold exposure alone but rather migration-related delayed presentation and structural vulnerabilities.[11-13]

In hospital-based series from Europe and North America, the proportion of migrant or homeless individuals among patients with severe frostbite has been reported to range between 35% and 62%.[8-10] In contrast, the remarkably high proportion of foreign nationals in our cohort (94.2%) highlights a substantially increased burden of frostbite-related vulnerability among populations affected by forced migration in border regions. Similarly, while previous studies have reported median ages ranging from 30 to 45 years,[15,16] the median age in our study was 23 years, suggesting that frostbite in this setting disproportionately affects younger adults. Notably, in their comprehensive clinical review, Handford et al.[17] emphasized that frostbite occurs most frequently among young men, particularly migrants, individuals with inadequate shelter conditions, and those compelled to work outdoors.

The near-exclusive male predominance in our cohort (98.1%) is consistent with the demographic distributions reported by Ervasti et al.[26] and Cauchy et al.,[19] both of whom identified frostbite as most prevalent among males aged 20–40 years. These findings further support the notion that frostbite is driven less by biological susceptibility and more by exposure duration, environmental risk factors, and adverse socioeconomic conditions.

The extent of extremity involvement represents another notable finding of this study. In our cohort, 83.8% of patients had involvement of two or more extremities, a proportion substantially higher than the approximately 52% reported by Ervasti et al.[26] in Finland and the 48% reported by Cauchy et al.[19] in Alpine Mountaineering Series. This discrepancy is likely attributable to prolonged cold exposure, inadequate protective clothing, and restricted mobility during irregular border crossings. Handford et al.[17] similarly reported that multi-extremity involvement reflects prolonged and severe cold exposure and is associated with poorer functional outcomes.

Delayed hospital presentation emerged as one of the most critical findings of our study. The pathophysiology of frostbite is classically described as a biphasic process consisting

of freezing and reperfusion phases.[3,4] During the freezing phase, extracellular ice crystal formation, capillary leakage, endothelial injury, and microthrombosis impair early tissue perfusion, whereas during the reperfusion phase, reactive oxygen species, inflammatory cytokines, and complement activation further exacerbate tissue damage.[5,21] In our cohort, only 26.6% of patients presented within the first 12 h, which likely facilitated the progression of these pathophysiological mechanisms.

Consistent with the findings of Cauchy et al.[19] and Regli et al.,[4] who reported that presentation beyond 24 h increases the risk of tissue loss by two- to fourfold, our data demonstrated a statistically significant association between prolonged presentation time and both frostbite severity ($p<0.001$) and the need for amputation ($p<0.001$). More than 70% of our patients presented after the first 12 h, in marked contrast to early presentation rates exceeding 50% as reported by tertiary care centers outside border regions.[26,27]

The high amputation rate observed in our study (77.3%) is considerably greater than that reported in most civilian series.[24-27] Wibbenmeyer et al.[2] reported an amputation rate of 28% in a multicenter U.S. cohort, while Regli et al.[4] reported an approximate rate of 31% in their meta-analysis. In contrast, Cauchy et al.[19] demonstrated that amputation rates in fourth-degree frostbite may reach 60–80%. The fact that all amputated patients in our series had fourth-degree frostbite is consistent with these observations.

The significantly elevated WBC levels observed in patients undergoing amputation support the role of an intense systemic inflammatory response in severe frostbite.[21,22] Although elevated WBC counts have previously been described as markers of tissue necrosis and secondary infection,[22] clinical evidence quantifying the relationship between WBC levels and amputation risk remains limited. In this context, our findings provide additional support for incorporating inflammatory markers into early prognostic assessment models.

From a therapeutic perspective, early intervention is of critical importance. Controlled rewarming, adequate analgesia, hydration, and trauma management constitute the foundation of standard care.[17,18] In advanced frostbite, thrombolytic therapy with tissue plasminogen activator, particularly when administered within the first 24 h, has been shown to significantly reduce amputation rates.[27-30] In the landmark studies by Bruen et al.,[27] Limb salvage rates of 60–80% were reported following thrombolytic therapy. However, in our study, the predominance of delayed presentation severely limited the applicability of thrombolytic treatment.

Advanced imaging modalities play an important role in assessing tissue viability in frostbite injuries. Nevertheless, in clinical practice, particularly among patients presenting at advanced stages, the decision for amputation is often based primarily on multidisciplinary clinical assessment rather than imaging findings.[20] In our cohort, surgical decision-making was guided by criteria including clinical progression of tissue necrosis, distal perfusion status, signs of infection, and tissue demarcation. Limited systematic access to advanced imaging and the high proportion of late-stage presentations resulted in surgical decisions being predominantly clinically driven. These findings indicate that the applicability of imaging-based algorithms is closely linked to both institutional resources and timing of presentation. Accordingly, clinical algorithms for frostbite management in border regions should be addressed through a multilayered public health approach that integrates not only medical care but also migrant health policies, early access to care, and effective referral systems.

Limitations of the Study

The primary limitation of this study is its retrospective, single-center design, which limits the generalizability of the findings and precludes causal inferences. The predominance of high-risk migrant and refugee individuals in the study population may result in findings that reflect a specific patient group rather than the general population.

The fact that a substantial proportion of patients presented late limited the evaluation of the effectiveness of advanced early-stage treatment options. In addition, certain variables, such as duration of environmental exposure and use of protective equipment, could not be objectively verified because they were based on patient history.

The inability to apply advanced imaging modalities uniformly to all patients and the lack of assessment of long-term functional and psychosocial outcomes represent additional limitations of this study.

CONCLUSION

This study provides clinical evidence that delayed hospital admission and higher frostbite grade at presentation are independent and strong predictors of amputation risk in patients with frostbite injuries.

In addition, hypotension at admission and elevated WBC levels were identified as significant biological markers associated with poor limb outcomes.

Our findings quantitatively demonstrate the protective role of early, controlled rewarming and timely medical intervention in limiting tissue necrosis and preserving limb integrity.

By analyzing a unique patient population from a border region, this study contributes novel data on the clinical course, treatment response, and prognostic factors of severe frostbite in real-world settings.

Compared with previous cohorts, our study reports one of the highest documented amputation rates, highlighting the critical impact of delayed access to care on clinical outcomes.

These results refine current understanding of frostbite pathophysiology and progression, support early risk stratification

based on presentation characteristics, and may assist clinicians in identifying high-risk patients who require aggressive monitoring and intervention.

Furthermore, our data suggest that incorporating simple clinical variables (time to presentation, blood pressure, WBC levels, and frostbite grade) into early decision-making algorithms may improve prognostic accuracy and guide resource allocation in emergency settings.

Furthermore, the study adds to the limited body of literature on predictors of amputation in frostbite and provides evidence-based parameters that can be incorporated into future clinical algorithms and management guidelines.

Multicenter observational studies using standardized data collection protocols are needed to validate these findings and clarify the impact of early thrombolytic therapy and advanced imaging on clinical outcomes.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Sınır bölgelerinde zorunlu hareket halindeki popülasyonlarda ekstremite donmalarının klinik seyri ve tedavisi

AMAÇ: Donma, derin doku hasarı ve amputasyona kadar ilerleyebilen ciddi bir soğuk yaralanmasıdır. Sınır bölgelerinde zorunlu hareket halinde bulunan mülteci ve göçmen popülasyonlarında vaka sayılarındaki artış, klinik seyir ve risk faktörlerinin ayrıntılı olarak değerlendirilmesini gerekli kılmaktadır. Bu çalışma, donmaya bağlı ekstremite yaralanmaları ile başvuran hastaların demografik özelliklerini, klinik seyirlerini, laboratuvar bulgularını ve tedavi sonuçlarını değerlendirmeyi amaçlamıştır.

GEREÇ VE YÖNTEM: Bu retrospektif çalışmaya, klinik olarak doğrulanmış donma ile başvuran toplam 154 hasta dahil edilmiştir. Hastalar üç önceden tanımlanmış sınıflandırmaya göre analiz edildi: tedavi yaklaşımı (konservatif, medikal ve ileri/girişimsel), donma yaralanmasının anatomik dağılımı ve hastaneye başvuru süresi (≤12 saat, 12–24 saat, 24–36 saat, 36–48 saat ve >48 saat). Demografik veriler, klinik bulgular, laboratuvar parametreleri, uygulanan tedavi yöntemleri ve klinik sonuçlar değerlendirildi. İstatistiksel analizler nonparametrik testler ve ki-kare analizi kullanılarak gerçekleştirildi.

BULGULAR: Hastaların ortanca yaşı 23 yıl olup, %94.2'si yabancı uyrukluydu. En sık hastaneye başvuru zamanı, soğuğa maruziyetten sonraki 12–24 saatler arasında (%61) idi. Hastaneye başvuru süresi uzadıkça, donma derecesi, etkilenen ekstremite sayısı, hipotansiyon sıklığı, beyaz kan hücresi (WBC) düzeyleri ve hastanede yatış süresi anlamlı olarak arttı ($p<0.001$). Hastaların %77.3'üne amputasyon uygulandı ve amputasyon yapılan tüm olgularda dördüncü derece donma mevcuttu. Amputasyon, gecikmiş başvuru, hipotansiyon, yüksek WBC düzeyleri, daha geniş donma alanı ve daha uzun hastanede yatış süresi ile anlamlı şekilde ilişkili bulundu ($p<0.05$).

SONUÇ: Gecikmiş başvuru ve ağır sistemik tutulum amputasyon riskini belirleyen en önemli faktörlerdir. Erken tanı, hızlı ve kontrollü yeniden ısıtma, uygun hasta transferi ve ileri tedavi seçeneklerine zamanında erişim, amputasyon oranlarının azaltılmasında kritik öneme sahiptir.

Anahtar sözcükler: Amputasyon; donma; halk sağlığı; mülteciler; soğuk yaralanması.

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ORIGINAL ARTICLE

Simulation-based evaluation of emergency medicine residents' preparedness for toxic terrorism

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ABSTRACT

BACKGROUND: Toxic terrorism is a rare but potentially catastrophic threat that can result in mass casualties and overwhelm healthcare systems. Effective management of such incidents requires specialized clinical competencies and preparedness that may be underemphasized in standard emergency medicine training. This study aimed to assess emergency medicine residents' competencies in toxic terrorism preparedness and emergency medical management using a structured simulation-based examination.

METHODS: Emergency medicine residents working in the emergency departments of two tertiary university hospitals in Trabzon participated in a simulation-based clinical assessment. The examination comprised five realistic, fully immersive objective structured clinical examination (OSCE) stations designed to evaluate diagnostic decision-making and treatment planning in toxic terrorism scenarios. Each station was scored using standardized checklists developed by medical toxicologists. Factors associated with improved performance were also examined.

RESULTS: Although 33.3% of participants successfully passed the botulism scenario (Station 3), no participant successfully completed all five stations. The radiation exposure scenario (Station 2) was the most challenging. Higher performance was significantly associated with having more than 24 months of residency training, prior chemical, biological, radiological, and nuclear (CBRN) training, and previous exposure to simulation-based education.

CONCLUSION: These findings suggest that current training may not adequately prepare emergency medicine residents to manage toxic terrorism incidents. Incorporating standardized simulation-based assessments, such as OSCEs, into residency curricula may help identify training gaps and improve preparedness for low-frequency, high-impact events.

Keywords: Chemical, biological, radiological, and nuclear; emergency medicine; simulation; toxic terrorism; toxicology; training.

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INTRODUCTION

Toxic terrorism refers to the use of chemical, biological, radiological, or nuclear (CBRN) agents as threats or weapons to cause panic, illness, injury, and death within civilian populations.[1] Incidents of toxic terrorism involving CBRN agents have become an increasing global concern. Although toxic syndromes are most commonly associated with chemical agents, biological (e.g., anthrax), radiological (e.g., internal contamination), and nuclear (e.g., acute radiation syndrome) exposures can also result in distinct, life-threatening clinical conditions that require rapid recognition and emergency intervention. The use of chemical agents in modern warfare has been extensively documented. In Syria, between 2013 and 2020, at least 234 chemical attacks were recorded, resulting in more than 13,000 injuries and 3,400 deaths; 211 of these attacks involved chlorine gas alone or in combination with other agents.[2,3] The United Nations and independent human rights organizations have documented multiple sarin and chlorine attacks, most of which targeted civilian populations. In the context of the Russia–Ukraine war, battlefield reports and open-source intelligence have raised concerns regarding the use of riot-control agents and toxic industrial chemicals, such as chloropicrin, allegedly deployed in enclosed environments in violation of international law. Additionally, Russia has a documented history of using chemical agents in targeted assassinations, including the 2018 Novichok poisoning of former spy Sergei Skripal in the United Kingdom and the 2020 poisoning of opposition leader Alexei Navalny.[4] Recent intelligence reports have suggested that Russia may be preparing a chemical or radiological attack against Ukraine, accompanied by disinformation campaigns intended to justify such actions.[5] These developments underscore the global need for preparedness against CBRN terrorism incidents across emergency healthcare systems. Diagnostic uncertainty and limited experience in emergency management may delay the initiation of life-saving interventions and increase patient morbidity and mortality during toxic terrorism incidents.

The current emergency medicine residency curriculum includes limited content on toxic terrorism preparedness and medical management, and the extent of coverage varies across training programs.[6] Effective preparedness for toxic terrorism requires a multilayered approach involving national strategies, interregional coordination, and institutional planning. National frameworks establish policies, allocate resources, and ensure alignment with international conventions.[7] Interregional preparedness promotes standardized protocols, mutual aid agreements, and coordinated response capabilities across healthcare systems. At the hospital level, operational readiness depends on structured training programs, adequate personal protective equipment, established decontamination procedures, and regular disaster drills.[8-10] Within this framework, simulation-based Objective Structured Clinical Examinations (OSCEs) represent an important method for evaluating individual clinical competence. By recreating rare but high-consequence scenarios, OSCEs can identify knowledge gaps, assess decision-making under pressure, and determine whether institutional preparedness translates into effective frontline performance.[11–14] Previous studies have demonstrated that simulation-based OSCE performance correlates with subsequent clinical performance across several competency domains, including emergency decision-making and procedural skills.[13]

Assessing physicians' clinical skills in rare but high-risk scenarios, such as CBRN terrorism incidents, is essential for evaluating healthcare system readiness and identifying deficiencies in current management practices that can inform targeted training interventions. Accordingly, this study sought to address the following research questions:

1. What is the level of clinical competence among emergency medicine residents in managing toxic terrorism scenarios involving chemical, biological, radiological, or nuclear agents?

2. How do prior experiences, such as simulation-based training or exposure to real-world CBRN incidents, affect residents' performance in OSCE scenarios?

3. Which domains of clinical management (e.g., overall assessment and stabilization, decontamination, diagnostic activities, and specific treatment) represent the most significant gaps in performance?

The aim of this study was to assess the performance of emergency medicine residents in toxic terrorism scenarios using structured simulation-based OSCEs, with a particular focus on overall assessment and stabilization, decontamination, diagnostic activities, and specific treatment.

MATERIALS AND METHODS

Study Setting and Population

This was an observational study using a simulation-based assessment. Emergency medicine residents from the Karadeniz Technical University, Faculty of Medicine, Department of Emergency Medicine, and the Trabzon University, Faculty of Medicine, Department of Emergency Medicine participated in the study. The study was conducted at the Karadeniz Technical University Medical Education and Training Simulation Center (KTU-MEDSIM), which is equipped with the technology and resources necessary to provide authentic and clinically relevant simulation experiences.

