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Ulusal Travma ve Acil Cerrahi Dergisi

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

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Abstract: The abstract should be structured and serve as an informative guide for the methods and results sections of the study. It must be prepared with the following subtitles: Background, Methods, Results and Conclusions. Abstracts should not exceed 200 words.

Figures, illustrations and tables: All figures and tables should be numbered in the order of appearance in the text. The desired position of figures and tables should be indicated in the text. Legends should be included in the relevant part of the main text and those for photomicrographs and slide preparations should indicate the magnification and the stain used. Color pictures and figures will be published if they are definitely required and with the understanding that the authors are prepared to bear the costs. Line drawings should be professionally prepared. For recognizable photographs, signed releases of the patient or of his/her legal representatives should be enclosed; otherwise, patient names or eyes must be blocked out to prevent identification.

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- Protect intellectual property and to defend the rights of the journal and author(s);
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The publication processes of the journal are conducted in accordance with the guidelines of International Committee of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), the Council of Science Editors (CSE), the Committee of Publication Ethics (COPE), the European Association of Science Editors (EASE) and National Information Standards Organization (NISO).

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The Turkish Journal of Trauma and Emergency Surgery, the scientific publication of the National Association of Trauma and Emergency Surgery, has now added the option of a Fast-track Publication Fee to meet the demand for an accelerated publication process. The charge for early publication is 10,000 TL for Turkish authors and 1000 USD for foreign authors.

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Starting with the first issue of 2024, the Turkish Journal of Trauma and Emergency Surgery will be introducing an Article Processing Charge (APC) of 200 USD for articles published in the journal. This charge is necessary to cover the costs associated with the publication services provided by the journal. These services include article management costs, the production of articles in PDF and other formats, and the distribution of published articles to various venues and other publishing functions.

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Editorial: 2025 in Review

Dear Colleagues,

We have successfully concluded another significant year in the publication journey of the Turkish Journal of Trauma and Emergency Surgery. In 2025, our journal received 400 manuscript submissions, comprising 299 original research articles, 54 case reports, 38 experimental studies, 4 case series, 3 letters to the editor, and 2 review articles. Throughout the year, we published a total of 173 peer-reviewed papers, including 132 original research articles, 23 experimental studies, 17 case reports, and 1 letter to the editor.

Global Reach and Scholarly Impact

The international influence of our journal continues to grow. In 2025, our website attracted 115,000 unique visitors, averaging approximately 7,000 per month. Our global readership is led by Türkiye (58,274), followed by the People's Republic of China (42,348), Singapore (17,743), the United States (3,685), and India (1,266). In terms of digital traffic, 85,000 users reached us via Google, 5,900 through PubMed, and nearly 900 through other academic search engines.

Our contributors' work continues to resonate within the scientific community. The most-viewed article on PubMed was "Evaluation of perfusion index in pediatric trauma patients" by Erdurmuş et al. (6,930 views), followed by "A dangerous tradition: retrospective analysis of celebratory gunfire-related injuries in three tertiary hospitals" by Çelikmen et al. (5,411 views). Additionally, Web of Science data identifies "Evaluation of systemic immune-inflammation index efficacy in predicting complicated appendicitis in pediatric emergency department" by Tekeli et al. as the most cited article over the last three years, with 14 citations.

The Backbone of Our Journal: Operational Excellence and the Peer-Review Process

As with many prestigious national and international journals, our operations—beyond the technical aspects of manuscript preparation and printing—rely fundamentally on the selfless, voluntary contributions of our academic community. The sustained growth in submissions has placed an immense and growing burden on our Section Editors and Reviewers, who serve as the true guardians of our journal's scientific integrity.

While our primary editorial objective remains the timely assessment of every manuscript to meet our authors' legitimate expectations, our priority is to achieve this without compromising the rigorous academic standards that define the Turkish Journal of Trauma and Emergency Surgery. We are acutely aware that this excellence is only possible through the invisible labor and profound expertise of our reviewers and editors, who dedicate their limited time to advancing our field.

To maintain this delicate balance, it is essential that reviewer assignments are completed within the 20-day timeframe. We believe that those of us who have experienced the anticipation of awaiting an editorial decision as authors can best appreciate the importance of punctuality. We kindly request that colleagues who find themselves unable to meet these commitments due to current workload constraints inform the Editorial Office so we may adjust our workflow accordingly.

Acknowledgements

On behalf of the Editorial Board, we express our deepest gratitude first and foremost to our Section Editors and Reviewers for their tireless efforts and intellectual guidance. We also thank our authors for choosing our journal as a platform for their research and our readers for their ongoing support.

We also extend our appreciation to the leadership of our professional community:

Prof. Dr. Mehmet Eryılmaz, President of the Turkish Association of Trauma and Emergency Surgery

The members of the Executive Board and Association Secretary Kerem Ayar

Mr. Metin Ateş and the LookUs team for their essential technical and infrastructure support

Mr. Ali Cangül and the staff of Kare Publishing for their unwavering commitment to our publication quality

Respectfully,

The Editorial Board

EXPERIMENTAL STUDY

Effect of calcium dobesilate on liver regeneration in rats undergoing partial hepatectomy

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ABSTRACT

BACKGROUND: To date, no study has evaluated the effects of calcium dobesilate on regenerative capacity after partial hepatectomy. Within the scope of this research, we aimed to elucidate the effects of calcium dobesilate (CD) on liver regeneration capacity and antioxidant pathways after partial hepatectomy.

METHODS: Thirty-six Sprague Dawley male rats weighing between 250-350 grams were used in the study. All animals underwent partial hepatectomy. The rats were randomly divided into four groups, each consisting of nine rats, as control groups (Groups 1 and 2) and study groups (Groups 3 and 4). Regeneration rate, histopathological parameters, immunohistochemical examination, and the apoptotic index (AI) were measured.

RESULTS: Tissue superoxide dismutase (SOD) levels were statistically significantly higher in the calcium dobesilate study groups compared to controls (p=0.03). Malondialdehyde (MDA) levels were statistically significantly higher in the study groups than in the control groups on both the second and seventh days (p=0.001). The regeneration rate (RR) was higher in the study group compared to the control group on the second day, and this difference was statistically significant (p<0.001). RR was also significantly higher in the study group on the second day compared to the seventh day (p<0.001). According to the Suzuki Scoring System, vacuolization and necrosis were not observed in the study groups (p<0.001 vs. p=0.034, respectively). The apoptotic index was significantly higher in the control groups compared to the study groups (p<0.001), and AI was statistically significantly lower on the seventh day (p=0.006). Ki-67 expression was statistically significantly higher in the groups receiving CD treatment on both the second and seventh days. In the control groups, Ki-67 expression was statistically significantly higher on the seventh day compared to the second day (p=0.006).

CONCLUSION: This research indicated the effects of calcium dobesilate on improving oxidative damage and liver regeneration in rats undergoing partial hepatectomy. The results of the present study showed that (preoperative-postoperative) CD improves oxidative stress and increases liver regeneration capacity after partial hepatectomy.

Keywords: Calcium dobesilate; liver regeneration; oxidative damage; partial hepatectomy; experimental.