The study protocol was approved by the Karadeniz Technical University Scientific Research Ethics Committee (Protocol No. 2021/216/ Date: 30.06.2021). The required sample size was calculated using G*Power version 3.1 software, assuming a medium effect size (f=0.25), an alpha level of 0.05, and a statistical power of 80% (1-β=0.80). Based on these parameters, the minimum required sample size was determined to be 42 participants. Both participating institutions followed the standard emergency medicine residency curriculum. In addition, the KTU, Department of Emergency Medicine offers a

structured toxicology training program consisting of monthly didactic lectures and daily bedside teaching delivered by a certified medical toxicologist. This training program is unique to KTU and is not available at the second participating institution. All emergency medicine residents actively working in either institution during the study period were eligible for inclusion, regardless of residency year. Residents who were on leave, rotating outside the emergency department, or unwilling to participate were excluded.

Study Design and Measurements

The simulation-based OSCE stations were developed by a panel of four experts. The research coordinator was an Associate Professor of Emergency Medicine with certification in simulation-based education and a PhD in toxicology. One researcher contributed to scenario development through an extensive literature review. Two additional medical educators with doctoral-level training and expertise in simulation-based education participated in the development process. One author had completed a one-year fellowship in medical education, while the other served as Co-Director of the KTU-MEDSİM and held a master's degree in medical education.

Development of OSCE Scenarios

The medical toxicologist served as the principal investigator and drafted the initial scenario framework. As this study was conducted as part of an emergency medicine residency dissertation, a comprehensive literature review was performed during the planning phase. Based on this review, a blueprint was developed to define the key topics and competencies to be assessed. Medical educators contributed to scenario development during the item-writing phase to ensure the clarity, relevance, and educational validity of the content. The researchers responsible for scenario development met repeatedly to refine and finalize the scenarios. Subsequently, three independent experts reviewed the scenarios and provided feedback to enhance their content validity and overall quality.

The OSCE consisted of five simulation-based stations: one utilizing a high-fidelity computerized manikin, two employing standardized patients, and two video-based scenarios. In the first three stations, residents were observed through live video and audio feeds from behind a one-way mirror, and their performance was evaluated across the management domains presented in Table 3 (recognition/diagnosis, PPE selection and decontamination, supportive treatment, and specific treatment). For the two video-based stations, participants viewed prerecorded footage and provided written responses. Developed by the research team, these scenarios depicted television news coverage of large-scale toxic incidents that were too complex to recreate within a single simulation station. The video scenarios were designed to convey the scale and severity of toxic agent attacks and to evaluate participants' management strategies in response to chemical terrorism incidents. To establish content validity, each scenario was reviewed by three independent experts.

Assessment forms for each scenario were developed based on the literature and expert consensus. These forms were subsequently reviewed by three independent experts, and revisions were made accordingly. The final assessment forms were completed in the simulation center control room by a team consisting of one medical toxicologist and five emergency medicine faculty members, all of whom had received training in simulation-based education.

Each station lasted 8 minutes, followed by a 2-minute transition period. These timings were established through pilot testing with residents who did not participate in the study. Entry and exit times were signaled by an audible buzzer. Two days before the assessment, all participants attended a standardized orientation session that included a video explaining station procedures and the capabilities of the high-fidelity computerized manikin.

No preparatory lectures, training sessions, or educational materials were provided before the OSCE because the objective was to assess baseline competence rather than evaluate an educational intervention. The only preparation permitted was a standardized orientation video describing the OSCE format, which was provided equally to all participants. This approach was intended to ensure a uniform level of familiarity with the examination process while minimizing the influence of external educational interventions. Factors potentially associated with performance included prior training in CBRN incidents, previous participation in simulation-based training, duration of residency training (>24 months), gender, and toxicology-related educational experiences. Potential confounding factors included baseline clinical competence, familiarity with similar scenarios, examination-related stress, and variability in the perceived realism of the simulations.

Although a formal interrater calibration session was not conducted before the study, all raters used standardized assessment checklists developed by experts in toxicology and simulation-based education. Participant performance was evaluated based on predefined critical actions ("golden steps") for each station. Any uncertainty or disagreement in ratings was resolved through post hoc review of video recordings and consensus discussion among the evaluators. This approach was intended to enhance rating consistency despite the absence of formal calibration.

This study was reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for cross-sectional studies.[15]

Simulation-Based OSCE Design

The simulation-based OSCE was conducted using a high-fidelity computerized manikin (Advanced HAL S3201; Gaumard Scientific, Miami, FL, USA) and standardized patients. A standardized patient is a trained actor who consistently portrays a predefined clinical role according to a scenario developed by subject-matter experts and course coordinators.[16]

A detailed summary of each station, including the scenario content, competencies assessed, and expected critical actions, is presented in Table 1. Photographic documentation of station setups is provided in Figure 1. The scenarios were specifically designed to assess residents' competencies in overall assessment and stabilization, decontamination, diagnostic activities, and specific treatment interventions.

All scenarios were designed to present a moderate level of clinical and cognitive difficulty consistent with the expected competencies of second-year and more senior emergency medicine residents. Scenario complexity was not modified according to training level. All participants received identical case content, event sequences, and decision-making requirements to ensure standardized assessment conditions across varying levels of experience. A faculty member from the Department of Emergency Medicine served as evaluator at each station. Video recordings were reviewed when necessary to verify or clarify performance assessments.

Data Collection

The study utilized a simulation-based OSCE that was reviewed and validated by three independent experts to assess clinical decision-making and medical management skills.



Figure 1. Simulation-based stations included in the study.

Table 1. Simulation-based OSCE scenarios for toxic terrorism preparedness

Station	Scenario description	Simulation modality	Key competencies assessed	Critical actions ("golden steps")
1	Organophosphate poisoning following exposure to an unknown liquid at a bus stop	High-fidelity manikin	Personal protective equipment (PPE) selection, toxidrome recognition, antidote administration	• Select appropriate PPE • Initiate patient decontamination • Recognize the cholinergic toxidrome • Administer atropine and an oxime antidote
2	Internal contamination following ingestion of radioactive material	Hybrid simulation (manikin + standardized patient [SP])	Decontamination, radiation emergency recognition, supportive management	• Select appropriate PPE • Recognize internal radioactive contamination • Initiate decontamination procedures • Establish the diagnosis and initiate appropriate treatment
3	Botulism presenting with ptosis and dysphagia following a shared meal	Standardized patient	Diagnostic reasoning, treatment initiation	• Recognize botulism • Request appropriate diagnostic tests • Initiate botulinum antitoxin therapy
4	Sulfur mustard exposure during a mass-casualty incident	Video-based scenario	Recognition of visual clinical findings, protective measures, symptomatic management	• Identify characteristic dermatologic findings • Initiate symptomatic treatment • Implement appropriate protective measures
5	Cyanide poisoning following an indoor explosion	Video-based scenario	Cyanide toxidrome recognition, antidote administration	• Recognize cyanide poisoning • Administer hydroxocobalamin • Initiate oxygen therapy

Assessment forms were developed based on published literature and expert consensus and were intended to evaluate both general professional competencies and scenario-specific clinical skills. Each station was evaluated using a predefined checklist developed by medical toxicologists. These checklists consisted of scenario-specific critical actions ("golden steps") considered essential for successful patient management. Participant performance at each station was classified into one of three categories: "Competent," "Partial competence," or "Failure." A participant was classified as "Competent" only if all golden steps were completed adequately. Performance was classified as "Partial Competence" if at least one critical step was partially completed or performed suboptimally. Performance was classified as "Failure" if critical actions were omitted or performed incorrectly.

For statistical analyses, "Partial Competence" and "Failure" were combined into a single category. No cumulative score was calculated across stations. Instead, performance was evaluated at the station level using a binary pass/fail framework. The decision to dichotomize performance ratings into a binary pass/fail classification was made a priori by the research team. This approach was intended to reflect the realities of high-stakes toxicological emergencies, in which the omission of a single critical action may result in adverse patient outcomes.

Because the study was designed as an assessment rather than an educational intervention, no real-time or post-scenario feedback was provided during the OSCE. To maintain standardization and minimize bias, facilitators did not offer guidance, commentary, or corrective feedback during the examination. Following completion of the study and data collection, all participants were offered the opportunity to review their performance and receive individualized formative feedback during one-on-one debriefing sessions.

Participants also completed written evaluations of their examination experience for internal quality improvement purposes; however, these data were not included in the study analyses.

Data Analysis

All statistical analyses were performed using SPSS version

Table 2. Participant characteristics

Variable	n=48	%
Gender		
Female	16	33.3
Male	32	66.7
Age group (years)		
20–24	1 / 1	2.1
25–29	36	75.0
30–35	10	20.8
36–41	1 / 1	2.1
Institution type		
Institution with a Medical Toxicology Unit	34	70.8
Institution without a Medical Toxicology Unit	14	29.2
Duration of residency training		
≤24 months	28	58.3
>24 months	20	41.7
Previous CBRN training		
Yes	17	35.4
No	31	64.6
Time since most recent CBRN training		
1 year	2	4.2
2 years	13	27.1
3 years	2	4.2
No previous CBRN training	31	64.6
Previous CBRN case management experience		
Yes	10	20.8
No	38	79.2
Previous simulation-based training experience		
Yes	24	50.0
No	24	50.0
Previous simulation-based CBRN training experience		
Yes	5	10.4
No	43	89.6
Performance by OSCE station	Competent	Not competent
Station 1: Organophosphate poisoning	2 (4.2)	46 (95.8)
Station 2: Internal radioactive (cesium) contamination	-	48 (100.0)
Station 3: Botulism poisoning	16 (33.3)	32 (66.7)
Station 4: Sulfur mustard exposure	13 (21.7)	35 (72.9)
Station 5: Cyanide poisoning	4 (8.3)	44 (91.7)
Number of stations at which participants achieved competence	n	%
None	28	58.3
1 station	9	18.8
2 stations	7	14.6
3 stations	4	8.3

Table 3. Participant performance across medical management domains by OSCE station

Station 1	Competent	Partial competence	Failure
Recognition of cholinergic toxidrome	30 (62.5)	-	18 (37.5)
PPE selection and decontamination	23 (47.9)	17 (35.4)	8 (16.7)
Supportive treatment	33 (68.8)	12 (25.0)	3 (6.3)
Specific treatment	2 (4.2)	11 (22.9)	35 (72.9)
Station 2			
Recognition of acute radiation syndrome	8 (16.7)	-	40 (83.3)
PPE selection and decontamination	3 (6.3)	1 (2.1)	44 (91.7)
Supportive treatment	9 (18.8)	1 (2.1)	38 (79.2)
Specific treatment	1 (2.1)	-	47 (97.9)
Station 3			
Recognition of botulism	30 (62.5)	-	18 (37.5)
Supportive treatment	40 (83.3)	8 (16.7)	-
Specific treatment	20 (41.7)	11 (22.9)	17 (35.4)
Station 4			
Recognition of sulfur mustard toxicity	15 (31.3)	-	33 (68.7)
PPE selection and decontamination	28 (58.3)	3 (6.3)	17 (35.4)
Supportive treatment	42 (87.5)	3 (6.3)	3 (6.3)
Specific treatment	28 (58.3)	3 (6.3)	17 (35.4)
Station 5			
Recognition of cyanide poisoning	8 (16.7)	-	40 (83.3)
Supportive treatment	39 (81.3)	9 (18.8)	-
Specific treatment	5 (10.4)	2 (4.2)	41 (85.4)

17 (35.4%) had previously received CBRN training, and 10 (20.8%) had managed at least one CBRN-related case. Table 2 also summarizes the number of stations at which residents achieved a competent performance. The highest success rate was observed at Station 3 (botulism), where 16 participants (33.3%) achieved competence. In contrast, Station 2 (radiation) was the most challenging scenario, with no participant achieving competence. Overall, 28 participants (58.3%) did not achieve competence at any station, whereas nine participants (18.8%) achieved competence at one station. No participant achieved competence across all five stations.

The numbers and proportions of participants rated as competent according to station and assessment domain are presented in Table 3. The highest rates of diagnostic success were observed at Stations 1 and 3, where 62.5% of participants correctly established the diagnosis. The highest rate of success in specific treatment was observed at Station 4 (58.3%), followed by Station 3 (41.7%). The lowest rate of success in supportive treatment was observed at Station 2, where only 18.8% of participants performed adequately. When participant characteristics were compared with performance at Station 1, residents who had previously managed a CBRN-related case were significantly more likely to achieve competence (p=0.040). No significant associations were identified for any other participant characteristics (p>0.05). Analysis of factors associated with performance at Station 3 demonstrated that participants aged 30 years or older and those with more than 24 months of residency training were significantly more likely to achieve competence (p=0.027 and p=0.003, respectively). Furthermore, residents who had received simulation-based training and simulation-based CBRN training achieved significantly higher success rates at this station (p=0.006 and p=0.037, respectively). For Station 4, residents who had received CBRN training, previously managed a CBRN-related case, or participated in simulation-based training demonstrated significantly higher success rates than their counterparts (p=0.006, p=0.016, and p=0.001, respectively).

The associations between participant characteristics and achieving competence in at least one station are presented in Table 4. Residents with more than 24 months of training, as well as those with prior CBRN training and simulation-based training experience, were significantly more likely to achieve competence in at least one station (Table 4).

Table 4. Association between participant characteristics and OSCE performance

	Competent in ≥1 station n=20 (41.7)	Not competent in any station n=28 (58.3)	p
Institution type			
Institution with a Medical Toxicology Unit	17 (50.0)	17 (50.0)	0.130
Institution without a Medical Toxicology Unit	3 (21.4)	11 (78.6)	
Duration of residency training			
≤24 months	5 (17.9)	23 (82.1)	0.001
>24 months	15 (75.0)	5 (25.0)	
Previous CBRN training			
Yes	12 (70.6)	5 (29.4)	0.007
No	8 (25.8)	23 (74.2)	
Previous CBRN case management experience			
Yes	7 (70.0)	3 (30.0)	0.070
No	13 (34.2)	25 (65.8)	
Previous simulation-based training experience			
Yes	16 (66.7)	8 (33.3)	0.001
No	4 (16.7)	20 (83.3)	

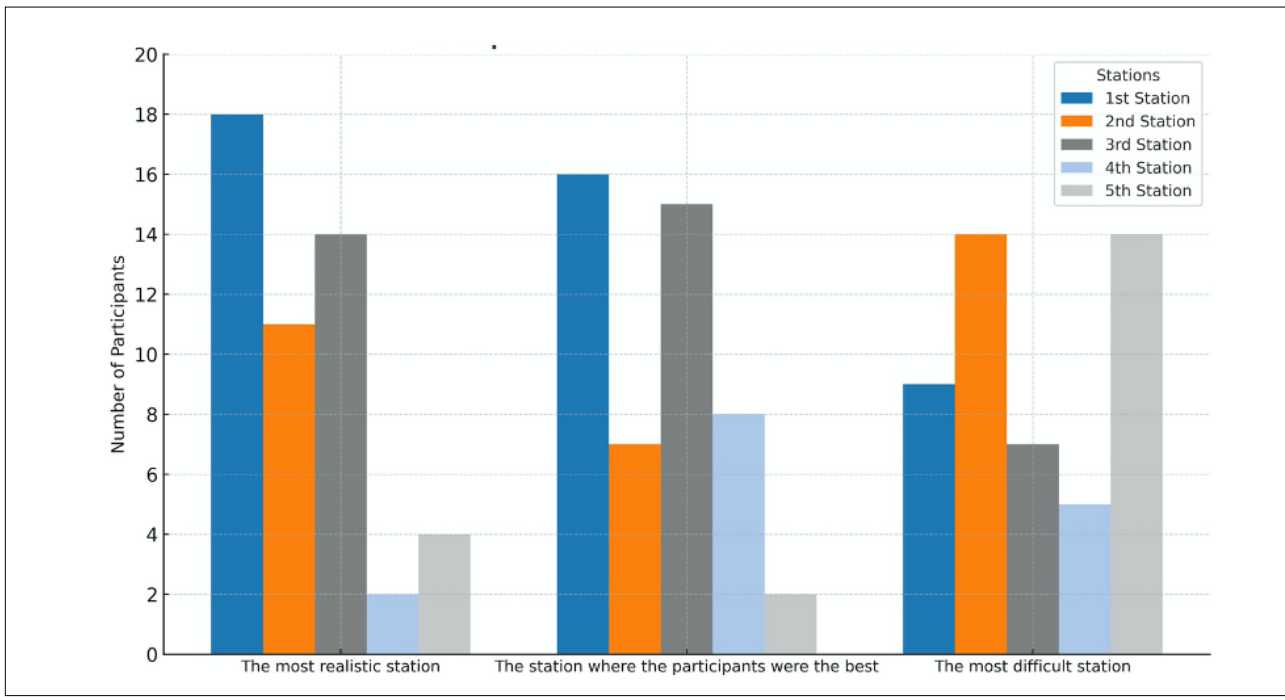


Figure 2. Participants' evaluations of the stations.

Participants were also asked to evaluate the realism and difficulty of the stations. Station 1 was rated as the most realistic scenario by 18 participants (37.5%), followed by Station 3 (29.2%) and Station 2 (22.9%). Participants most frequently reported feeling most successful in Station 1 (n=16, 33.3%) and Station 3 (n=15, 31.3%). Stations 2 and 5 were identified as the most difficult scenarios by 14 participants (29.2%) each (Fig. 2).

DISCUSSION

In this study, emergency medicine residents' clinical competencies in managing toxic terrorism scenarios were evaluated using a simulation-based OSCE. The results revealed that a substantial proportion of participants were unable to demonstrate adequate performance across critical domains, including overall stabilization, diagnosis, decontamination, and specific treatment. These findings suggest important gaps in toxic terrorism preparedness among emergency medicine residents and underscore the need for standardized, reproducible educational modules addressing CBRN incidents within emergency medicine residency curricula.

In the present study, residents with more than 24 months of training, prior CBRN education, and previous simulation-based training were significantly more likely to achieve competence in at least one OSCE station. Ryan et al.[17] reported that mean examination scores assessing medical knowledge and overall clinical competence among 59 emergency medicine residents increased significantly with advancing years of residency training. Our findings are consistent with previous evidence demonstrating that clinical knowledge and performance improve with increasing training experience. Dönmez [18] reported that 61.8% (n=268) of emergency medicine providers had not received any formal CBRN training. Similarly, Stevens et al.,[19] evaluated the perceived preparedness of 663 healthcare workers to respond to CBRN incidents and found significantly higher readiness scores among those who had received recent CBRN training. Kako et al.[12] demonstrated that simulation-based CBRN training can improve healthcare professionals' knowledge and preparedness for emergency response. In the present study, 31 residents (64.6%) had never received formal CBRN training, and prior CBRN training was significantly associated with higher proficiency rates. Compared with the existing literature, the relatively low proficiency rates observed in our study may reflect several educational deficiencies, including limited emphasis on CBRN terrorism within standard emergency medicine curricula, insufficient use of simulation-based training for high-risk and low-frequency scenarios, and the rarity of real-world CBRN exposures during residency training. Previous studies have shown that structured and repeated educational interventions—including realistic simulations, disaster drills, and scenario-based exercises—can substantially improve preparedness and performance in managing such events. Our findings further support the integration of standardized toxic terrorism and CBRN preparedness modules into emergency medicine residency programs.

Numerous studies have demonstrated the effectiveness of simulation-based CBRN training. In this study, participants rated the organophosphate poisoning station as the most realistic scenario; however, it was also associated with one of the highest failure rates. Errors involving critical interventions, such as the administration of atropine, suggest deficiencies in both practical skills and theoretical knowledge. Similarly, Eason et al.[20] found that sarin gas simulation exercises effectively improved healthcare workers' administrative and clinical competencies. A pilot study by Subbarao et al.,[21] utilizing both manikin-based and video-based simulations, demonstrated significant improvements in participants' knowledge following training. Furthermore, a virtual reality–based educational program that included practical decontamination procedures for radiation-contaminated patients provided substantial learning benefits through opportunities for individualized practice.[22] Collectively, these findings highlight the importance of practical and modular training approaches to reduce performance deficiencies in complex toxicological emergencies.

Among the five stations, the radiation exposure scenario (Station 2) was perceived, together with the cyanide scenario (Station 5), as the most difficult by participants. This finding is consistent with previous literature highlighting the complexity of radiation-related emergencies and the limited training opportunities available in this area. Ebeling et al.[23] reported that only 25% of participants, including 22 emergency medicine residents and one pharmacy resident, correctly diagnosed acute radiation syndrome (ARS) in a highly realistic simulation without explicit warning cues. Similarly, Sheikh et al.[24] found that only 37% of emergency medicine residents had received radiation-related training within the previous five years, suggesting that inadequate training negatively affects diagnostic and intervention competence. Together, these findings emphasize the need to increase awareness of radiation emergencies, strengthen diagnostic skills, and implement targeted educational strategies to improve preparedness.

Decontamination practices were also evaluated in this study. Although most participants recognized the need for decontamination, deficiencies in the selection and use of appropriate personal protective equipment (PPE) were common. In a survey conducted by Szarpak et al.,[25] only 26.1% of 510 physicians, nurses, and paramedics reported adequate knowledge of patient decontamination procedures. Consistent with these findings, cross-sectional studies of prehospital healthcare workers have identified significant readiness gaps and emphasized the need for additional training in decontamination procedures.[26,27] While participants in our study generally recognized the importance of decontamination, many failed to select appropriate PPE to protect themselves, highlighting a critical area for educational improvement.

Participants who achieved competence in at least one OSCE station were significantly more likely to have previous experience with simulation-based training. Approximately half of the residents had participated in such training, and these individuals demonstrated significantly higher proficiency rates. This finding reinforces the value of simulation-based education not only as a teaching modality but also as a reliable method for assessing clinical competence. Chen et al.[28] evaluated 68 emergency medicine residents using written examinations, oral assessments, and immersive simulation scenarios across

eight training periods. Similarly, Liu et al.[29] demonstrated that immersive simulation training was associated with superior end-of-training examination performance among nine emergency medicine residents. In rare but high-consequence toxicological scenarios, simulation within a structured and standardized OSCE framework offers distinct advantages because it evaluates clinical reasoning, decision-making, and procedural performance beyond simple knowledge recall.[30]

This study also has important implications for medical educators and emergency preparedness planners. First, our findings demonstrate that simulation-based OSCEs can effectively identify deficiencies in CBRN preparedness among emergency medicine residents, particularly in settings where direct clinical exposure is limited. Second, the combination of immersive simulation and video-based scenarios provided a cost-effective and scalable approach for evaluating core clinical competencies. Importantly, residents with prior simulation experience or formal toxicology training performed significantly better, supporting the integration of structured and repetitive simulation-based learning experiences into residency curricula. These findings align with recent recommendations advocating competency-based disaster education and support the use of modular, video-based training and assessment approaches.[31–33] Educational leaders and policymakers in comparable healthcare systems may consider adopting similar approaches to enhance preparedness for toxic terrorism, a rare but potentially devastating public health threat.

A review of the literature did not identify any previous studies evaluating the clinical competencies of emergency medicine physicians in the diagnosis and management of toxic terrorism incidents using a structured simulation-based assessment. Consequently, this study contributes to the literature by developing and applying a simulation-based clinical skills assessment focused on toxic terrorism preparedness.

Limitations

This study has several limitations. First, although the five scenarios were designed to represent key CBRN terrorism situations, they do not encompass the full spectrum of potential clinical presentations. A larger and more diverse scenario pool would improve generalizability. Second, the assessments were conducted on consecutive days to minimize information sharing among participants; however, informal communication and discussion of scenario content among residents could not be completely prevented. Third, although emergency medicine residency curricula are theoretically standardized across institutions in Türkiye, differences in local implementation and toxicology exposure may have influenced participant performance. Fourth, senior residents are more likely to encounter and manage CBRN-related incidents in clinical practice, which may limit the applicability of the findings to junior residents. Fifth, although the study sought to compare residents exposed to simulation-based education with those receiving structured toxicology training, only one participating institution offered formal toxicology rotations, limiting the strength of these comparisons. Sixth, the study was conducted at only two emergency medicine residency programs in Türkiye, which may limit the international generalizability of the findings. Seventh, the assessment instrument was not pilot tested before implementation. Although the scenarios and assessment forms underwent expert review, the absence of pilot testing limits the extent of formal validation. Finally, this study employed a cross-sectional design and assessed participants at a single time point; therefore, long-term knowledge retention and the effects of subsequent educational interventions could not be evaluated.

Although the simulation-based findings provide valuable insights into residents' preparedness for toxic terrorism incidents, their direct applicability to real-world clinical performance remains uncertain. Simulation environments cannot fully replicate the complexity of actual clinical practice, including patient interactions and environmental pressures. Future studies should examine the relationship between simulation-based performance and real-world clinical outcomes.

CONCLUSION

This study developed and implemented a standardized simulation-based assessment to evaluate emergency medicine residents' clinical competencies in the management of toxic terrorism incidents. The findings of this study highlight the need for a standardized core curriculum addressing CBRN and toxic terrorism preparedness within emergency medicine residency programs. Regular, competency-based training interventions should be incorporated to ensure that residents acquire the necessary competencies. Standardized, reproducible simulation-based assessments should be routinely incorporated into residency training to evaluate and reinforce preparedness for toxic terrorism, a rare but potentially high-consequence public health threat.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Acil tıp asistanlarının toksik terörizme hazırlıklı olma durumunun simülasyon tabanlı değerlendirilmesi

AMAÇ: Toksik terörizm, nadir görülmesine rağmen kitlesel yaralanmalara ve sağlık sistemlerinin hızla kapasitesini aşmasına neden olabilecek yıkıcı bir tehdit oluşturmaktadır. Bu tür olayların yönetimi, standart acil tıp eğitiminde genellikle yeterince vurgulanmayan özel klinik beceriler ve hazırlık gerektirir. Bu çalışma, yapılandırılmış simülasyon temelli bir sınav aracılığıyla acil tıp asistanlarının toksik terörizme hazırlık ve acil tıbbi yönetim konusundaki klinik yeterliliklerini değerlendirmeyi amaçlamıştır.
GEREÇ VE YÖNTEM: Trabzon'daki iki üçüncü basamak üniversite hastanesinin acil tıp kliniklerinde görev yapan acil tıp asistanları simülasyon temelli klinik değerlendirmeye katılmıştır. Sınav, toksik terörizm senaryolarında tanısal karar verme ve tedavi planlamasını ölçmek üzere tasarlanmış, gerçekçi ve tamamen immersif beş istasyondan oluşan bir nesnel yapılandırılmış klinik sınav formatındaydı. Her istasyon, medikal toksikologlar tarafından geliştirilen standartlaştırılmış kontrol listeleri kullanılarak puanlanmıştır. Ayrıca performansı artıran faktörler de incelenmiştir.
BULGULAR: Katılımcıların %33.3'ü botulizm senaryosunu (İstasyon 3) başarıyla tamamlamış olsa da hiçbir katılımcı beş istasyonun tamamını geçememiştir. En zorlanan istasyon radyasyon maruziyeti senaryosu (İstasyon 2) olmuştur. Daha iyi performans, 24 aydan uzun asistanlık deneyimi, önceden alınmış kimyasal, biyolojik, radyolojik ve nükleer (KBRN) eğitim ve daha önce simülasyon temelli eğitime katılmış olmak ile anlamlı olarak ilişkili bulunmuştur.
SONUÇ: Bulgular, mevcut eğitimin acil tıp asistanlarını toksik terörizm senaryolarını yönetmek için yeterince hazırlamadığını göstermektedir. Nesnel yapılandırılmış klinik sınav gibi standartlaştırılmış simülasyon temelli değerlendirmelerin eğitim müfredatına dahil edilmesi, eğitimdeki eksiklikleri belirlemeye ve düşük sıklıkta görülen ancak yüksek etkili olaylara hazırlığı artırmaya yardımcı olabilir.

Anahtar sözcükler: Acil tıp; eğitim; radyolojik ve nükleer; simülasyon; toksikoloji; toksik terörizm.

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ORIGINAL ARTICLE

Long-term outcomes following scaphoid nonunion surgery: the role of structural severity, avascular necrosis, and surgical timing

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ABSTRACT

BACKGROUND: This study aimed to evaluate the long-term clinical and radiological outcomes of patients undergoing surgical treatment for scaphoid nonunion and to examine the independent effects of surgical timing and preoperative avascular necrosis (AVN) on postoperative recovery.

METHODS: This retrospective cohort study included 71 adult patients who underwent surgical treatment for scaphoid nonunion between 2011 and 2020 and had a minimum follow-up of five years. Variables included demographic characteristics, surgical timing, preoperative AVN, and radiographic severity. Clinical outcomes were assessed using the Visual Analog Scale (VAS), Patient-Rated Wrist Evaluation (PRWE), and Mayo Wrist Score (MWS). Radiological evaluation included scaphoid nonunion advanced collapse (SNAC) staging, scapholunate angle (SLA), radiolunate angle (RLA), and carpal height index. Multivariate linear and logistic regression analyses were performed to identify independent predictors of functional improvement, union, complications, and reoperation.

RESULTS: The mean patient age was 34.4±7.1 years, and the mean follow-up duration was 78.4±10.3 months. Preoperative AVN was present in 29.6% of patients. Union was achieved in 76.1% of patients, while complication and reoperation rates were 26.8% and 18.3%, respectively. In univariate analysis, surgery performed within 12 months of injury was associated with greater improvement in resting pain ($p=0.046$), and the absence of AVN was associated with greater improvement in pain scores and MWS ($p<0.05$). After adjustment for baseline pain and radiographic severity, surgical timing was no longer independently associated with pain improvement ($p=0.056$), whereas AVN remained an independent predictor of reduced symptomatic recovery ($p<0.001$). No variable independently predicted union. The preoperative SNAC stage was associated with complications ($p=0.007$), and Schernberg classification predicted reoperation ($p=0.011$). Radiographic parameters were not associated with functional outcomes. These findings suggest that biological and structural disease burden may have a greater influence on long-term recovery than surgical timing alone. Although vascular compromise appears to limit symptomatic improvement despite surgical intervention, structural severity influences the risk of adverse postoperative events. The absence of a correlation between radiographic healing and functional outcomes underscores the complex and multifactorial nature of recovery after scaphoid nonunion surgery.