INTRODUCTION

Partial hepatectomy (PH) is frequently used in the treatment of liver tumors and in donors for organ transplantation. Studies using the PH model have shown that many factors influence the formation of the regenerative response.[1] Liver regeneration after PH is associated with the activation of inflammatory signaling molecules and the induction of oxidative stress.[2] PH, the model that most clearly demonstrates liver regeneration capacity, is considered the most potent stimulator of liver regeneration. PH stimulates DNA replication, and mitosis accelerates immediately afterward. Significant regeneration occurs within the first 10 days, and this process is completed in 4-5 weeks. Unlike humans, it takes 7-10 days for the rat liver to

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regenerate and return to normal.[3]

Calcium dobesilate (CD) (2,5 dihydroxybenzenesulfonate) is a pharmacological agent with angioprotective, anti-inflammatory, and antioxidant properties. The antioxidant and anti-inflammatory properties of CD are associated with decreased lipid peroxidation (LPO) caused by free oxygen radicals (FOR) and reduced inflammatory cytokine release, such as platelet-activating factor (PAF). It has also been shown that CD improves microvascular dysfunction, reduces FOR, and increases endothelial nitric oxide (eNO) synthesis.[4] CD, known to have angioprotective and antioxidant effects and to increase endothelial nitric oxide (NO), may positively affect liver regeneration.[5]

The impact of CD on regenerative capacity during the post-hepatectomy period remains unexplored. Within the scope of this research, we aimed to elucidate the effects of CD on liver regeneration capacity and antioxidant pathways after PH.

MATERIALS AND METHODS

This experimental study was conducted at Sakarya University's Experimental Medicine Applications and Research Center. It was initiated after approval from the Sakarya University Animal Experiments Local Ethics Committee, with protocol number 36 dated 02/10/2019. The principles regarding the care and use of laboratory animals included in the Declaration of Helsinki were applied throughout the study.

Thirty-six Sprague Dawley male rats weighing between 250 and 350 grams were used in the study. The rats were randomly divided into four groups, each consisting of nine rats.

• Control Groups:

o Group 1: Planned as the control group of Group 3. Saline (2 ml/day) was administered by oral gavage as the first dose 2 hours before the operation.

o Group 2: Planned as the control group of Group 4. Saline (2 ml/day) was administered by oral gavage as the first dose 2 hours before the operation.

• Study Groups:

o Group 3: Planned as a two-day study group. CD was administered by oral gavage at a dose of 100 mg/kg/day, given 2 hours before the operation.

o Group 4: Planned as a seven-day study group. CD was administered by oral gavage at a dose of 100 mg/kg/day, given 2 hours before the operation.

At the end of two hours, all rats were anesthetized with intraperitoneal ketamine (50 mg/kg) and xylazine (10 mg/kg). A laparotomy with a 2 cm midline incision was performed in all rats. The pedicles of the left lateral and median lobes of the liver were ligated with 3/0 polyglactin, and PH was performed as described by Higgins and Anderson.[6] The removed liver tissue was weighed, and its weight was recorded. Saline (2 ml/day) was given to Group 1, and 100 mg/kg/day CD was given to Group 3 via oral gavage for two days postoperatively. Saline (2 ml/day) was given to Group 2, and 100 mg/kg/day CD was given to Group 4 via oral gavage for seven days postoperatively.

Groups 1 and 3 underwent relaparotomy under intraperitoneal anesthesia at the end of the second day, and Groups 2 and 4 at the end of the seventh day. An average of 1.5 ml of blood was collected into a standard biochemistry tube for biochemical analysis. Afterwards, a high volume of 0.09% NaCl was administered to the aorta with the help of an intracatheter for liver perfusion. After liver perfusion was achieved, a high volume of blood was collected from the abdominal aorta, and sacrifice was achieved through hypovolemia. The remaining liver tissue was removed without compromising its integrity and weighed. Some liver tissue was stored at -80°C until the day of analysis for superoxide dismutase (SOD), glutathione (GSH), and malondialdehyde (MDA) measurements. The remaining liver tissue samples were fixed in 10% buffered formalin for histopathological examination.

Biochemical Parameters

Biochemical evaluation was performed at the Sakarya University Biochemistry Department Laboratory. Oxidative damage was assessed by measuring GSH, SOD, and MDA levels in liver tissue samples and serum. Rat Superoxidase Dismutase ELISA (enzyme-linked immunosorbent assay) Kit, Rat Malondialdehyde ELISA Kit, and Glutathione ELISA Kit (YLbiont®) were used to evaluate parameters in both tissue and serum.

Regeneration Rate (RR)

The 70% liver tissue resected during hepatectomy was weighed, and the total liver weight was calculated as follows: "Resected tissue (g) = 0.70 × initial total liver weight (g)." Using this formula, the liver weights of all rats before resection were estimated. At 2 and 7 days after PH, the remnant liver tissue was removed and weighed after sacrifice. The regeneration rate was calculated using the formula "Liver regeneration rate (%) = Remnant liver weight / Total liver weight × 100." This formula is known as the Kwon formula.[7]

Histological and Immunohistochemical Evaluation

Histological and immunohistochemical examinations of the liver tissues were performed at the Sakarya University Medical Faculty Histology and Embryology Department Laboratory. The Suzuki Scoring System was used for histopathological examinations.[8]

The evaluated parameters included histopathological changes in the liver assessed with hematoxylin-eosin (HE) and Masson trichrome (MTT) staining, apoptotic index (AI) determined by TUNEL (terminal deoxynucleotidyl transferase–mediated dUTP nick end labeling) staining, and Ki-67 expression assessed by immunohistochemical staining. The apoptotic index with TUNEL staining was calculated as AI = (apoptotic cell count / total cell count) × 100.

Statistical Analysis

Data collected within the scope of the study were analyzed using the IBM Statistical Package for the Social Sciences (SPSS) for macOS version 30.0 (IBM Corp., Armonk, NY). Frequency and percentage were used for categorical data, and mean and standard deviation for continuous data as descriptive values. The normality of variables was evaluated using the Shapiro-Wilk test. Multivariate analysis of variance (Multivariate ANOVA) was used to evaluate whether there were differences in biochemical measurements, regeneration rate, apoptotic index, and Ki-67 measurements between rats in the study and control groups with different treatment durations. The chi-square test was used to compare categorical variables. Results were considered statistically significant when the p value was less than 0.05.

RESULTS

The distribution of SOD, GSH, and MDA measurements in the serum and tissue of rats in the experimental and control groups with different treatment periods is shown in Table 1. Upon examination of the table, statistically significant differences were found in tissue SOD and tissue MDA measurements ($p<0.05$). In tissue SOD measurements, statistically significant differences were observed between the study group and the control group at different treatment times, while no statistically significant differences were observed in the interaction between group and treatment time. The tissue SOD value in the study group was higher than that in the control group, and the measurements on the second day were higher than those on the seventh day. Similarly, in tissue MDA measurements, a statistically significant difference was observed between the study group and the control group at different treatment times, while no statistically significant difference was observed in the interaction between group and treatment time. The tissue MDA value in the study group was higher than that in the control group, and the measurements on day 2 were higher than those on day 7. No statistically significant differences were observed in other serum and tissue measurements between groups and treatment times.

The distribution of regeneration rates, apoptotic indices, and Ki-67 measurements in the study and control groups of rats with different treatment durations is shown in Table 2. Upon examination of the table, statistically significant differences were observed between the study and control groups, between different treatment times, and in the interaction between group and treatment time in terms of regeneration rate and Ki-67 measurements ($p<0.05$). For apoptotic index measurements, statistically significant differences were observed between the study group and the control group and between different treatment times; however, no statistically significant differences were observed in the interaction between group and treatment time.

In terms of regeneration rate, the values in the study group were higher than those in the control group, and the mea-

Table 1. Distribution of biochemical measurements between groups

Parameters	Group	Time	Mean±SD	p-value
Serum SOD	Control	2nd day	3.7±0.5	
		7th day	4.8±2.8	
	Study	2nd day	3.2±0.6	
		7th day	4.3±2.2	
	Group			0.505
	Time			0.138
	Group*Time			0.989
Tissue SOD	Control	2nd day	2.2±0.6	
		7th day	1.2±0.3	
	Study	2nd day	3.1±1.1	
		7th day	2±0.8	
	Group			0.003
	Time			0.001
	Group*Time			0.881
Serum GSH	Control	2nd day	667.4±156	
		7th day	520.2±165	
	Study	2nd day	592.9±98.7	
		7th day	535±278.9	
	Group			0.665
	Time			0.145
	Group*Time			0.519
Tissue GSH	Control	2nd day	3.7±0.5	
		7th day	4.8±2.8	
	Study	2nd day	3.2±0.6	
		7th day	4.3±2.2	
	Group			0.505
	Time			0.138
	Group*Time			0.989
Serum MDA	Control	2nd day	0.4±0.2	
		7th day	0.4±0.2	
	Study	2nd day	0.3±0.2	
		7th day	0.3±0.1	
	Group			0.223
	Time			0.736
	Group*Time			0.806
Tissue MDA	Control	2nd day	0.7±0.1	
		7th day	0.4±0.2	
	Study	2nd day	1.2±0.5	
		7th day	0.8±0.3	
	Group			0.001
	Time			0.001
	Group*Time			0.872

Table 2. Distribution of intergroup regeneration rate, apoptotic index, and Ki-67 measurements

Parameters	Group	Time	Mean±SD	p-value
Regeneration Rate	Control	2nd day	0.50±0.05	
		7th day	0.53±0.04	
	Study	2nd day	0.70±0.13	
		7th day	0.55±0.05	
	Group			<0.001
	Time			0.014
	Group*Time			<0.001
Apoptotic Index	Control	2nd day	35.9±4.5	
		7th day	34.6±4.7	
	Study	2nd day	15.8±2.4	
		7th day	10±1.5	
	Group			<0.001
	Time			0.005
	Group*Time			0.071
Ki-67	Control	2nd day	11.8±1.6	
		7th day	12.7±1.6	
	Study	2nd day	27±1.1	
		7th day	32.6±3.8	
	Group			<0.001
	Time			<0.001
	Group*Time			0.004

surements on the second day were higher than those on the seventh day. In the combined effect of groups and treatment times, the rates were higher on day 2 in the study group and on day 7 in the control group.

For the apoptotic index measurements, the values in the control group were higher than those in the study group, and the measurements on the second day were higher than those on the seventh day. TUNEL-positive stained cells are shown in Figure 1.

Regarding Ki-67 values, the measurements in the study group were higher than those in the control group, and the values on day 7 were higher than those on day 2. In the combined effect of groups and treatment times, the measurements on day 7 were higher in both the study and control groups. Cells stained by immunohistochemical (IHC) staining for Ki-67 are shown in Figure 2.

When histopathological changes were graded according to the Suzuki Scoring System,[8] the distribution of sinusoidal obstruction, necrosis, and vacuolization in the experimental and control groups is shown in Table 3. Upon examination of the table, a statistically significant relationship was observed between the groups in all histopathological results ($p<0.05$). Sinusoidal obstruction was observed in groups 0 and 1 in the experimental group and in groups 2 and 3 in the control group. Similarly, necrosis and vacuolization were observed in all rats in the experimental group, while necrosis was observed in groups 0, 1, and 2 in the control group, and vacuolization was observed in groups 0 and 1.

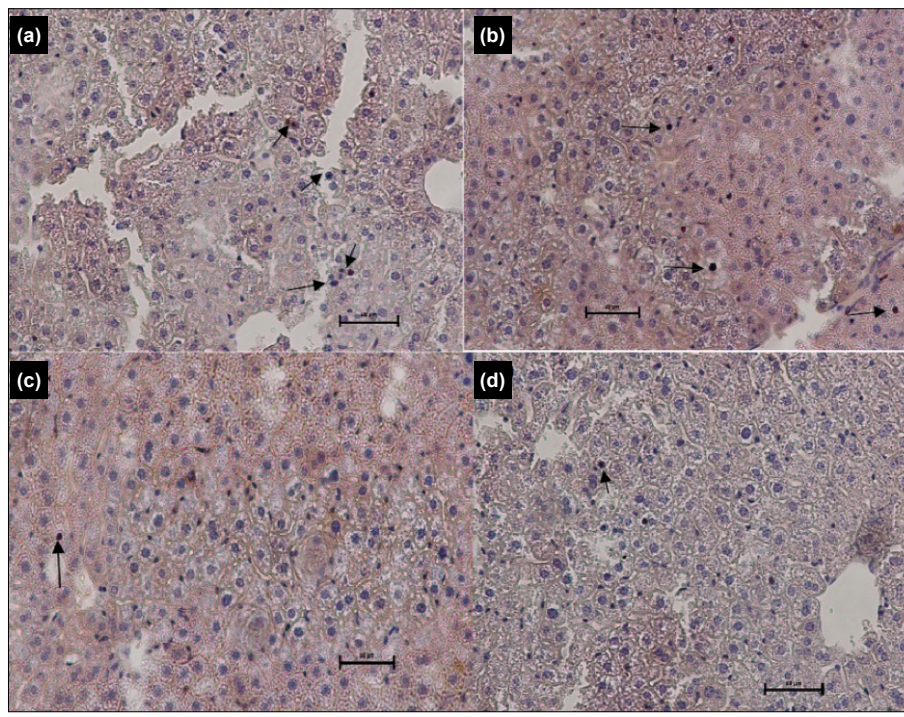

Figure 1. TUNEL cell staining. TUNEL-positive cells are marked with black arrows. **(a)** and **(b)**: Control groups (Groups 1 and 2, respectively), showing more TUNEL-positive cells. **(c)** and **(d)**: Calcium dobesilate-treated groups (Groups 3 and 4), showing fewer TUNEL-positive cells.

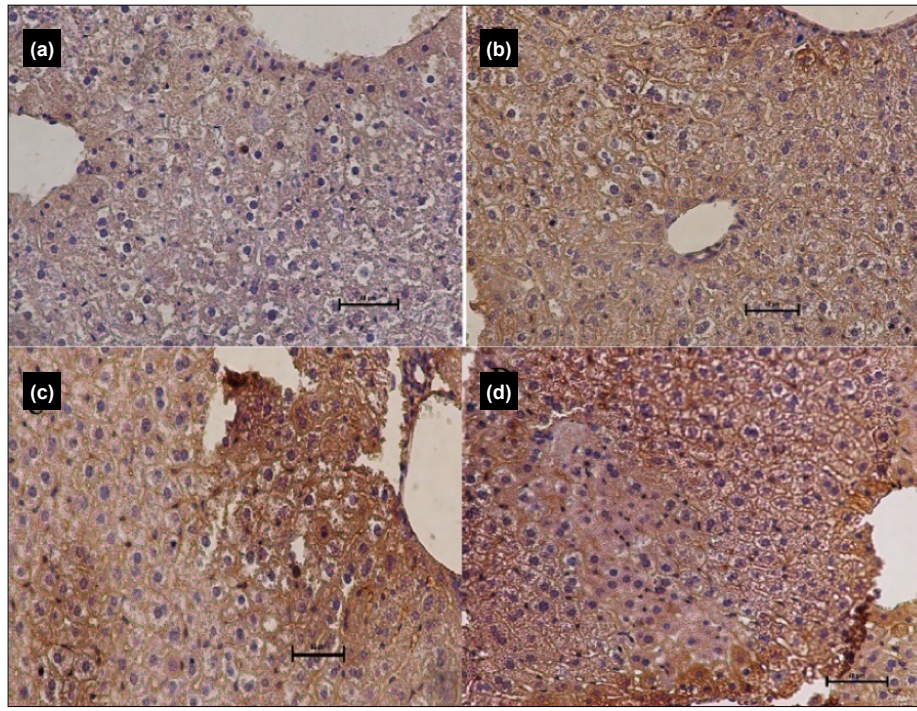

Figure 2. Ki-67 immunohistochemical staining (200× magnification). Cells showing division activity are observed as brown-stained (Ki-67-positive). **(a)** and **(b)**: Groups 1 and 2, respectively. **(c)** and **(d)**: Groups 3 and 4.