CONCLUSION: Surgical timing and radiographic union were not independently associated with long-term functional recovery. In contrast, preoperative AVN predicted less symptomatic improvement, whereas structural severity, reflected by SNAC stage and Schernberg classification, was associated with postoperative complications and reoperation.

Keywords: Avascular necrosis; nonunion; scaphoid; scaphoid nonunion advanced collapse (SNAC); union rate.

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INTRODUCTION

Scaphoid nonunion is defined as the absence of radiographic or advanced imaging evidence of bone healing six months after injury.[1] It develops in approximately 2%–15% of scaphoid fractures, with higher rates observed in proximal pole injuries.[2-4] Established risk factors include avascular necrosis (AVN), fracture displacement or instability, fracture location, and delayed treatment.[5,6]

Scaphoid nonunion is associated with persistent pain, functional impairment, and progressive carpal collapse. If left untreated, it may progress to scaphoid nonunion advanced collapse (SNAC) and secondary wrist arthritis.[3] The primary goals of treatment are restoration of carpal alignment, achievement of union, and durable functional recovery.

Surgical management is influenced by fracture location, deformity, vascular status, and patient-related factors.[4,7] Various techniques have been described, including deformity correction, bone grafting, rigid internal fixation, and the use of vascularized and nonvascularized grafts.[8-10] Despite these approaches, there is no clear consensus regarding the optimal surgical strategy or the prognostic significance of factors such as AVN.[7,10,11]

Although short-term outcomes are generally favorable, long-term clinical and radiographic outcomes remain insufficiently characterized, particularly regarding the independent effects of surgical timing and preoperative vascular status.[7,10,11] Therefore, the present study aimed to evaluate long-term outcomes following surgical treatment of scaphoid nonunion and to examine the effects of surgical timing and preoperative AVN on postoperative recovery.

MATERIALS AND METHODS

This retrospective single-center cohort study included consecutive adult patients who underwent primary surgical treatment for scaphoid nonunion between 2011 and 2020, with a minimum postoperative follow-up of five years. Ondokuz Mayıs University Clinical Research Ethics Committee (Date: 12.09.2024, Decision no: 2024/360).

All preoperative, intraoperative, and postoperative data were obtained from institutional medical records.

Inclusion criteria were age ≥18 years, radiographically confirmed scaphoid nonunion, and availability of at least five years of follow-up. Patients with previous failed scaphoid surgery, advanced carpal collapse requiring salvage procedures, complex wrist trauma, systemic inflammatory disease, or incomplete clinical data were excluded. A total of 102 patients were initially identified; after application of the inclusion and exclusion criteria, 71 patients were eligible for final analysis.

All patients were treated using a modified Matti–Russe technique through a volar approach. A longitudinal incision was made along the radial border of the flexor carpi radialis tendon, followed by capsulotomy to expose the nonunion site. After thorough debridement of fibrous tissue and sclerotic bone, a corticocancellous iliac crest bone graft was inserted to restore scaphoid length and alignment. Internal fixation was performed using a headless compression screw, and stability was confirmed intraoperatively under fluoroscopic guidance.

Postoperatively, patients were immobilized in an arm cast for 4 weeks, followed by splint immobilization from weeks 4 to 6. Progressive active range-of-motion exercises were initiated after week 6. Clinical and radiographic evaluations were performed at 2, 4, 8, and 12 weeks and at 6 months postoperatively. Radiographic follow-up continued until bone healing was confirmed. Final assessment was performed at the most recent available follow-up visit, with a minimum postoperative follow-up of 5 years.

Standard posteroanterior (PA), lateral, ulnar-deviated PA, and semipronated radiographs were obtained during follow-up. Nonunion location was categorized as proximal pole, waist, or distal pole. Degenerative changes were classified according to the scaphoid nonunion advanced collapse staging system. Scapholunate (SL) angle, radiolunate (RL) angle, and carpal height index were measured on standard radiographs. Bone union was assessed using at least two postoperative radiographic views.

All patients had established scaphoid nonunion preoperatively. At final follow-up, bone healing status was categorized as union or non-union. Union was defined as cortical bridging with trabecular continuity across the fracture site and disappearance of the fracture line on at least two radiographic views. Nonunion was defined as the absence of cortical bridging with persistence of the fracture line at final follow-up. Computed tomography (CT) was obtained only when standard radiographs were inconclusive or when clinical–radiographic discordance was suspected. Because CT was not routinely performed, it was not incorporated into the primary outcome assessment. Preoperative avascular necrosis was diagnosed using magnetic resonance imaging (MRI) and defined as low signal intensity on T1-weighted images within the scaphoid, as assessed by an experienced musculoskeletal radiologist.

Clinical outcomes were assessed using the Visual Analog Scale (VAS) for pain at rest and during activity, the Patient-Rated Wrist Evaluation (PRWE), and the Mayo Wrist Score (MWS). Active wrist range of motion (ROM), including radial and ulnar deviation, was measured using a standard goniometer. Grip strength was assessed using a hydraulic hand dynamometer (Model SH5001, Masan, Korea) and expressed as a percentage of the contralateral side. Changes (Δ) in clinical scores were calculated as the difference between preoperative and final follow-up values. Postoperative complications and reoperation rates were recorded. Persistent pain was defined as pain at final follow-up requiring medical treatment,

activity modification, or additional clinical evaluation.

Statistical Analysis

Statistical analyses were performed using SPSS version 22. Continuous variables are presented as mean ± standard deviation, and categorical variables as frequency and percentage. Comparisons between groups (<12 vs. ≥12 months and AVN vs. non-AVN) were performed using the Mann–Whitney U test or the chi-square/Fisher's exact test. Multivariate linear regression analysis was used to identify predictors of improvement in resting pain (ΔVAS), adjusting for baseline pain and radiographic severity. Logistic regression analysis was performed to identify predictors of union, complications, and reoperation. Variables with clinical relevance or a univariate p value <0.10 were included in the analysis. A p value <0.05 was considered statistically significant.

RESULTS

A total of 71 patients were included, with a mean age of 34.4±7.1 years and a mean follow-up duration of 78.4±10.3 months. Baseline demographic and surgical characteristics (Fig. 1), including the prevalence of preoperative AVN and overall rates of union, complications, and reoperation (76.1%, 26.8%, and 18.3%, respectively), are summarized in Table 1. No significant associations were identified between demographic variables and complication rates or clinical outcomes (p>0.05).

A total of 26 complications occurred in 19 patients. Persistent pain was the most common complication (n=13), followed by persistent nonunion (n=8) and postoperative AVN (n=3). Less frequent complications included iliac crest donor-site pain (n=3), donor-site infection (n=1), hematoma (n=1), and lateral femoral cutaneous nerve deficit (n=1). Reopera-



Figure 1. A 26-year-old woman who underwent surgical treatment for scaphoid nonunion using the modified Matti–Russe technique. Five-year postoperative radiographs demonstrate complete osseous union, with trabecular continuity across the fracture site and no evidence of graft resorption, sclerosis at the fracture margins, or implant-related complications.

Table 1. Demographic and baseline characteristics of the study population

Characteristic	Value
Age, mean (SD)	34.4±7.1
Follow-up duration, mean (SD), months	78.4±10.3
Sex (male/female)	61 (85.9%)/10 (14.1%)
Injured hand (dominant/non-dominant)	56 (78.9%)/15 (21.1%)
Smoking status (current smoker/non-smoker)	24 (33.8%)/47 (66.2%)
Occupation (manual labor/non-manual labor/not working)	34 (47.9%)/30 (42.3%)/7 (9.3%)
Preoperative SNAC stage (no arthritis/stage 1/stage 2)	29 (40.8%)/30 (42.3%)/12 (16.9%)
Schernberg classification (type 1/type 2/type 3)	9 (12.7%)/36 (50.7%)/26 (36.6%)
Time from injury to surgery (months)	11.2±4.3
Time to surgery (<12months/≥12 months)	42 (59.2%)/29 (40.8%)
Preoperative AVN (present/absent)	21 (29.6%)/50 (70.4%)
Union status at final follow-up (union/nonunion)	54 (76.1%)/17 (23.9%)
Postoperative SNAC stage (no arthritis/stage 1/stage 2)	20 (28.1%)/32 (45.1%)/19 (26.8%)
Postoperative complications (present/absent)	19 (26.8%)/52 (73.2%)
Reoperation (yes/no)	13 (18.3%)/58 (81.7%)

SNAC: Scaphoid nonunion advanced collapse; AVN: Avascular necrosis.

Table 2. Univariate analysis of factors associated with postoperative complications

Variable	Complication (n=19)	No complication (n=52)	p
Occupation (manual labor/non-manual labor/not working, %)	52.6%/42.1%/5.3%	46.2%/42.3%/11.5%	0.710
Injured hand (dominant/non-dominant, %)	78.9%/21.1%	78.8%/21.2%	0.192
Schernberg classification (type 1/type 2/type 3, %)	10.5%/31.6%/57.9%	13.5%/57.7%/28.8%	0.039
Preoperative SNAC stage (no arthritis/stage 1/stage 2, %)	21.1%/42.1%/36.8%	48.1%/42.3%/9.6%	0.014
Time to surgery (<12 months/≥12 months, %)	47.4%/52.6%	63.5%/36.5%	0.222
Preoperative AVN (present/absent, %)	42.1%/57.9%	25.0%/75.0%	0.162

SNAC: Scaphoid nonunion advanced collapse; AVN: Avascular necrosis.

tion was required in 13 patients, most commonly revision surgery with bone grafting (n=8).

Univariate Analysis

Proximal nonunion localization and preoperative SNAC stage 2 were associated with higher complication rates (p=0.039 and p=0.014, respectively) (Table 2). Surgical treatment within 12 months of injury was associated with a greater reduction in resting pain (ΔVAS −6.6±1.1 vs. −5.7±1.3; p=0.046) (Table 3), whereas no significant differences were observed in other clinical or event-related outcomes.

Patients without preoperative AVN demonstrated greater improvements in resting pain, activity-related pain, MWS, and grip strength (p<0.05) (Table 4). Union status was not associated with long-term clinical or radiographic outcomes (Table 5).

Multivariate Analysis

In multivariate linear regression adjusted for baseline resting pain and radiographic severity, surgical timing was not independently associated with improvement in resting pain (β=−0.372, 95% confidence interval [CI]: −0.754 to 0.010; p=0.056). In contrast, preoperative AVN independently predicted reduced pain improvement (β=0.731, 95% CI: 0.336 to 1.126; p<0.001). Baseline resting pain was independently associated with greater postoperative pain reduction (β=−0.767, 95% CI: −1.019 to −0.516; p<0.001). The preoperative SNAC stage was not independently associated with pain improvement.

In logistic regression analysis, no independent predictors of radiographic union were identified. Surgical timing (odds ratio [OR]: 1.16, 95% CI: 0.36–3.68; p=0.805), preoperative AVN

Table 3. Clinical outcomes according to surgical timing

Outcome	<12 months (n=42)	≥12 months (n=29)	p
Δ Resting VAS	−6.6±1.1	−5.7±1.3	0.046
Δ Activity VAS	−5.0±0.7	−4.7±1.2	0.178
Δ PRWE	−32.2±20.9	−25.6±16.2	0.282
Δ MWS	+13.8±7.5	+11.2±8.4	0.121
Δ ROM (°)	+25.8±12.3	+22.7±9.6	0.490
Δ Grip strength (%)	+28.8±3.1	+26.4±3.5	0.702
Union status at final follow-up	78.6%/21.4%	72.4%/27.6%	0.582
Complications	9 (21.4%)	10 (34.5%)	0.222
Reoperation	5 (11.9%)	7 (24.1%)	0.154

VAS: Visual Analog Scale; PRWE: Patient-rated wrist evaluation; MWS: Mayo wrist score; ROM: Range of motion.

Table 4. Clinical outcomes according to preoperative avascular necrosis status

Outcome	No AVN (n=50)	AVN (n=21)	p
Δ Resting VAS	−5.2±1.2	−4.3±1.0	0.031
Δ Activity VAS	−6.4±1.9	−5.6±1.4	0.042
Δ PRWE	−16.6±8.0	−12.8±7.5	0.145
Δ MWS	+25.1±21.4	+14.8±23.9	0.046
Δ ROM (°)	+28.4±19.0	+31.2±20.9	0.571
Δ Grip strength (%)	+38.1±8.1	+21.8±7.5	0.036
Union status at final follow-up	80%/20%	66.7%/33.3%	0.240
Complications	11 (22.0%)	8 (38.1%)	0.162
Reoperation	7 (14.0%)	5 (23.8%)	0.320

VAS: Visual Analog Scale; PRWE: Patient-rated wrist evaluation; MWS: Mayo wrist score; ROM: Range of motion; AVN: Avascular necrosis.

Table 5. Long-term clinical and radiological outcomes according to union status

Outcome	Union (n=54)	Nonunion (n=17)	p
Δ Resting VAS	−5.0±1.0	−4.6±0.7	0.165
Δ Activity VAS	−6.3±1.0	−5.9±1.5	0.437
Δ PRWE	−24.1±23.4	−17.9±20.2	0.581
Δ MWS	+13.9±8.3	+11.8±4.4	0.612
Δ ROM (°)	+40.2±20.3	+36.4±17.3	0.739
Δ Grip strength (%)	+18.9±5.6	+18.8±4.9	0.946

VAS: Visual Analog Scale; PRWE: Patient-rated wrist evaluation; MWS: Mayo wrist score; ROM: range of motion.

(OR: 0.47, 95% CI: 0.14–1.51; p=0.204), and preoperative SNAC stage (OR: 0.71, 95% CI: 0.32–1.56; p=0.388) were not significantly associated with union.

The preoperative SNAC stage independently increased the risk of postoperative complications (OR: 3.05, 95% CI: 1.36–6.82; p=0.007), whereas Schernberg classification and AVN were not significant predictors. Schernberg classification independently predicted reoperation risk (OR: 5.18, 95% CI:

Table 6. Multivariate regression analyses of clinical and structural outcomes

Outcome	Variable	Effect size (β or OR)	95% CI	p
Δ Resting VAS	Surgery <12 months	β=−0.372	−0.754 to 0.010	0.056
(linear regression)	Preoperative AVN	β=0.731	0.336 to 1.126	<0.001
	Preoperative SNAC stage	β=−0.030	−0.289 to 0.230	0.820
	Baseline resting VAS	β=−0.767	−1.019 to −0.516	<0.001
Radiographic union	Surgery <12 months	OR=1.16	0.36–3.68	0.805
(logistic regression)	Preoperative AVN	OR=0.47	0.14–1.51	0.204
	Preoperative SNAC stage	OR=0.71	0.32–1.56	0.388
Postoperative complications	Preoperative SNAC stage	OR=3.05	1.36–6.82	0.007
(logistic regression)	Schernberg classifica-tion	OR=1.80	0.71–4.57	0.214
	Preoperative AVN	OR=1.45	0.41–5.10	0.562
Reoperation	Schernberg classification	OR=5.18	1.47–18.30	0.011
(logistic regression)	Preoperative SNAC stage	OR=1.89	0.79–4.53	0.156
	Preoperative AVN	OR=1.91	0.47–7.75	0.364

AVN: Avascular necrosis; SNAC: Scaphoid nonunion advanced collapse; VAS: Visual Analog Scale; CI: Confidence interval

1.47–18.30; p=0.011), whereas preoperative SNAC stage and AVN were not independently associated with reoperation (Table 6).