Table 3. Distribution of histopathological findings between groups

Parameters	Control n (%)	Study n (%)	p-value
Sinusoidal congestion			<0.001
0	0 (0)	10 (55.6)	
1	0 (0)	8 (44.4)	
2	9 (50)	0 (0)	
3	9 (50)	0 (0)	
Necrosis			<0.001
0	5 (27.8)	18 (100)	
1	12 (66.7)	0 (0)	
2	1 (5.6)	0 (0)	
Vacuolization			0.034
0	14 (77.8)	18 (100)	
1	4 (22.2)	0 (0)	

DISCUSSION

Partial hepatectomy, the model that most clearly demonstrates liver regeneration capacity, is considered the most potent stimulator of liver regeneration.[9,10] Therefore, the partial hepatectomy model was chosen. Weight measurement, proliferating cell nuclear antigen (PCNA), and the mitotic index are the most commonly used parameters for the evaluation of liver regeneration. In our study, we selected the regeneration weight ratio (according to the Kwon formula), mitotic count, and Ki-67 proliferation index for evaluating regeneration, as these are the most widely used parameters in the literature.

To prevent oxidative damage, mammalian cells have developed an elaborate antioxidant defense system that includes enzymatic activities such as superoxide dismutase, catalase, and glutathione peroxidase/reductase. Studies conducted on various tissues have shown that CD acts as a radical scavenger, reduces FOR, increases eNOS, and decreases LPO.[11,12] However, there is no study in the literature evaluating the effect of CD treatment on liver regeneration in the PH model.

Karaman et al.[13] investigated the effect of leflunomide, an antioxidant and anti-inflammatory agent, on liver regeneration in the PH model; on day 2, liver tissue SOD values were higher in the PH+leflunomide group than in the group treated with PH alone. The current findings are consistent with those observed in the second-day study and control groups. In the study by Kanter et al.,[14] quercetin treatment, a flavonoid, was evaluated. When the effect of quercetin on liver regeneration in the PH model was examined by comparing the PH+quercetin and PH groups, the seventh-day tissue SOD value was higher in the PH+quercetin group than in the PH group alone. These findings are similar to the seventh-day tissue SOD values in our study. The tissue SOD value was high-

er in the seven-day study group than in the control group, and this effect was even more pronounced in the two-day study group compared to the control group, indicating that CD may be effective on the enzymatic antioxidant defense system and may benefit regeneration. Özden et al.[15] evaluated the effect of hyperbaric oxygen (HBO) treatment on liver regeneration; tissue SOD values were compared on days 2, 4, and 7, and it was shown that tissue SOD values in the PH-only group were lower from day 2 to day 7, while these values increased from day 2 to day 7 with HBO treatment. Similar results were found in our study in terms of tissue SOD values. The antioxidant enzyme levels decreased in the control groups due to an increase in superoxide anions from day 2 to day 7, and the increased SOD levels after treatment with CD suggest that this treatment provides support to the antioxidant system. In our study, serum SOD values increased from the second day to the seventh day in the control groups and did not increase in the study groups receiving CD treatment. Enzyme results showed opposite trends in tissue and serum in both the control and study groups. In a study conducted by Saitoh et al.,[16] changes in tissue and plasma levels of SOD were investigated in a burn rat model, and SOD values in different tissues at various times were compared with plasma values during the same periods; different plasma and SOD values that increased at different time points were recorded for each tissue.

Free oxygen radicals attack polyunsaturated fatty acids in membrane lipids and lead to lipid peroxidation. Elevated MDA concentrations in tissue and plasma are well-known hepatocyte damage markers reflecting the level of LPO. Although LPO may be a primary toxicity mechanism for cell membrane damage, it is also a physiological process. It is known that LPO begins to appear at a very early stage of liver regeneration.[17] In light of these findings, as it is known that treatments with antioxidant properties prevent LPO in liver tissue, tissue MDA levels were expected to be lower in the groups receiving treatment in our study. However, tissue MDA levels were higher in both the study and control groups. The effects of peroperative and preoperative CD use on regeneration in a hepatic ischemia-reperfusion (I/R) injury model were evaluated by Ünal et al.[18] In that study, total sulfhydryl (SH) levels, MDA, and fluorescent oxidation products (FOP) were measured as oxidative stress parameters, and the highest MDA levels were found in the control group. The authors concluded that preoperative and peroperative CD treatment significantly reduced liver tissue MDA levels. Although an I/R injury model was used, the CD-related reduction in tissue MDA levels showed an opposite trend in our study. However, serum MDA levels in our study were lower in the groups receiving treatment than in those undergoing PH alone, regardless of the day of measurement.

In a study conducted by Andersen et al.,[19] PH was applied to healthy rats to systematically examine the natural course of liver regeneration. They reported that PH induced a rapid regenerative response at a maximum rate between days 1 and 4, and that liver regeneration was completed by day 8. Again, in the same study, it was observed that liver regeneration rate (RO) showed a stable increasing course until day 7 after PH and reached its final peak on day 7, albeit with lower acceleration. Our results in the control groups are consistent with the literature in this respect, as the regeneration rate increased from day 2 to day 7. The RO of the treated groups was higher. The difference between the ROs of the control and study groups on days 2 and 7 is thought to be due to CD and its contribution to liver regeneration.

The Suzuki Scoring System was used for histopathological grading in our study. Ünal et al.[18] used the same scoring system in their study evaluating the effects of CD on hepatic I/R injury, and reported that CD significantly reduced sinusoidal congestion scores, that there was no significant difference in vacuolization scores, and that necrosis was not observed in any group. Oğuz et al.[20] investigated the effect of Urtica dioica (UD) on regeneration in the PH model and found that vacuolization was widespread in the PH group on the seventh day, while sinusoids were larger than those in the PH+UD group. In our study, sinusoidal congestion was absent or mild in the study groups, vacuolization and necrosis were not observed, and all findings were statistically significant for all variables. These results suggest that CD protects liver tissue during regeneration and helps to form a histological structure more similar to normal liver tissue.

The role of apoptosis in the liver after hepatectomy is controversial. Apoptosis begins at the peak of regeneration. Li et al.[21] showed that the level of apoptosis after liver regeneration is directly proportional to the level of regeneration. In another study, Kırımlıoğlu et al.[22] showed increased apoptosis after PH in rats. We did not find any study in the literature evaluating the effect of CD on hepatic regeneration and apoptosis. Sowa et al.[23] evaluated apoptosis on the second and seventh days after 70% PH and showed that apoptosis occurred earlier and in parallel with regeneration. Their outcomes were consistent with our study in terms of time selection. Our findings in the control groups are also consistent with the literature. Kanter et al.[14] compared PH+quercetin and PH groups in their study and found that the seventh-day AI value was lower in the PH+quercetin group than in the PH-only group. In our study, the CD group had lower AI values on the second and seventh days than the control groups. This result suggests that CD may reduce cell damage after PH.

Karaman et al.[13] evaluated the KI-67 proliferation index in terms of liver regeneration on the second day after PH in their study with leflunomide; Ki-67 proliferation index values were significantly higher in the PH+leflunomide group compared to the PH group. They concluded that leflunomide use after PH probably increased liver regeneration through its antioxidant effect. These findings are in line with our results, although the agents used for treatment differ. CD increases cell proliferation in tissue repair and supports regeneration.

CONCLUSION

In our study, the effects of calcium dobesilate on oxidative damage and liver regeneration in rats undergoing PH were evaluated using biochemical and histological methods. The increased tissue SOD levels after calcium dobesilate treatment suggest that this treatment provides support to the antioxidant system and contributes to liver regeneration. In addition, histopathological examination under light microscopy showed decreased sinusoidal congestion and vacuolization with calcium dobesilate treatment, supporting its potential benefit in regeneration and its protective effect on liver tissue. Furthermore, calcium dobesilate was observed to effectively suppress the tendency for apoptosis after PH and thus significantly contribute to regeneration.

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DENEYSEL ÇALIŞMA - *ÖZ*

Parsiyel hepatektomi yapılan sıçanlarda kalsiyum dobesilatın karaciğer rejenerasyonu üzerine etkisi

AMAÇ: Bugüne kadar hiçbir çalışma, kalsiyum dobesilatın parsiyel hepatektomi sonrası rejeneratif kapasite üzerindeki etkilerini değerlendirmemiştir. Bu araştırma kapsamında, kalsiyum dobesilatın (KD) parsiyel hepatektomi sonrası karaciğer rejenerasyon kapasitesi ve antioksidan yolakları üzerindeki etkilerini açıklamayı amaçladık.

GEREÇ VE YÖNTEM: Çalışmada 250 ile 350 gram ağırlığında otuz altı Spraque Dawley erkek sıçan kullanıldı. Tüm hayvanlara parsiyel hepatektomi uygulandı. Sıçanlar rastgele dört gruba ayrıldı, her grup kontrol grubu (Grup 1 ve 2) ve çalışma grubu (Grup 3 ve 4) olmak üzere 9 sıçandan oluşuyordu. Rejenerasyon oranı, histopatolojik parametreler, immünohistokimyasal inceleme ve apoptotik indeks (Aİ) ölçüldü.

BULGULAR: Doku süperoksit dismutaz (SOD) seviyesi, çalışma gruplarında kontrol gruplarına kıyasla istatistiksel olarak anlamlı derecede yüksekti (p=0.03). Çalışma gruplarında malondialdehit (MDA) hem 2. hem de 7. günde kontrol gruplarına kıyasla istatistiksel olarak anlamlı derecede yüksekti (p=0.001). İkinci günde rejenerasyon oranı (RO), çalışma grubunda kontrol grubuna kıyasla daha yüksekti ve bu fark istatistiksel olarak anlamlıydı (p<0.001). İkinci günde RO, KD grubunda 7. gün grubuna kıyasla anlamlı derecede yüksekti (p<0.001). Suzuki skorlama sistemine göre çalışma gruplarında vakuolizasyon ve nekroz gözlenmedi (sırasıyla, p<0.001'e karşı p=0.034). Apoptotik indeks (Aİ), kontrol gruplarında çalışma gruplarına kıyasla anlamlı derecede yüksekti (p<0.001) ve AI, 7. günde istatistiksel olarak anlamlı derecede düşüktü (p=0.006). Ki67 ekspresyonu çalışma gruplarında 2. ve 7. günde istatistiksel olarak anlamlı derecede yüksekti. Kontrol gruplarında 7. günde 2. güne göre istatistiksel olarak anlamlı derecede daha yüksekti (p=0.006).

SONUÇ: Bu araştırma, kalsiyum dobesilatın parsiyel hepatektomi uygulanan sıçanlarda oksidatif hasarı iyileştirme ve karaciğer rejenerasyonunu artırma üzerindeki etkilerini ortaya koymuştur. Mevcut çalışmanın sonuçları (ameliyat öncesi ve sonrası), KD'nin parsiyel hepatektomi sonrası oksidatif stresi iyileştirdiğini ve karaciğer rejenerasyon kapasitesini artırdığını göstermiştir.

Anahtar sözcükler: Deneysel; kalsiyum dobesilat; karaciğer rejenerasyonu; oksidatif hasar; parsiyel hepatektomi.

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EXPERIMENTAL STUDY

Neuroprotective effects of pregabalin in experimental spinal cord injury: An investigation of oxidative stress and antioxidant enzymes in blood and neural tissue

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ABSTRACT

BACKGROUND: This study aimed to evaluate the neuroprotective potential of pregabalin (PB) and methylprednisolone (MP) in a rat model of spinal cord injury (SCI) by assessing serum and spinal cord levels of superoxide dismutase (SOD) and glutathione peroxidase (GPx), markers of oxidative stress, and neurological recovery outcomes.

METHODS: Forty-four rats were randomized into six groups: sham, PB control (40 mg/kg), SCI alone, MP-treated SCI (30 mg/kg), and PB-treated SCI (40 and 80 mg/kg). SCI was induced at the T10 level using the Allen weight-drop method. PB and MP were administered intraperitoneally for three days post-injury. Neurological recovery was assessed using the Tarlov scale and inclined plane test. Although 44 rats were initially allocated, mortality and technical loss resulted in a final cohort of 35 animals; however, post hoc power remained >90% for key biochemical outcomes.

RESULTS: SOD levels were significantly reduced in the MP+SCI group compared with the sham (p=0.006), SCI (p=0.015), 40 PB (p=0.004), and 80 PB+SCI (p=0.028) groups. Additionally, the SCI group exhibited lower SOD activity than the 40 PB group (p=0.007). Serum glutathione peroxidase levels were significantly lower in both the SCI (p=0.018) and 80 PB+SCI (p=0.009) groups compared with the sham group, whereas the 40 PB group showed higher GPx activity than the SCI (p=0.010) and 80 PB+SCI (p=0.006) groups. In spinal cord tissue, SOD activity in the 40 PB+SCI group was significantly lower than in the SCI group (p=0.007). Additionally, SOD activity in the SCI group was significantly higher than in the 40 PB group (p=0.007). Spinal cord GPx levels were significantly elevated in the SCI group compared with the sham (p=0.007), MP+SCI (p=0.010), 40 PB (p=0.003), 40 PB+SCI (p=0.003), and 80 PB+SCI (p=0.028) groups. Furthermore, the MP+SCI group demonstrated higher GPx activity than the sham group (p=0.045). Pregabalin improved inclined-plane performance but did not produce significant changes in Tarlov motor scores, indicating selective enhancement of postural stability rather than full locomotor recovery. Histopathological analysis revealed no significant differences between the trauma groups.

CONCLUSION: Pregabalin mitigated oxidative stress and partially improved functional stability in experimental spinal cord injury, suggesting possible clinical applicability pending further validation.

Keywords: Pregabalin; spinal cord injury; superoxide dismutase; glutathione peroxidase; antioxidant; methylprednisolone.

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INTRODUCTION

Spinal cord injury (SCI) is a devastating condition that can cause permanent motor, sensory, and autonomic dysfunctions.[1] SCI progresses in two phases: the primary phase, characterized by irreversible structural damage, and the secondary phase, driven by inflammation, oxidative stress, and excitotoxicity.[2,3] These secondary mechanisms exacerbate neuronal loss and drive long-term disability, making them critical therapeutic targets.

Reactive oxygen species (ROS) function as central mediators of secondary injury. ROS accumulation induces lipid peroxidation, protein and DNA damage, and mitochondrial dysfunction, ultimately triggering apoptosis and inflammation. Endogenous antioxidant enzymes, such as superoxide dismutase (SOD) and glutathione peroxidase (GPx), counteract these processes; however, this function is often insufficient in SCI.[4] Pregabalin (PB), an antiepileptic drug widely prescribed to treat neuropathic pain, binds to the α2-δ subunit of voltage-gated calcium channels, thereby reducing excitatory neurotransmitter release.[5-7] Beyond its analgesic properties, PB exerts neuroprotective effects by modulating oxidative stress and inflammatory responses.[5,8] In contrast, methylprednisolone (MP) is still used as a conventional treatment option, even though its efficacy and safety remain controversial.[9]

We hypothesized that PB would mitigate secondary injury after SCI by strengthening endogenous antioxidant defenses through modulation of SOD and GPx and by reducing excitotoxicity, thereby exerting neuroprotective effects equivalent or superior to those of MP. To test this hypothesis, the present study compared the effects of PB on antioxidant enzyme activity, histopathological alterations, and functional recovery with those of MP in an experimental SCI model in a dose-dependent manner.

MATERIALS AND METHODS

This study was conducted in accordance with the Guide for the Care and Use of Laboratory Animals (NIH publication no. 85-23, revised 1996). Ethical approval was obtained from the Experimental Animals Ethics Committee of İnönü University Faculty of Medicine (approval no. 2011 A-108).