DISCUSSION

Scaphoid nonunion remains a challenging clinical condition, and the existing literature is dominated by retrospective studies employing heterogeneous surgical techniques and varying definitions of union.[12,13] These methodological differences limit direct comparison across studies. In our cohort, the overall union rate of 76% falls within the broad range reported in previous systematic reviews and single-center series (53%–100%).[9,14,15] Notably, multivariate analysis demonstrated that structural disease severity, reflected by preoperative SNAC stage and Schernberg classification, independently increased the risk of complications and reoperation, whereas preoperative AVN adversely affected symptomatic recovery.

The overall complication rate of 26.8% was higher than rates reported by Slade, Delamarre, and Pinder.[2,9,16] This difference may be attributable to the relatively high proportion of structurally advanced cases and the extended follow-up period in our cohort. In multivariate analysis, preoperative SNAC stage independently increased the risk of postoperative complications (OR: 3.05, 95% CI: 1.36–6.82; p=0.007), while Schernberg classification independently predicted reoperation (OR: 5.18, 95% CI: 1.47–18.30; p=0.011). These findings suggest that adverse long-term outcomes are more strongly associated with baseline structural severity and fracture morphology than with surgical timing. The prognostic importance of degenerative progression and structural severity in scaphoid nonunion has been highlighted in previous studies.[12,17,18]

Although early surgery (<12 months) was associated with greater improvement in resting pain in univariate analysis, this association was no longer significant after adjustment for baseline pain and radiographic severity (p=0.056). The impact of surgical timing remains controversial.[9,19-21] Slade et al.[19] reported faster union in patients treated within 6 months (p<0.02), whereas Somerson et al.[20] found that treatment delays of at least one year were associated with worse DASH (Disabilities of the Arm, Shoulder and Hand) and pain scores. In contrast, other studies have reported no significant relationship between surgical timing and long-term functional outcomes.[9,21] Consistent with these findings, our multivariate analysis suggests that surgical timing may not independently determine long-term functional recovery.

Preoperative AVN independently predicted less improvement in resting pain, indicating that vascular compromise negatively affects symptomatic recovery. However, AVN was not independently associated with union, complications, or reoperation. This suggests that AVN may influence clinical recovery without necessarily determining structural healing. Higher baseline resting pain was also independently associated with greater postoperative improvement, likely reflecting the influence of initial symptom severity on the magnitude of change.

The impact of AVN on union and functional outcomes remains inconsistent in the literature. Some studies have reported lower union rates in AVN-associated nonunions treated with nonvascularized grafts,[22] whereas others have demonstrated acceptable union rates using vascularized grafts.[23,24] Fergu-

son et al.[11] reported union rates of 74% with vascularized grafts and 62% with nonvascularized grafts in patients with AVN. However, systematic reviews have not consistently demonstrated superiority of either graft type within AVN subgroups.[25] This variability may reflect differences in AVN definitions (MRI-based versus intraoperative assessment), the extent of proximal pole involvement, graft selection, and methods used to assess union.[26] Because all patients in our cohort were treated with nonvascularized bone grafting, our findings should be interpreted within this surgical context.

Multivariate analysis identified no independent predictors of radiographic union, and union status was not associated with long-term clinical or radiographic outcomes. These findings are consistent with previous studies demonstrating limited correlation between radiographic measures and patient-reported outcomes.[27-29] Restoration of osseous continuity and radiographic alignment alone may not fully capture the multifactorial determinants of wrist function, including cartilage integrity, soft-tissue adaptation, neuromuscular control, and patient perception.

Radiographic progression of degenerative changes was observed during follow-up despite structural reconstruction. This observation is consistent with long-term studies demonstrating that arthritic progression may continue even after technically successful surgery.[17,18] Therefore, achieving union does not necessarily prevent long-term degenerative evolution.

This study has several limitations. Its retrospective design introduces the potential for selection and information bias, and the single-center setting may limit generalizability. Although multivariate analyses were performed, the relatively small sample size may have reduced statistical power, particularly for subgroup analyses. Additionally, radiographic assessment was based primarily on standard radiographs, which may be subject to measurement variability.

CONCLUSION

Neither surgical timing nor radiographic union was independently associated with long-term functional recovery after scaphoid nonunion surgery. In contrast, preoperative AVN predicted reduced symptomatic improvement, whereas structural disease severity, reflected by SNAC stage and Schernberg classification, was associated with postoperative complications and reoperation.

Ethics Committee Approval: Ethical approval was obtained from the Ondokuz Mayıs University Clinical Research Ethics Committee (Date: 12.09.2024, Decision No: 2024/360).

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ORİJİNAL ÇALIŞMA - *ÖZ*

Skafoid kaynamamada uzun dönem sonuçlar: Yapısal hastalık şiddeti, avasküler nekroz ve cerrahi zamanlamanın rolü

AMAÇ: Bu çalışmanın amacı, skafoid kaynamama nedeniyle cerrahi tedavi uygulanmış hastaların uzun dönem klinik ve radyolojik sonuçlarını değerlendirmek ve cerrahi zamanlama ile preoperatif avasküler nekrozun (AVN) postoperatif iyileşme üzerindeki bağımsız etkilerini analiz etmektir.
GEREÇ VE YÖNTEM: Bu retrospektif kohort çalışmasına, 2011–2020 yılları arasında skafoid kaynamama nedeniyle cerrahi tedavi uygulanmış ve en az 5 yıl takip süresi bulunan 71 erişkin hasta dahil edildi. Değerlendirilen değişkenler arasında demografik özellikler, cerrahi zamanlama, preoperatif AVN ve radyografik şiddet yer aldı. Klinik sonuçlar Vizüel Analog Skala (VAS), Hasta Tarafından Değerlendirilen El Bileği Ölçeği (PRWE) ve Mayo El Bileği Skoru (MWS) ile değerlendirildi. Radyolojik incelemede skafoid kaynamama ileri kollapsı (SNAC) evrelemesi, skafo-lunat açı (SLA), radio-lunat açı (RLA) ve karpal yükseklik indeksi kullanıldı. Fonksiyonel iyileşme, kaynama, komplikasyon ve reoperasyon için bağımsız belirleyicileri saptamak amacıyla çok değişkenli lineer ve lojistik regresyon analizleri yapıldı.
BULGULAR: Hastaların ortalama yaşı 34.4±7.1 yıl, ortalama takip süresi 78.4±10.3 ay idi. Preoperatif AVN hastaların %29.6'sında mevcuttu. Kaynama, komplikasyon ve reoperasyon oranları sırasıyla %76.1, %26.8 ve %18.3 idi. Tek değişkenli analizde, 12 ay içinde uygulanan cerrahinin istirahat ağrısında daha fazla azalma ile ilişkili olduğu saptandı (p=0.046). AVN bulunmaması, ağrı skorlarında ve MWS'de daha fazla iyileşme ile ilişkiliydi (p<0.05). Ancak başlangıç ağrısı ve radyografik şiddet için düzeltme yapılan çok değişkenli analizde, cerrahi zamanlama ağrı iyileşmesi ile bağımsız olarak ilişkili bulunmadı (p=0.056), buna karşılık AVN varlığı semptomatik iyileşmenin daha sınırlı olması ile bağımsız olarak ilişkiliydi (p<0.001). Kaynamayı bağımsız olarak öngören herhangi bir değişken saptanmadı. Preoperatif SNAC evresi komplikasyonları (p=0.007), Schernberg sınıflaması ise reoperasyonu (p=0.011) öngördü. Radyolojik parametreler fonksiyonel sonuçlarla ilişkili değildi. Bu bulgular, cerrahi zamanlamadan ziyade biyolojik ve yapısal hastalık yükünün uzun dönem iyileşmede daha belirleyici olabileceğini göstermektedir. Vasküler bozulmanın cerrahi müdahaleye rağmen semptomatik iyileşmeyi sınırlayabileceği, yapısal şiddetin ise olumsuz sonuç riskini artırabileceği anlaşılmaktadır. Radyografik iyileşme ile fonksiyonel sonuçlar arasındaki ilişkinin olmaması, skafoid kaynamama cerrahisi sonrasında iyileşmenin karmaşık ve çok faktörlü bir süreç olduğunu göstermektedir.
SONUÇ: Cerrahi zamanlama ve radyografik kaynama uzun dönem fonksiyonel iyileşme ile bağımsız olarak ilişkili değildir. Buna karşılık preoperatif AVN daha sınırlı semptomatik iyileşmeyi öngörmekte, yapısal şiddet ise komplikasyon ve reoperasyon ile ilişkili bulunmaktadır.

Anahtar sözcükler: Avasküler nekroz, kaynama oranı, kaynamama, Skafoid, SNAC.

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CASE REPORT

A novel variant of pancreaticobiliary maljunction: Complete opening of the common bile duct into the duct of Santorini in a patient with pancreas divisum

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ABSTRACT

Pancreaticobiliary maljunction (PBM) is a rare congenital anomaly in which the pancreatic and bile ducts unite outside the duodenal wall, forming an abnormally long common channel that permits reciprocal reflux of pancreatic juice and bile. This leads to a high risk of recurrent pancreatitis, cholangitis, biliary stone formation, and biliary tract malignancy. Type D PBM, particularly when associated with complete pancreas divisum and aberrant bile duct drainage, represents an exceptionally rare and complex variant. We report the case of a 20-year-old female with a long-standing history of recurrent cholestasis and acute pancreatitis who presented with fever, jaundice, and abdominal pain accompanied by laboratory findings consistent with cholangitis and pancreatitis. Cross-sectional imaging and magnetic resonance cholangiopancreatography demonstrated type D PBM, complete pancreas divisum, and anomalous drainage of the common bile duct into the duct of Santorini with intraductal sludge. Emergency endoscopic retrograde cholangiopancreatography confirmed the diagnosis, and endoscopic sphincterotomy with biliary stenting led to clinical improvement. Given the persistent risk of malignancy and refractory clinical course, extrahepatic bile duct resection with Roux-en-Y hepaticojejunostomy was performed. Despite initial improvement, intermittent episodes of acute pancreatitis persisted, ultimately necessitating a pylorus-preserving pancreaticoduodenectomy. Histopathological examination revealed chronic inflammatory changes without dysplasia or malignancy. The patient recovered uneventfully and remains asymptomatic. This rare case illustrates the complexity of type D PBM associated with complete pancreas divisum and highlights the importance of early anatomical recognition and a stepwise, individualized treatment strategy. In patients with refractory symptoms and complex ductal anomalies, surgical intervention beyond endoscopic management may be required to prevent recurrent disease and reduce the risk of malignant transformation.

Keywords: Acute pancreatitis; endoscopic retrograde cholangiopancreatography; hepaticojejunostomy; pancreas divisum; pancreaticobiliary maljunction.

INTRODUCTION

Pancreaticobiliary maljunction (PBM) is a rare congenital anomaly in which the pancreatic and bile ducts join outside the duodenal wall, resulting in an abnormally long common channel that allows bidirectional reflux of bile and pancreatic juice. This pathological reflux predisposes patients to chronic inflammation, biliary stone formation, recurrent pancreatitis, and an increased risk of biliary tract malignancy.

PBM is generally classified into four morphological types: A (stenotic), B (non-stenotic), C (dilated channel), and D (complex). In addition, cases are further stratified based on the presence or absence of extrahepatic bile duct dilatation, a key determinant in both clinical prognosis and surgical decision-making. Notably, the reported risk of malignancy is approximately 21.6% in patients with bile duct dilatation and rises to 42.4% in those without dilatation.[1-10]

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The coexistence of PBM and pancreas divisum is a highly potent anatomical combination that significantly increases the risk of pancreatitis through the simultaneous effect of two separate pathophysiological mechanisms: pancreatic drainage disorder and bile reflux. While PBM is known to increase the risk of chronic inflammation and malignancy due to abnormal mixing of bile and pancreatic enzymes, pancreas divisum has been reported to lead to recurrent pancreatitis attacks due to inadequate drainage through the minor papilla. The coexistence of these two anomalies increases the inflammatory load as described in the literature, leading to a more resistant, recurrent, and progressive clinical course.

In this report, we describe a rare case of type D PBM in a young adult with concomitant complete pancreas divisum and an anomalous drainage of the common bile duct into the duct of Santorini. The patient was managed using a staged surgical approach, beginning with extrahepatic bile duct resection and ultimately requiring a pylorus-preserving pancreaticoduodenectomy due to refractory pancreatitis. This case highlights the critical importance of early anatomical recognition and individualized surgical planning in the management of complex PBM variants.

CASE REPORT

A 20-year-old woman, born in 2002, was referred to our institution on May 05, 2022, for endoscopic retrograde cholangiopancreatography (ERCP) with a preliminary diagnosis of bile duct-related cholangitis. She presented with abdominal pain, nausea, vomiting, jaundice, and fever. Physical examination revealed icterus and tenderness in the epigastric and right upper quadrants without rebound tenderness.

One month prior, she had been hospitalized for 14 days with acute pancreatitis and cholangitis and was discharged following partial clinical improvement. Her symptoms worsened in the 2 days preceding admission. Laboratory evaluation showed leukocytosis (12,000/μL), elevated pancreatic enzymes (amylase: 341 U/L; lipase: 981 U/L), increased liver function markers (Aspartate transaminase: 126 U/L, alanine transaminase: 162 U/L, alkaline phosphatase: 288 U/L, gamma-glutamyl transferase: 234 U/L, total bilirubin: 3.2 mg/dL, direct bilirubin: 3.0 mg/dL), and markedly elevated inflammatory markers (C-reactive protein [CRP]: 281 mg/L; procalcitonin: 2.47 ng/mL). Empirical intravenous piperacillin–tazobactam therapy was initiated.