Experimental Groups

Forty-four male Sprague–Dawley rats (250-400 g), all free of neurological deficits, were obtained from the İnönü University Experimental Animal Center. The study included six experimental groups: sham (laminectomy only, n=6), PB only (40 mg/kg, n=6), SCI (spinal cord injury and 0.5 cc saline, n=8), MP+SCI (30 mg/kg, n=8), PB+SCI (40 mg/kg, n=8), and PB+SCI (80 mg/kg, n=8). SCI was induced using the Allen weight-drop method in all groups except the sham and PB-only groups. Treatments were administered intraperitoneally at 30 minutes and 12, 24, 36, and 48 hours post-injury.

Anesthesia and Surgical Procedures

All rats were anesthetized with intraperitoneal xylazine (10 mg/kg) and ketamine (50 mg/kg). Following shaving and povidone–iodine disinfection, a midline incision was made at T9–L1. The paravertebral muscles were bluntly dissected, and T9–T11 laminectomies were performed. SCI was induced by exposing the intact dura and dropping a 5-g weight (2-mm tip) from a height of 10 cm onto the T10 level, according to the Allen weight-drop method (Fig. 1).

Drug Administration

PB (Lyrica®, 150-mg capsules) and MP (Sopharma) were administered intraperitoneally at 30 minutes and at 12, 24, 36, and 48 hours. PB powder was accurately weighed, suspended in sterile 0.9% saline, vortexed for homogeneity, and administered at doses of 40 or 80 mg/kg depending on group allocation.

Neurological Assessment

Motor function was evaluated on postoperative days 1–3 by a blinded neurosurgeon using the Tarlov scale and inclined plane test.[10,11] The Tarlov scale (0–5) was used to grade function as follows: 0=no movement (paraplegia), 1=minimal movement, 2=sitting with assistance, 3=sitting independently, 4=ambulation with abnormal gait, and 5=normal ambulation. Hind limb performance was further assessed using the inclined plane test, in which rats were positioned perpendicular to the platform, and the maximum angle maintained for ≥5 seconds without falling was recorded. Each rat was tested three times, and the mean value was used for analysis.

Sacrifice and Tissue Collection

At 72 hours, rats were anesthetized with intraperitoneal xylazine (10 mg/kg) and ketamine (50 mg/kg) and sacrificed by thoracotomy. Blood (2 mL) was drawn from the heart, centrifuged at 3000 rpm for 10 minutes, and the serum was collected and stored at −30°C. Spinal cords were harvested

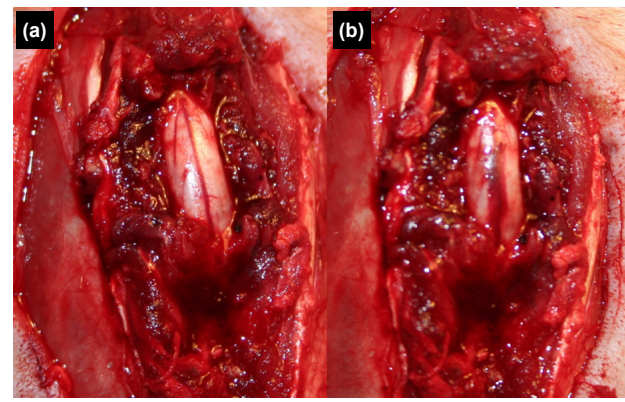

Figure 1. Postoperative laminectomy and induction of spinal cord injury at the T10 level. **(a)** Dorsal view following T9–T11 laminectomy, showing the intact dura mater. **(b)** Contusive spinal cord injury generated at the T10 level via the Allen weight-drop method, demonstrating traumatic disruption of neural tissue.

and divided into a 1-cm segment from the T10 lesion site for histopathology and a 2-cm caudal segment for biochemical analysis, both stored at −30°C.

Histopathological Evaluation

The T10 spinal cord segments were fixed in 10% formaldehyde, embedded in paraffin, and sectioned at 6 µm thickness. Hematoxylin–eosin–stained transverse sections were examined under a Leica DFC 280 microscope using image analysis software. The extent of hemorrhage, necrosis, and edema was graded semi-quantitatively based on the proportion of the affected area relative to the total cross-sectional area of the spinal cord as follows: 0, no damage; +, <25%; ++, 25–50%; +++, 50–75%; and ++++, >75%. This scoring system enabled standardized assessment of histopathological injury severity across experimental groups.

Biochemical Analysis

Superoxide dismutase and glutathione peroxidase activities were measured in spinal cord homogenates and serum. All samples were stored at −30°C until further analysis.

Preparation of Tissues for Biochemical Analysis

On the day of analysis, spinal cord tissues stored at −30°C were thawed, weighed, and homogenized (10% weight/volume [w/v]) in a phosphate buffer at 12,000 rpm for 1–2 minutes on ice. Homogenates were centrifuged at 5000 rpm for 30 minutes at 4°C, and the supernatants were collected for analysis.

Measurement of Enzyme Activities

SOD activity was determined using the method described by Sun et al.,[12] based on nitro blue tetrazolium (NBT) reduction. GPx activity was measured by monitoring the decrease in absorbance at 340 nm due to NADPH (nicotinamide adenine dinucleotide phosphate) oxidation during enzymatic activity, according to the method described by Paglia and George.[13]

Impact of Animal Losses on Statistical Power

Although the initial study design included 44 rats, losses reduced the final number to 35, creating some imbalance among groups. Nevertheless, post hoc power analysis demonstrated >90% power for key biochemical parameters, confirming the statistical robustness of our findings.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). Due to small group sizes and non-normal data distributions, non-parametric tests were applied, including the Kruskal–Wallis test followed by Mann–Whitney U tests for pairwise comparisons. Effect sizes were reported as η^2H for Kruskal–Wallis tests and r for Mann–Whitney U tests, together with 95% confidence intervals. A two-tailed p-value <0.05 was considered statistically significant. Post hoc power analysis was conducted using G*Power (version 3.1; Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany) and demonstrated statistical power exceeding 90% for the primary biochemical outcomes.

RESULTS

Final Sample Size

Due to mortality, technical issues, or inadequate samples, the final group sizes were as follows: sham, n=5; PB 40 mg, n=6; SCI, n=7; MP+SCI, n=6; PB 40 mg+SCI, n=6; and PB 80+SCI, n=5.

Inclined Plane Test

Performance on the inclined plane test was significantly impaired in all trauma groups compared to controls on day 1 ($p<0.01$), confirming effective SCI induction. Both pregabalin-treated groups demonstrated superior motor recovery compared to the saline (SCI) and methylprednisolone (MP+SCI) groups. On days 1, 2, and 3, the 40 mg PB+SCI and 80 mg PB+SCI groups both showed significantly higher inclined plane angles than the SCI ($p<0.004$) and MP+SCI groups ($p<0.006$). Conversely, the 80 mg PB+SCI group showed no significant difference from the 40 mg PB+SCI group ($p>0.05$). A progressive, dose-dependent improvement was observed across three days, indicating enhanced motor recovery with pregabalin treatment compared to the MP and untreated trauma groups. The methylprednisolone (MP) group demonstrated statistically significant improvement in inclined-plane performance on post-injury days 2 and 3 compared with the saline-treated SCI group ($p=0.008$ and $p=0.013$, respectively) (Fig. 2).