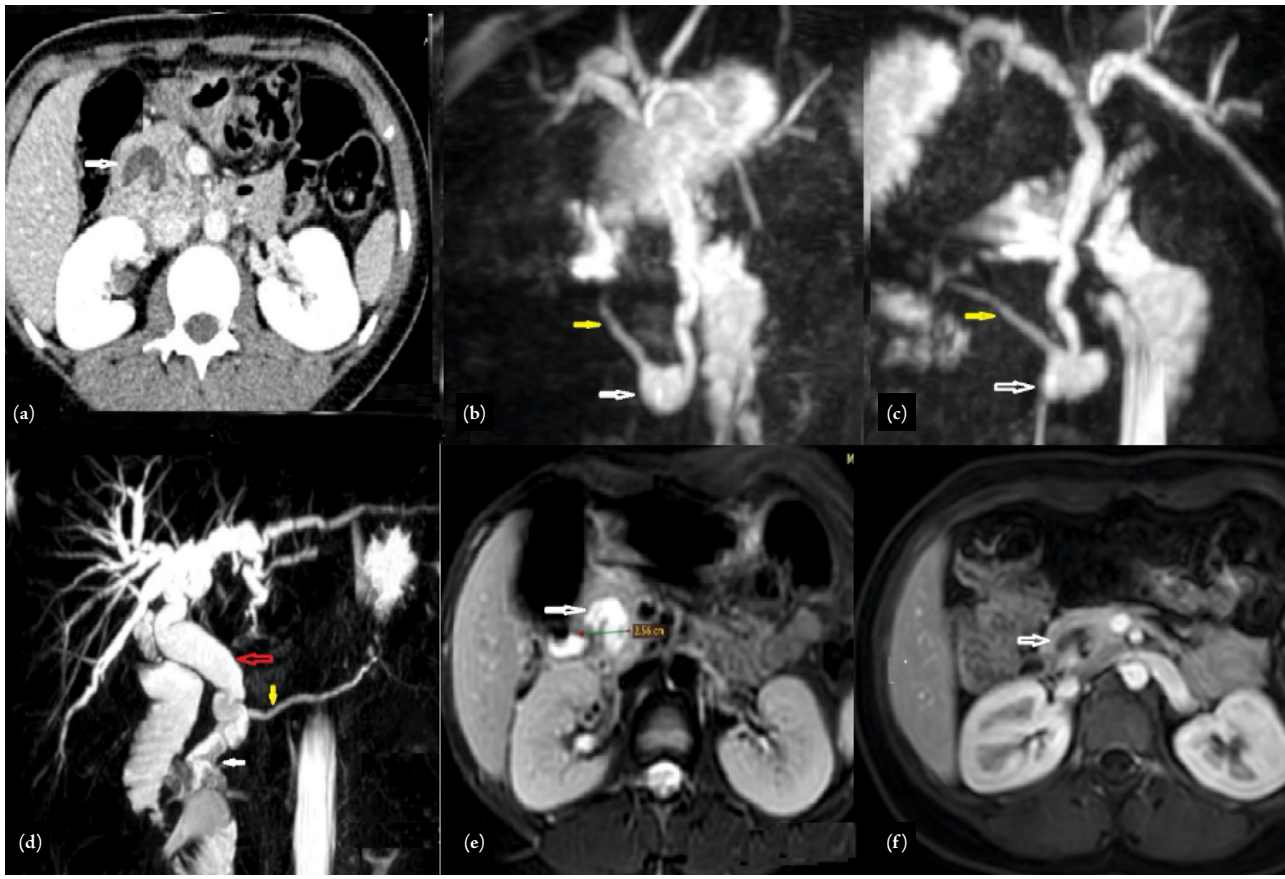


Figure 1. (a) Contrast-enhanced computed tomography showing a dilated common duct (white arrow) located in the head of the pancreas, **(b-d)** Magnetic resonance cholangiopancreatography images demonstrating the dilated common duct in the pancreatic head (white arrows), the pancreatic duct extending through the corpus and tail of the pancreas (yellow arrows) and common bile duct (red arrow), **(e and f)** Magnetic resonance imaging revealing the dilated common duct in the pancreatic head (white arrows), with visible intraductal sludge.

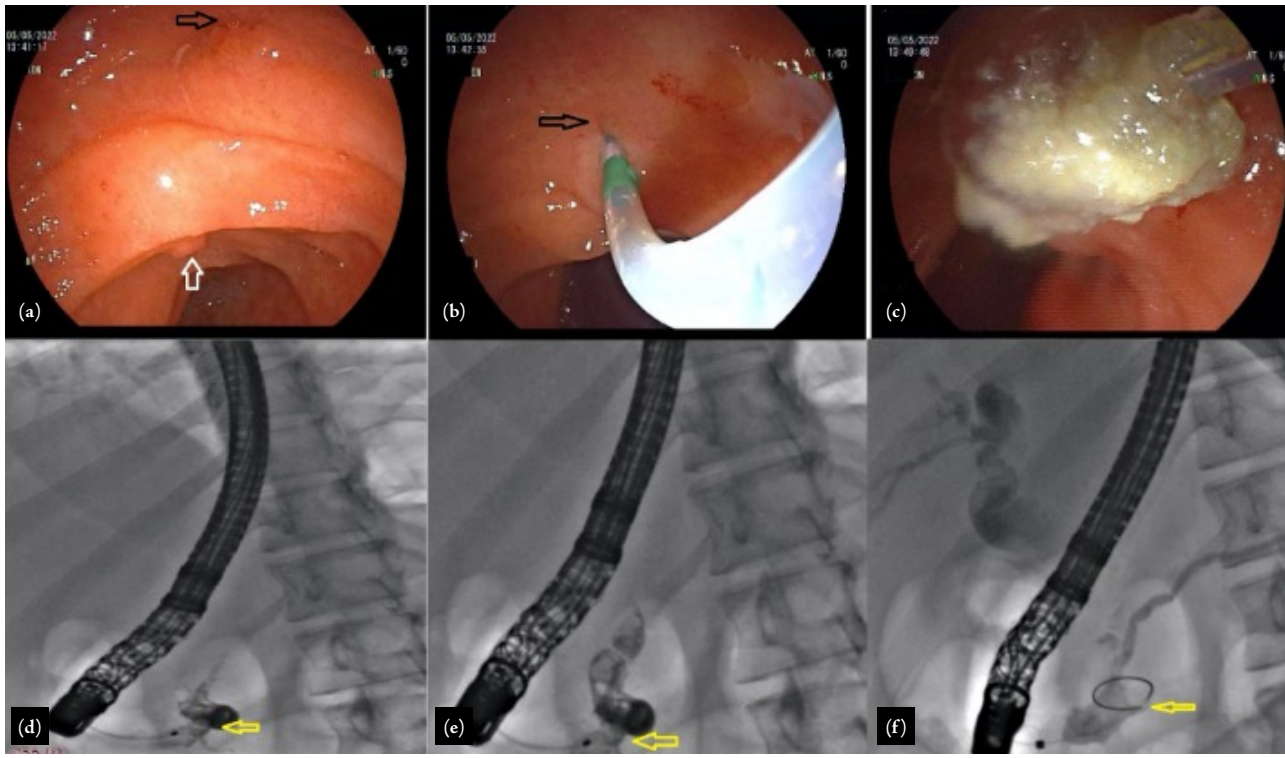


Figure 2. (a and b) Endoscopic views of the major papilla (white arrow) and minor papilla (black arrow), **(c)** Proteinaceous sludge evacuated from the common channel using a balloon catheter, **(d-f)** Fluoroscopic images showing the dilated common channel containing sludge, the dilated and tortuous distal common bile duct opening into the duct of Santorini, and the pancreatic duct extending into the corpus and tail regions of the pancreas.

Computed tomography, magnetic resonance imaging, and magnetic resonance cholangiopancreatography demonstrated type D PBM with complete pancreas divisum and anomalous drainage of a dilated common bile duct into the duct of Santorini. Intraluminal filling defects compatible with proteinaceous sludge were also identified (Fig. 1). An emergency ERCP was therefore performed.

The patient's medical history was notable for recurrent cholestatic episodes beginning at 2 years of age. After exclusion of Wilson's disease, cystic fibrosis, and metabolic and autoimmune liver disorders, benign recurrent intrahepatic cholestasis was diagnosed. A liver biopsy at the age of 5 revealed canalicular cholestasis, bile duct proliferation, and portal fibrosis. She experienced her first episode of acute pancreatitis at the age of 12 years, followed by a second episode 1 year later. At that time, a presumed cystic pancreatic lesion prompted exploratory surgery including cholecystectomy and pancreatic head biopsy, both yielding benign findings.

Despite these interventions, she continued to experience recurrent episodes of acute pancreatitis and cholangitis, occurring 3–4 times/year. ERCP in 2016 identified pancreas divisum without intervention. Genetic analysis later revealed a heterozygous mutation in the SPINK1 gene, while CFTR and PRSS1 mutations were excluded. In 2019, a minor papilla sphincterotomy and placement of a 5-Fr pancreatic stent in the duct of Santorini resulted in temporary symptom resolution.

During the emergency ERCP in May 2022, contrast injection via the minor papilla revealed a 2.5-cm dilated common bile duct containing proteinaceous sludge, which was cleared using balloon and basket catheters. A 10-Fr, 8-cm plastic stent was subsequently placed in the bile duct (Figure 2), resulting in rapid clinical improvement. CRP levels decreased significantly, and the patient completed a 2-week antibiotic regimen.

Given the markedly increased risk of malignancy associated with PBM and the history of recurrent inflammation, extrahepatic bile duct resection with Roux-en-Y hepaticojejunostomy was performed in May 2022. Histopathological analysis demonstrated epithelial hyperplasia, fibrosis, and wall thickening, without dysplasia or malignancy.

Despite surgery, the patient experienced occasional mild episodes of pancreatitis. Repeat ERCP in August 2022 revealed further sludge formation, and an 8.5-Fr pancreatic stent was placed following balloon dilation of the minor papilla. The stent was ultimately removed after another mild attack in May 2023.

Persistence of symptoms despite optimal endoscopic and biliary surgical management led to the decision to perform a pylorus-preserving pancreaticoduodenectomy in November

2024. Histopathology revealed chronic inflammatory changes without evidence of malignancy. The post-operative course was uneventful, and the patient remains symptom-free to date.

DISCUSSION

PBM is a rare congenital anomaly in which the pancreatic and biliary ducts unite anatomically outside the duodenal wall, resulting in an abnormally long common channel. This structural configuration allows reciprocal reflux of bile and pancreatic juice, predisposing the biliary epithelium and pancreatic ductal system to chronic inflammation, biliary stone formation, recurrent pancreatitis, and malignant transformation.[1,3,7,9]

Clinically, PBM is classified based on the presence or absence of extrahepatic bile duct dilatation, a distinction that has important implications for both cancer risk and surgical management. A large nationwide study from Japan demonstrated that the incidence of biliary tract cancer was significantly elevated in adults with PBM, reported as 21.6% in those with bile duct dilatation and up to 42.4% in those without it. In addition, PBM accompanied by bile duct dilatation has been strongly associated with both gallbladder cancer (62.3%) and bile duct cancer (32.1%), whereas PBM without dilatation is predominantly associated with gallbladder cancer (88.1%) and only rarely with bile duct malignancy (7.3%).[4,6,10]

At the molecular level, carcinogenesis in PBM has been linked to the accumulation of genetic alterations such as K-ras and p53 mutations in both malignant and non-malignant biliary epithelium. These changes support the classical "hyperplasia–dysplasia–carcinoma" sequence, initiated by prolonged epithelial exposure to refluxed pancreatic enzymes and bile acids, perpetuating chronic injury and abnormal cellular proliferation.[7,9]

In our patient, the heterozygous SPINK1 mutation likely acted as a disease-modifying factor that amplified the clinical impact of her underlying anatomical abnormalities. SPINK1 normally prevents premature intrapancreatic trypsin activation, and variants that reduce its function are known to increase susceptibility to pancreatic inflammation. Although heterozygous mutations alone rarely cause disease, they significantly enhance vulnerability when additional stressors such as pancreas divisum or PBM are present—an association also supported by large cohort studies showing earlier onset and more recurrent attacks in SPINK1 carriers. Experimental models further demonstrate that heterozygous loss of SPINK1 increases the severity of acute injury and promotes progression toward chronic pancreatitis, consistent with the persistent relapsing course observed in our case. Therefore, the coexistence of PBM, pancreas divisum, and a heterozygous SPINK1 mutation in the present case may have created a multifactorial predisposition to recurrent pancreatitis, with genetic susceptibility interacting synergistically with ductal anatomical abnormalities.[11,12]

Given this substantial malignant potential, current consensus, particularly from Japanese and East Asian expert panels, recommends early prophylactic surgical intervention following diagnosis of PBM, even in asymptomatic individuals. The standard operative strategy in patients with bile duct dilatation consists of cholecystectomy, complete resection of the extrahepatic bile duct, and Roux-en-Y hepaticojejunostomy. Importantly, excision should extend to the intrapancreatic portion of the bile duct to prevent remnant disease and stone formation. In morphologically complex PBM subtypes (particularly type B and D), intraoperative cholangiography and endoscopic guidance may be necessary to achieve complete resection.[4,9]

The present patient exhibited a type D PBM, an infrequently reported variant, concomitant with complete pancreas divisum. Uniquely, the common bile duct drained entirely into the duct of Santorini, an anatomical configuration that, to our knowledge, lacks prior documentation in the literature. Although no malignancy was detected histopathologically, the presence of epithelial hyperplasia, fibrosis, and chronic inflammatory change closely aligns with the early stages of PBM-related carcinogenesis, thereby supporting the appropriateness of the initial prophylactic surgical approach.[2,5,7,9,10]

Despite definitive biliary surgery, recurrent episodes of acute pancreatitis persisted. This clinical course has been described in PBM cases associated with pancreas divisum and is believed to stem from inadequate pancreatic duct drainage through the minor papilla, in combination with continued biliopancreatic reflux. In addition, the formation of proteinaceous plugs, resulting from premature trypsinogen activation and insoluble lithostathine aggregation, may contribute to ductal obstruction, elevated intraductal pressure, and recurrent inflammation.[1,2,5,9]

Given the refractoriness of symptoms to repeated endoscopic interventions, including minor papilla sphincterotomy and temporary stenting, a pylorus-preserving pancreaticoduodenectomy was ultimately performed.

The decision to perform pylorus-preserving pancreaticoduodenectomy (PPPD) in this patient is supported by current evidence indicating that PBM and pancreas divisum create a persistent inflammatory environment that often becomes refractory to endoscopic management. Surgical treatment is recommended when recurrent pancreatitis continues despite optimal endoscopic and biliary interventions, particularly in the presence of structural anomalies that perpetuate ductal obstruction and enzyme reflux.[11,12] Moreover, PBM is associated with increased long-term malignancy risk, making definitive resection essential once inflammation becomes chronic and difficult to control.[12] In our case, repeat episodes of pancreatitis and cholangitis despite sphincterotomy, stenting, and extrahepatic bile duct resection fit well within accepted indications for surgical escalation, reinforcing PPPD as an evidence-based and clinically justified intervention.

Although conventionally reserved for malignancy, this procedure is increasingly recognized as a valid therapeutic option in selected young patients suffering from disabling, refractory pancreatitis secondary to complex congenital ductal anomalies.[6,10] Final histopathological analysis demonstrated features of chronic pancreatitis without dysplasia or neoplasia, and the patient has remained asymptomatic following surgery.

Emerging data underscore PBM as a dominant etiological factor in early-onset biliary tract malignancies, reinforcing the concept that congenital anatomical derangements play a greater role than environmental exposures in these patients.[6,10] This further emphasizes the necessity of early recognition, careful surveillance, and timely prophylactic intervention in individuals diagnosed with PBM, particularly in children and young adults presenting with recurrent cholangitis or pancreatitis.

CONCLUSION

This case presents a rare and previously undescribed anatomical variant of PBM, characterized by complete drainage of the common bile duct into the duct of Santorini in the presence of pancreas divisum. The coexistence of bile duct dilatation, recurrent pancreatitis, and the well-established malignant potential of PBM justified definitive surgical management. Initial prophylactic extrahepatic bile duct resection was undertaken to mitigate cancer risk, followed by pylorus-preserving pancreaticoduodenectomy due to persistent post-operative pancreatitis.

This report highlights the critical importance of early recognition of PBM in young patients with recurrent pancreatobiliary symptoms. Detailed anatomical assessment and a multidisciplinary, individualized therapeutic approach are essential to optimize outcomes and prevent long-term complications, including biliary tract malignancy.

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Informed Consent: Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

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OLGU SUNUMU - *ÖZ*

Pankreatikobiliyer malformasyonun yeni bir varyantı: Pankreas divizumu olan bir hastada ortak safra kanalının santorini kanalına tam açılması

Pankreatikobiliyer maljunksiyon (PBM), pankreatik ve safra kanallarının duodenum duvarının dışında birleştiği, anormal derecede uzun bir ortak kanalın oluştuğu nadir bir konjenital anomalidir. Bu durum, pankreatik sıvı ile safranın karşılıklı reflüsüne izin vererek tekrarlayan pankreatit, kolanjit, safra taşı oluşumu ve biliyer trakt maligniteleri için yüksek risk oluşturur. Tip D PBM, özellikle tam pankreas divizumu ve anormal safra kanalı drenajıyla birlikte olduğunda son derece nadir ve kompleks bir varyanttır. Uzun süredir tekrarlayan kolestaz ve akut pankreatit öyküsü bulunan 20 yaşında bir kadın hasta; ateş, sarılık ve karın ağrısı şikâyetleri ile birlikte kolanjit ve pankreatit ile uyumlu laboratuvar bulguları eşliğinde başvurdu. Kesitsel görüntüleme ve manyetik rezonans kolanjiyopankreatografi (MRKP), tip D pankreatikobiliyer maljunksiyon, komplet pankreas divizumu ve ortak safra kanalının Santorini kanalına anormal drenajını, ayrıca intraduktal sludge varlığını gösterdi. Acil yapılan endoskopik retrograd kolanjiyopankreatografi (ERCP) ile tanı doğrulandı ve endoskopik sfinkterotomi ile biliyer stent yerleştirilmesi sonrası klinik düzelme sağlandı. Persistan malignite riski ve dirençli klinik seyir nedeniyle ekstrahepatik safra kanalı rezeksiyonu ve Roux-en-Y hepatikojejunostomi uygulandı. Başlangıçta düzelme sağlanmasına rağmen, aralıklı akut pankreatit atakları devam etti ve nihayetinde pilor koruyucu pankreatikoduodenektomi (Whipple prosedürü) yapılmasını gerektirdi. Histopatolojik incelemede displazi veya malignite saptanmazken kronik inflamatuvar değişiklikler izlendi. Hastanın postoperatif iyileşme süreci sorunsuz seyretti ve halen asemptomatiktir. Bu nadir olgu, tam pankreas divizumu ile birlikte görülen tip D pankreatikobiliyer maljunksiyonun karmaşıklığını ortaya koymakta ve erken anatomik tanı ile basamaklı, bireyselleştirilmiş bir tedavi stratejisinin önemini vurgulamaktadır. Dirençli semptomları ve kompleks duktal anomalileri olan hastalarda, tekrarlayan hastalıkların önlenmesi ve malign dönüşüm riskinin azaltılması için endoskopik tedavinin ötesinde cerrahi girişim gerekebilir.

Anahtar sözcükler: Akut pankreatit; ERCP; Hepatikojejunostomi; Pankreatikobiliyer maljunksiyon; Pankreas divizumu.

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CASE REPORT

Trauma-related simultaneous asymmetric bilateral hip dislocation: A case report

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ABSTRACT

Trauma-related simultaneous asymmetric bilateral hip dislocations (SABHDs) are extremely rare cases. High-energy trauma plays a role in their etiology. Traumatic hip dislocations account for 2–5% of all dislocations. Of all hip dislocations, 90% are posterior and 10% anterior. Bilateral traumatic hip dislocation is exceedingly rare. Asymmetric dislocations are even rarer, accounting for approximately 0.01–0.02% of all joint dislocations. This study aimed to evaluate a patient with trauma-related SABHD through a case presentation and discuss therapeutic options. A 27-year-old male patient was diagnosed with dislocation of both hips (left hip anterior and right hip posterior) following high-energy trauma. The patient was prepared for general anesthesia under emergency conditions and was taken to the operating room 2 h after admission to the emergency department without waiting for the fasting period. Under general anesthesia, left anterior and right posterior hip dislocations were reduced using the Allis and Boehler maneuvers. Direct radiography, computed tomography, and spiral tomography performed after the procedure demonstrated a successful reduction in both hips. While no bony pathology was observed in the right hip, a small fracture of the anterior acetabular wall and a non-displaced fissure line in the subcapital region of the femoral head were detected in the left hip; however, surgical intervention was not considered for either pathology. Since SABHD is caused by high-energy trauma, patients should be managed with a multidisciplinary approach. To prevent or minimize potential complications, the dislocations must be reduced as soon as possible.

Keywords: Femoral head; fractures; hip dislocation; hip osteoarthritis; trauma.

INTRODUCTION

The hip joint is the strongest and most stable joint in the human body. The stability of the hip joint is maintained by the joint capsule, the strong ligamentous structures and muscles surrounding the capsule, and the deep acetabular socket. Any trauma that disrupts the stability of the hip joint is consistently a high-energy trauma.[1,2] The most common injury mechanism leading to hip dislocation is posterior dislocation, caused by force transmitted proximally along the femoral shaft from the knee to the hip when the hip is flexed, adducted, and internally rotated. Anterior hip dislocations occur when the hip is forced into external rotation while in abduction or adduction.[3,4] Traumatic hip dislocations account for 2–5% of all dislocations. Of all hip dislocations, 90% are posterior and 10% anterior. Bilateral traumatic hip dislocation is exceedingly rare. Asymmetric dislocations are even rarer, accounting for approximately 0.01–0.02% of all joint dislocations. These injuries are frequently associated with other pathologies, including acetabular fractures, femoral fractures (5% of patients), knee ligament injuries, patellar or proximal tibial fractures (20%), femoral artery injury, venous thrombo-

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sis, and sciatic nerve injury (9–18%).[4-6] Traumatic hip dislocation is more common in young male patients. The rarity of asymmetric dislocation arises from the fact that the forces required to produce an anterior hip dislocation are the opposite of those necessary to produce a posterior dislocation, which makes the likelihood of an individual being exposed to both mechanisms simultaneously exceedingly uncommon. Most reported cases, especially those associated with motor vehicle accidents, are high-energy injuries.[5,6] Direct radiographs and physical examination findings are decisive in the preliminary diagnosis. Computed tomography (CT) and three-dimensional spiral tomography reveal the extent of trauma in detail and serve as critical tools for diagnosis and treatment planning. The common principle is that reduction must be performed as soon as possible to prevent complications.[6,7] Ideally, reduction should always be performed under general anesthesia. For posterior dislocations, the Boehler maneuver is applied, whereas for anterior dislocations, the Allis maneuver is preferred. In general, the risk of avascular necrosis of the femoral head after anterior or posterior hip dislocation ranges from 8% to 15%, whereas this rate may rise to 40% following open surgical reduction.

CASE REPORT

A 27-year-old male patient presented to the emergency department with severe pain in both hips and deformity of the lower extremities following a high-energy trauma caused by drunk driving. Radiographs taken in the emergency department revealed dislocations in both hips, and pelvic CT was requested for further evaluation (Fig. 1). However, due to the lower extremity and pelvic deformity caused by the dislocation, CT imaging of the hip region could not be obtained. Based on the pelvic anteroposterior radiographs, the patient was diagnosed with bilateral asymmetric (left hip anterior and right hip posterior) hip dislocation. Except for a mild hematoma in the lungs, no additional fractures or pathologies were

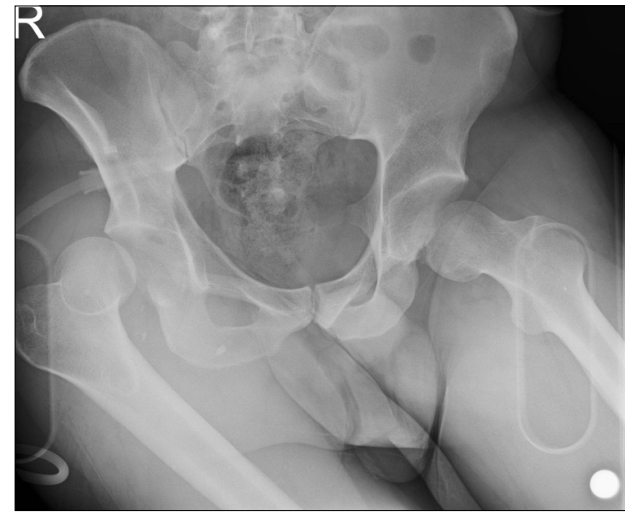


Figure 1. Radiographic image taken before reduction.



Figure 2. Three-dimensional spiral tomography images taken after reduction.

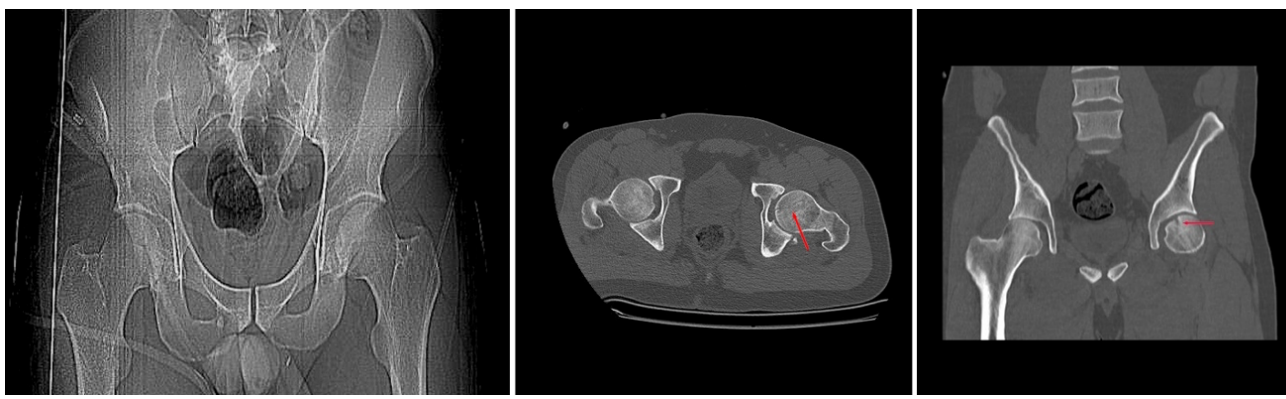


Figure 3. Computed tomography image taken after reduction.

detected on radiographs or physical examination. The severely intoxicated patient was prepared for general anesthesia under emergency conditions and was taken to the operating room 2 h after admission to the emergency department without waiting for the fasting period. Under general anesthesia, the left anterior and right posterior hip dislocations were reduced using the Allis and Boehler maneuvers. Direct radiographs, CT, and spiral tomography performed after the procedure demonstrated a successful reduction in both hips (Fig. 2). While no bony pathology was observed in the right hip, a small fracture of the anterior acetabular wall and a non-displaced fissure line in the subcapital region of the femoral head were detected in the left hip; however, surgical intervention was not considered for either pathology (Fig. 3). Since there was no fracture compromising acetabular stability, neither skin nor skeletal traction was applied. During follow-up, the patient was prescribed 3 weeks of bed rest. From the 2nd week, bed-based passive exercises were initiated. At the end of the 4th week, active exercises were started, and by the 6th week, the patient was mobilized through bedside sit-to-stand exercises. Full weight-bearing was allowed at the end of the 8 weeks. At the 6-month follow-up, complete hip joint range of motion was observed without neurovascular deficits. The patient continues to attend follow-up visits. The patient was informed of the details of her case, and consent was obtained for its presentation.

DISCUSSION

Cases of trauma-related simultaneous asymmetric bilateral hip dislocations (SABHDs) are extremely rare. Since high-energy trauma plays a role in their etiology, other organ and skeletal pathologies are frequently encountered. They are generally observed in young male individuals.[6-8] In such cases, early diagnosis and treatment are crucial to prevent complications that may arise in the future. Therefore, traumatic hip dislocation cases must be reduced as soon as possible. In our case, consistent with the literature, the patient was a 27-year-old young male. A rapid diagnosis was established through examinations, and within 2 h of admission to the emergency department, the patient was stabilized by performing bilateral reduction under general anesthesia.

There are very few published articles in the literature on this subject, and nearly all of those available are in the form of case reports. In their study, Buckwalter et al.[8] conducted a detailed review of trauma-related asymmetric bilateral hip dislocation. They reported that, from the first case described by Singowitz in 1830 up to 2015, approximately 104 case reports had been published. Meena et al.[9] reported that between 2015 and 2021, a total of 16 cases, including their own three cases, had been documented. Thus, from the initial report in 1830 until 2021, the cumulative number of reported cases of SABHD is 120. The fact that only 120 cases have been reported over a span of nearly 200 years demonstrates the rarity of this injury. In their case report, Hachicha et al.[10] emphasized that asymmetric bilateral hip dislocation is a rare injury, that hip osteoarthritis might be inevitable in the long term, and that, to optimize prognosis, reduction must invariably be performed within the first 6 h following trauma. Huang et al.[11] noted that asymmetric bilateral hip dislocation might be accompanied by hemodynamic instability and destabilization of the pelvic ring, which significantly increased the patient's life-threatening risks. Lo stated that such traumas were exceedingly rare and that a prompt attempt at closed reduction should be made, with open reduction pursued only if the initial attempt failed. The author further highlighted that delayed reduction increased the risk of avascular necrosis of the femoral head as well as major nerve injuries, such as sciatic or peroneal nerve damage.[12]

CONCLUSION

Since SABHDs result from high-energy trauma, patients should be managed with a multidisciplinary approach. To prevent or minimize potential complications, dislocations must be reduced as soon as possible. We hope that this case report will guide future studies on SABHD treatment. Further research with larger patient cohorts and additional parameters is needed.

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Informed Consent: The patient was informed of the details of her case, and consent was obtained for its presentation.

Conflict of Interest: None declared.

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OLGU SUNUMU - *ÖZ*

Travmaya bağlı eşzamanlı bilateral asimetrik kalça çıkığı: Olgu sunumu

Travmaya bağlı eşzamanlı bilateral asimetrik kalça çıkıkları (EBAKÇ) son derece nadir görülen vakalardır. Etiyolojilerinde yüksek enerjili travmalar rol oynamaktadır. Travmatik kalça çıkıkları tüm çıkıkların %2-5'ini oluşturur. Tüm kalça çıkıklarının ise %90'ını posterior çıkıklar, %10'unu anterior çıkıklar oluşturur. Bilateral travmatik kalça çıkığı son derece nadir görülen bir durumdur. Asimetrik çıkıklar ise daha da nadirdir ve tüm eklem çıkıklarının yaklaşık %0.01-0.02'sini oluşturur. Çalışmamızın amacı, travma sonucu gelişen EBAKÇ olgusunu ve tedavi seçeneklerini olgu sunumu eşliğinde değerlendirmektir. Yirmi yedi yaşında erkek hastaya, yüksek enerjili travma sonucu her iki kalçasında (sol kalça anterior, sağ kalça posterior) çıkık tanısı kondu. Hasta, acil şartlarda genel anesteziye hazırlanarak açlık süresi beklenmeden acile başvurusundan 2 saat sonra ameliyathaneye alındı. Genel anestezi altında sol anterior ve sağ posterior kalça çıkıkları Allis ve Boehler manevraları ile redükte edildi. İşlem sonrası çekilen direkt grafi, bilgisayarlı tomografi ve spiral tomografide her iki kalçada redüksiyonun sağlandığı görüldü. Sağ kalçada herhangi bir kemiksel patoloji görülmezken, sol kalçada asetabulum anterior duvarında küçük bir kemik segmentinde fraktür ve sol femur başının subkapital bölgesinde nondeplase fissür hattı tespit edildi; ancak her iki patoloji için de cerrahi düşünülmedi. EBAKÇ yüksek enerjili travma ile oluştuğundan hastalara multidisipliner bir yaklaşım uygulanmalıdır. İleride oluşabilecek komplikasyonların önlenmesi veya minimuma indirilebilmesi için çıkıklar mümkün olan en kısa sürede redükte edilmelidir.
Anahtar sözcükler: Femoral baş; fraktür; kalça çıkığı; kalça osteoartrit; travma.