Neurological Motor Function Results

Motor scores remained normal in the control and 40 mg PB-only groups (5.0±0.0). All trauma groups showed complete paralysis on day 1 (mean score of 0). By day 3, a dose-dependent trend of motor function improvement was observed in the pregabalin-treated groups, with the 80 mg PB+SCI group reaching the highest mean score (0.80±0.83), followed by the 40 mg PB+SCI group (0.5±0.83). However, these observed

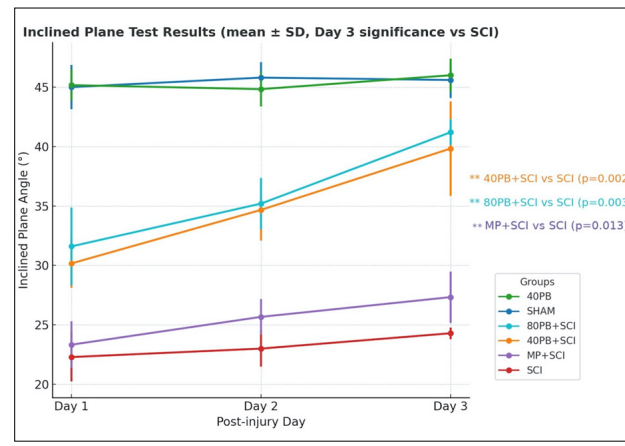

Figure 2. Inclined plane test outcomes (mean±SD) and corresponding p-values across experimental groups.

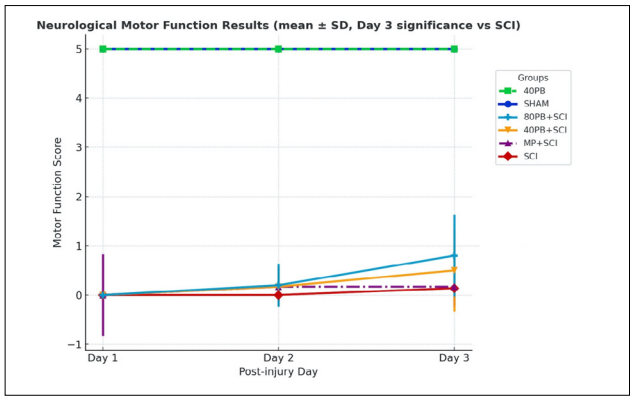

Figure 3. Neurological motor function outcomes (mean±SD) in experimental groups.

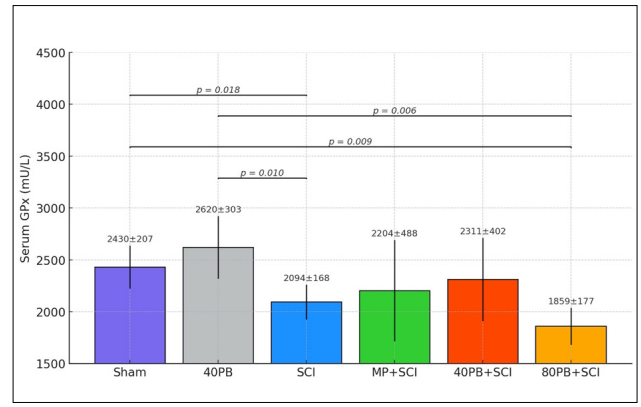

Figure 5. Serum glutathione peroxidase (GPx) levels (mean±SD) with corresponding p-values across experimental groups.

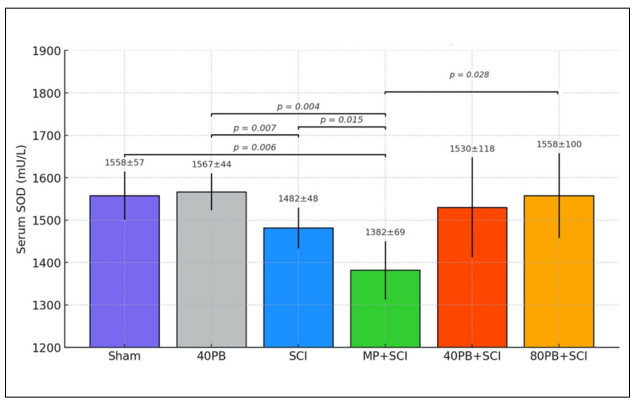

Figure 4. Serum superoxide dismutase (SOD) levels (mean±SD) with corresponding p-values across experimental groups.

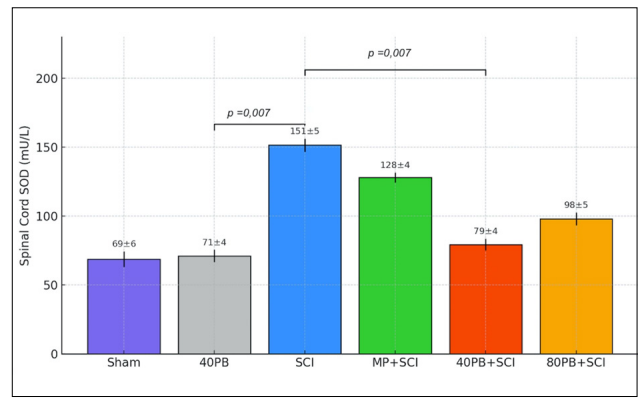

Figure 6. Spinal cord superoxide dismutase (SOD) levels (mean±SD) with corresponding p-values across experimental groups.

improvements did not reach statistical significance when compared to the SCI group (40 mg PB vs. SCI, p=0.383; 80 mg PB vs. SCI, p=0.097; MP vs. SCI, p=0.909 on day 3). Therefore, while a positive trend was noted, statistically significant locomotor recovery was not demonstrated within the 72-hour observation period (Fig. 3).

Serum SOD

Serum SOD levels differed significantly among the groups (Kruskal–Wallis H=15.40, p=0.009, η^2H=0.45, large effect). The MP+SCI group showed significantly lower values than the sham (p=0.006), SCI (p=0.015), and 40 mg PB (p=0.004) groups. The SCI group showed lower levels than the 40 mg PB group (p=0.007), and serum SOD levels were also significantly lower in the MP+SCI group compared with the 80 mg PB+SCI group (p=0.028). No other significant differences were observed (p>0.05). Post hoc power analysis confirmed high reliability (1–β=0.98) despite the reduced sample size (Fig. 4).

Serum GPx

Serum GPx levels also varied significantly (Kruskal–Wallis H=14.81, p=0.011, η^2H=0.44, large effect). Specifically, the SCI group showed significantly lower levels than the sham (p=0.018) and 40 mg PB (p=0.010) groups, whereas the 80 mg PB+SCI group showed significantly lower levels than the sham (p=0.009) and 40 mg PB (p=0.006) groups. No other significant differences were observed (p>0.05). Post hoc power analysis confirmed strong reliability (1–β=0.97) of the findings (Fig. 5).

Spinal Cord SOD

Spinal cord SOD levels differed significantly among the groups (Kruskal–Wallis H=13.06, p=0.023, η^2H=0.38, large effect). Spinal cord SOD levels in the SCI group were significantly higher than those in both the 40 mg PB+SCI group (p=0.007) and the 40 mg PB group (p=0.007). No other pairwise comparisons were statistically significant (p>0.05). Post hoc analysis indicated adequate statistical power (1–β=0.92) (Fig. 6).