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CASE REPORT

Spontaneous splenic rupture in a patient with congenital factor XIII deficiency: A case report and literature review

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ABSTRACT

Spontaneous (atraumatic) splenic rupture is a rare but potentially life-threatening clinical condition. Most reported cases of spontaneous splenic rupture are associated with splenomegaly due to infectious, neoplastic, or inflammatory diseases. Spontaneous rupture in the absence of these conditions is extremely rare. There is often an underlying trauma history. Factor XIII deficiency, a rare autosomal recessive bleeding disorder, is associated with abnormal fibrin stabilization despite normal routine coagulation parameters. Therefore, it can also lead to defects in wound healing. For the same reason, spontaneous splenic rupture has rarely been reported in patients with Factor XIII deficiency. We report a 32-year-old male with congenital Factor XIII deficiency who presented to the emergency room with hypovolemic shock following sudden-onset abdominal pain. The case was complicated by spontaneous splenic rupture and severe intra-abdominal bleeding. Contrast-enhanced abdominal computed tomography revealed a large perisplenic hematoma. Despite intensive blood transfusion and replacement therapy with fresh frozen plasma and cryoprecipitate, the patient required surgical intervention, and a splenectomy was performed. Histopathological examination revealed no underlying splenic pathology. Spontaneous splenic rupture is extremely rare in patients with factor XIII deficiency, but it should be considered in the differential diagnosis in this patient group presenting with an acute abdomen. Suspicion, early recognition, and supportive care with appropriate blood products and factors, along with prompt surgical intervention, are crucial to prevent mortality.

Keywords: Atraumatic rupture; Factor XIII deficiency; hemorrhage; splenectomy; spontaneous splenic rupture.

INTRODUCTION

The spleen is an intraperitoneal organ located in the upper left quadrant of the abdomen. It is the largest lymphoid organ in the human body and plays essential roles in filtering aged erythrocytes, blood storage, immune surveillance, and lymphocyte production. Splenic rupture most commonly occurs secondary to blunt or penetrating abdominal trauma. Spontaneous (atraumatic) splenic rupture, first described by Orloff and Peskin[1] in 1958, is a rare and potentially fatal condition, often associated with infections, hematologic malignancies, or inflammatory disorders.[1] However, spontaneous rupture in the absence of these risk factors is extremely uncommon and may occur due to congenital or acquired coagulation disorders.

Factor XIII (fibrin-stabilizing factor) is a transglutaminase enzyme involved in the final stage of the coagulation cascade, catalyzing the cross-linking of fibrin monomers to stabilize the clot.[2] Factor XIII deficiency, which may be congenital or acquired, results in defective clot stabilization despite normal standard coagulation parameters. Clinical manifestations include delayed wound healing, recurrent pregnancy loss, and life-threatening bleeding episodes, including intracranial hemorrhage.[3] The global prevalence of congenital Factor XIII deficiency is estimated at 1/3–5 million individuals.[4]

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Herein, we present a rare case of spontaneous splenic rupture in a patient with congenital Factor XIII deficiency, review the diagnostic challenges, and discuss management strategies.

CASE REPORT

A 32-year-old male with a known diagnosis of congenital Factor XIII deficiency presented to the emergency department with sudden-onset abdominal pain and nausea. He reported a similar episode 10 years prior and had last received fresh frozen plasma (FFP) replacement therapy 6 months earlier. He also has an epileptic disorder which is controlled with levetiracetam.

Clinical Examination

On admission, the patient was pale, diaphoretic, and in distress. Physical examination revealed marked tenderness and guarding in the left upper quadrant, progressive abdominal distension, tachycardia (105 bpm), and hypotension (80/45 mmHg).

Laboratory Findings

Initial tests revealed hemoglobin and platelet counts within normal ranges and normal coagulation parameters. White blood cell count was 14.37×103/μL, and C-reactive protein was 12.7 mg/L. His latest factor XIII activity is 10%.

Imaging

Contrast-enhanced abdominal computed tomography (CT) demonstrated irregular splenic margins, perisplenic fluid collection, and a heterogeneous hyperdense lesion (140×110×100 mm), consistent with a large hematoma extending into the mid-abdominal region. The spleen's size and position were normal. Radiological findings are shown in Figure 1.

Management

The patient was admitted to the intensive care unit for hemodynamic monitoring. Preoperatively, the patient received 3 units of packed red blood cells, 2 units of FFP, and 4 units of cryoprecipitate. Despite aggressive fluid and blood component therapy, hemoglobin decreased to 8.7 g/dL, hematocrit to 24.9%, and hypotension persisted. Following stabilization with packed red blood cells, an emergency laparotomy was performed. Intraoperative findings included approximately 2 liters of hemoperitoneum and a laceration at the lower pole of the spleen. Splenectomy was performed. Intraoperatively and postoperatively, an additional 6 units of packed red blood cells, 3 units of FFP, and 4 units of cryoprecipitate were administered.

Histopathology

Microscopic and macroscopic examinations revealed no underlying pathology except for fibrohyalinized tissue and calcifications in the splenic hilum.

Outcome

The post-operative course was uneventful. The patient received appropriate immunizations within 2 weeks and was discharged in stable condition.

DISCUSSION

The concept of spontaneous splenic rupture was first proposed by Orloff and Peskin (1958), who defined four diagnostic criteria: absence of trauma, absence of perisplenic adhesions, no underlying splenic pathology, and normal histology of the spleen.[1] Crate and Payne (1991) later added a fifth criterion – exclusion of viral etiologies.[5] Our patient met all modified criteria for true spontaneous rupture.

Although spontaneous splenic rupture has been reported in association with hematological malignancies, infections, and inflammatory disorders, its occurrence in congenital Factor XIII deficiency is exceedingly rare. Factor XIII deficiency is characterized by impaired fibrin stabilization, leading to de-

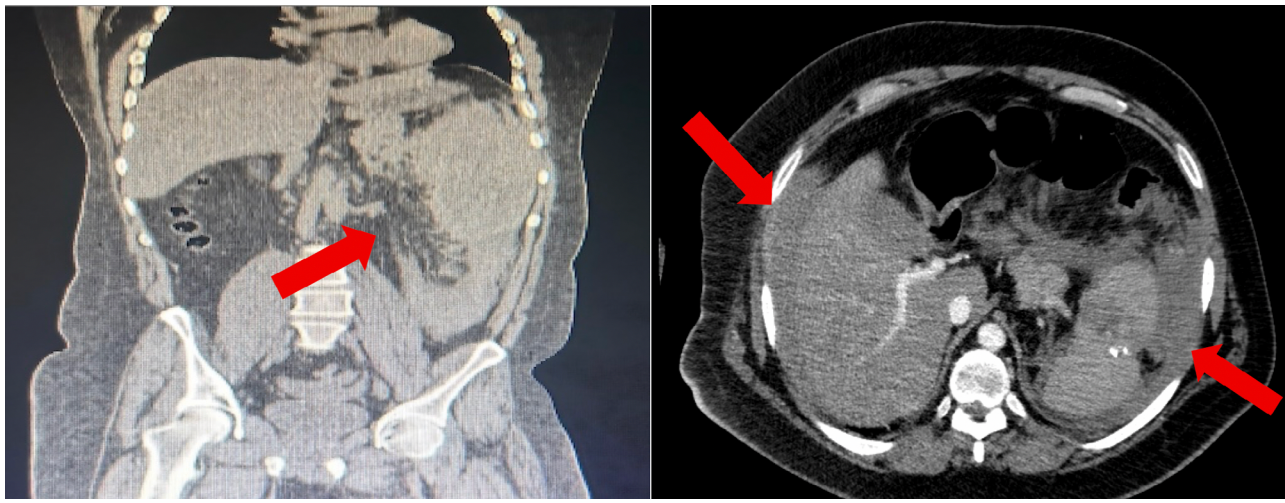


Figure 1. Abdominal computed tomography (CT) of the patient demonstrating free fluid consistent with hemorrhage in the perihepatic and perisplenic regions. Active bleeding from the inferior pole of the spleen due to splenic rupture is indicated by red arrows in both CT slices.

fective clot formation despite normal prothrombin time, activated partial thromboplastin time, and thrombin time. Clinical manifestations range from umbilical stump bleeding in neonates to intracranial hemorrhage in adults.[6,7]

In our case, the absence of splenomegaly and histological abnormalities highlights the role of coagulation instability as the primary mechanism. This suggests that even minor, clinically inapparent trauma may precipitate catastrophic hemorrhage in these patients. Probably, this was the second spontaneous rupture of the spleen. Ten years ago, he experienced a similar clinical scenario. Fortunately, the first rupture was self-limiting. The patient had intellectual disability, but the underlying cause had not been clarified so far. Retrospectively, cranial CT scans were reviewed and revealed multiple cerebromalacic areas. Our hypothesis is that these radiological findings are related to old intracranial hemorrhages, which may also be the origin of the epileptic foci. There was no family history of epilepsy; the patient was the first known case in his family. All these findings were compatible with Factor XIII deficiency and the expected bleeding complications. Fibrogammine is a widely used replacement therapy. However, we were unable to use this replacement therapy because we did not have access to it in our country. We gave the patient FFP and cryoprecipitate support instead of fibrogammine. Thankfully, he was able to recover from the splenic rupture that caused hypovolemic shock with this support.

Management Considerations

Treatment involves aggressive resuscitation, Factor XIII replacement therapy, and prompt surgical intervention when conservative measures fail. Splenectomy remains the definitive treatment for uncontrolled bleeding.

CONCLUSION

Spontaneous splenic rupture is a rare but life-threatening complication in patients with congenital Factor XIII deficiency. Clinicians should maintain a high index of suspicion for atraumatic splenic rupture in these patients presenting with acute abdomen and hemodynamic instability. Early diagnosis and timely surgical intervention are critical for survival.

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Informed Consent: Written informed consent was obtained from the patient for the publication of clinical details and accompanying images.

Conflict of Interest: None declared.

Financial Disclosure: The author declared that this study has received no financial support.

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OLGU SUNUMU - *ÖZ*

Konjenital faktör XIII eksikliği olgusunda spontan dalak rüptürü: Bir olgu sunumu ve literatür derlemesi

Spontan (atravmatik) dalak rüptürü nadir görülen ancak potansiyel olarak yaşamı tehdit eden bir klinik durumdur. Spontan dalak rüptürü bildirilen olguların çoğu enfeksiyöz, neoplastik veya inflamatuar hastalıklara bağlı splenomegali ile ilişkilidir. Bu durumların yokluğunda spontan rüptür son derece nadirdir. Çoğu kez altta travma öyküsü vardır. Nadir görülen otozomal resesif kanama bozukluğu olan Faktör XIII eksikliği, normal rutin pıhtılaşma parametrelerine rağmen anormal fibrin stabilizasyonu ile ilişkilidir. Bu yüzden yara yeri iyileşmesinde de defektlere yol açabilmektedir. Aynı nedenle de Faktör XIII eksikliği bulunan olgularda nadiren spontan dalak rüptürlerinin olduğu bildirilmiştir. Ani başlangıçlı karın ağrısınının ardından acile hipovolemik şokla başvuran, konjenital Faktör XIII eksikliği bulunan 32 yaşında bir erkek hasta sunulmaktadır. Olgu spontane dalak rüptürü ile ağır batın içi kanama ile komplike olmuştur. Kontrastlı karın bilgisayarlı tomografisinde, büyük bir perisplenik hematom saptanmıştır. Yoğun kan desteği ve taze dondurulmuş plazma, kriyopresipitat ile replasman tedavisine rağmen hastaya cerrahi müdahale gerekmiştir ve splenektomi yapılmıştır. Histopatolojik incelemede altta yatan bir dalak patolojisi saptanmamıştır. Faktör XIII eksikliği olan hastalarda spontan dalak rüptürü oldukça nadirdir, ancak bu hasta grubunda akut karın tablosu ile başvurularında ayırıcı tanıda düşünülmelidir. Mortaliteyi önlemek için şüphe etmek, erken tanımak ve uygun kan ürünü ve faktörlerle desteklemek, hızlı cerrahi müdahale etmek çok önemlidir.

Anahtar sözcükler: Atravmatik rüptür; Faktör XIII eksikliği; kanama; splenektomi; spontan dalak rüptürü.

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LETTER TO THE EDITOR

Predicting acute biliary pancreatitis severity

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Dear Editor,

I read with interest the study by Tolan et al.,[1] published in a previous issue of the Turkish Journal of Trauma and Emergency Surgery (TJTES), which investigated the role of NLR and PLR in predicting the severity of acute biliary pancreatitis (ABP). The use of these simple, inexpensive, and rapid biomarkers for early severity prediction is of great importance, especially in resource-limited settings. However, there are several methodological and clinical interpretation points that warrant consideration.

1. Case Selection and Limited Generalizability: The study's limitation to only 161 cases over a 10-year period (2015-2024) is noteworthy. Furthermore, the exclusive inclusion of biliary etiology pancreatitis restricts the generalizability of the findings to other etiologies such as alcoholic, hypertriglyceridemic, or idiopathic pancreatitis. This narrow selection weakens the applicability of the results to the broader pancreatitis population.

2. Clinical Severity vs. Radiological Severity (Revised Atlanta Criteria): The authors utilized only the Balthazar scoring system (radiological severity) as a severity indicator. However, according to the current Revised Atlanta Classification, the severity of pancreatitis is primarily determined by the presence and duration of organ failure, not solely by radiology.[2,3] Focusing only on radiological severity may not fully reflect the patient's true clinical status (mortality, need for intensive care).

3. Lack of ROC Analysis and Clinical Applicability: While the study reports statistical significance (p-values) for NLR and PLR, it fails to provide the most critical data for clinical decision-making: "cut-off points" and their corresponding sensitivity/specificity (AUC) values. For a physician to practically use these biomarkers in the emergency department (e.g., "NLR above X predicts severe pancreatitis"), ROC analysis results are essential. This omission severely limits the clinical applicability of the study.[4,5]

In conclusion, while the study by Tolan et al. highlights the potential of NLR and PLR in predicting ABP severity, the limitations in case selection, the disregard for the Revised Atlanta Criteria in severity assessment, and the absence of clinical cut-off values restrict the study's scientific contribution and practical utility.

Sincerely

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