Spinal Cord GPx

Spinal cord GPx levels differed significantly among the experimental groups (Kruskal–Wallis H=17.75, p=0.003, η^2H=0.52, large effect). Compared with the sham group, GPx levels

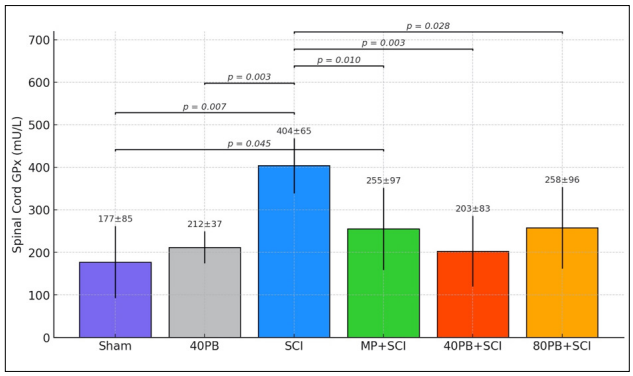

Figure 7. Spinal cord glutathione peroxidase (GPx) levels (mean±SD) with corresponding p-values across experimental groups.

were significantly elevated in the SCI (p=0.007) and MP+SCI (p=0.045) groups, indicating a trauma-induced oxidative response. Furthermore, GPx levels in the SCI group were significantly higher than those in the 40 mg PB (p=0.003) group, as well as the MP+SCI (p=0.010), 40 mg PB+SCI (p=0.003), and 80 mg PB+SCI (p=0.028) groups. These findings suggest that pregabalin and methylprednisolone mitigated spinal cord oxidative stress when administered after injury. MP+SCI animals showed slightly higher GPx activity than sham controls (p=0.045); however, this effect did not follow the overall trend of oxidative suppression and may reflect transient compensatory enzyme induction rather than true antioxidant improvement. Post hoc analysis confirmed excellent statistical power (1–β=0.997), reinforcing the robustness of these results (Fig. 7).

Histopathology

Histopathological evaluation revealed preserved spinal cord architecture in the control and 40 mg PB-only groups, with no evidence of hemorrhage, necrosis, or edema. In contrast, all trauma-induced groups (SCI, MP+SCI, 40 mg PB+SCI, and 80 mg PB+SCI) exhibited moderate-to-severe parenchymal damage, corresponding to histopathological scores of +++ (50–75%). These lesions were characterized by widespread hemorrhage, necrosis, and edema throughout the spinal cord. No statistically significant differences were observed among the treatment groups, indicating comparable structural injury patterns across all SCI models (Fig. 8).

DISCUSSION

Spinal cord injury leads to irreversible neuronal loss and paralysis, resulting in high morbidity and mortality.[3,14] Secondary injury mechanisms, including edema, ROS production, neuroinflammation, lipid peroxidation, calcium overload, and apoptosis, all play a central role in the progression of tissue damage.[2,3,15,16] Antioxidant enzymes such as SOD and GPx are critical for mitigating these processes; however, their activities can be suppressed under severe injury conditions.[17]

The present study evaluated the effects of PB and MP on

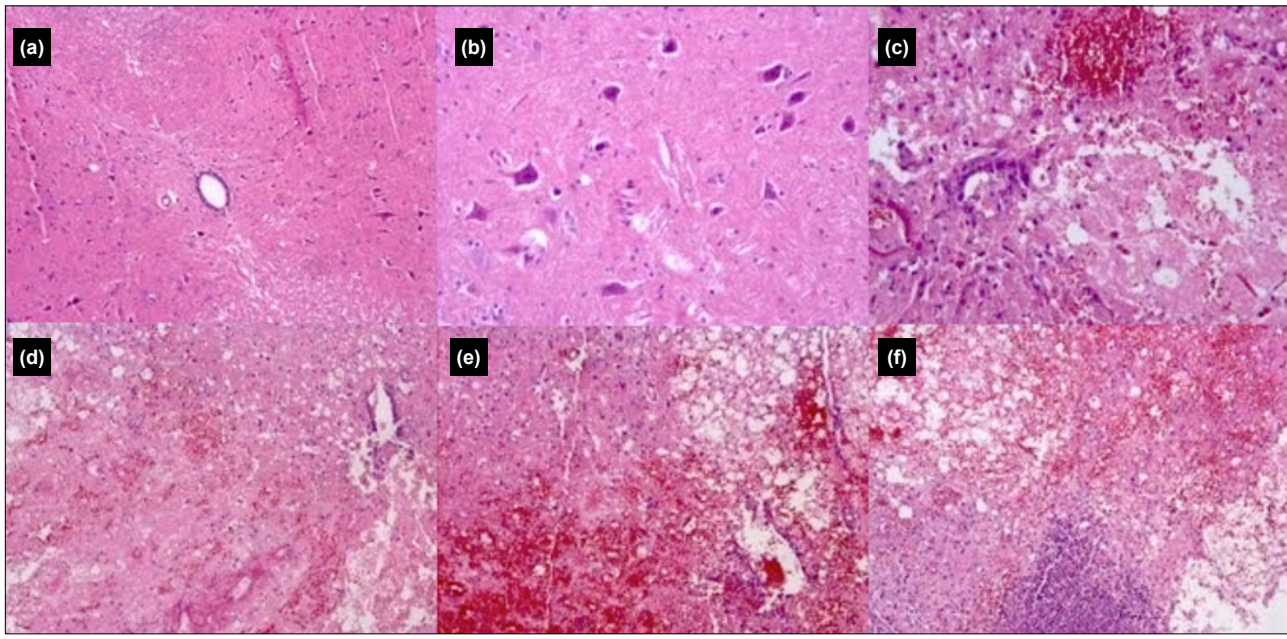

Figure 8. Histopathological abnormalities in hematoxylin and eosin-stained (H&E-stained) spinal cord sections from the study groups. Hematoxylin and eosin staining analyses of all groups: **(a)** Sham: Normal histoarchitecture with intact gray and white matter; **(b)** 40 PB: Preserved neuronal morphology in the substantia grisea. **(c)** SCI: Extensive hemorrhage and necrosis with disruption of central canal integrity; **(d)** MP+SCI: Diffuse hemorrhagic and necrotic areas accompanied by structural degeneration; **(e)** 40 PB+SCI: Widespread hemorrhage, necrosis, and edema with central canal disruption; **(f)** 80 PB+SCI: Severe hemorrhage and necrosis with prominent polymorphonuclear cell infiltration.

SOD and GPx activity in the serum and spinal cord tissue of SCI rats, as well as on their functional recovery. Pregabalin attenuated the SCI-induced elevation of spinal cord GPx activity at both doses while markedly suppressing SOD levels, particularly at 40 mg/kg. However, these changes were not evident in the serum, likely due to systemic dilution and pharmacokinetic factors. Although pregabalin showed partial modulation of serum antioxidant levels-particularly higher GPx activity in the 40 mg PB group compared to the SCI and 80 mg PB+SCI groups-these systemic effects were inconsistent relative to the localized spinal tissue response, likely due to dilution and pharmacokinetic variability. MP decreased serum SOD activity, indicating a distinct tissue-specific antioxidant profile. Although MP+SCI animals exhibited a marginal increase in spinal GPx compared with the sham group ($p=0.045$), this isolated fluctuation was inconsistent with the overall oxidative suppression trend and was therefore interpreted as a transient compensatory response rather than a genuine therapeutic effect. Overall, the antioxidant action of PB appears to be dose-dependent and predominantly localized to spinal tissue. Although the 80 mg PB+SCI group showed a paradoxical reduction in serum SOD compared with the MP+SCI group ($p=0.028$), this deviation from the expected dose-dependent trend may reflect pharmacokinetic saturation or a transient oxidative rebound at higher doses. Similar nonlinear antioxidant responses to pregabalin and other calcium channel modulators have been reported in previous neuroprotective models, suggesting that optimal dosing may require narrower therapeutic windows.

Methylprednisolone is a corticosteroid that reduces inflammation and limits tissue damage in SCI; however, its benefits for functional recovery remain controversial.[9,18,19] Although both PB and MP act through antioxidant and anti-inflammatory mechanisms, the clinical use of MP is limited by serious adverse effects, such as infection and gastrointestinal bleeding.[18]

Experimental models have highlighted the antioxidant potential of PB. In diabetic rats, PB increases brain SOD levels without affecting GPx, whereas nano-formulated PB increases SOD and glutathione levels in a fibromyalgia model.[8,20,21] Similarly, PB increases SOD and GPx activity in epilepsy and diabetic neuropathy models, thereby reducing oxidative stress.[8,20,22] In a spinal cord ischemia–reperfusion model, PB provided superior histopathological protection compared to MP.[7,23] These findings indicate that the antioxidant effects of PB vary depending on the experimental model and the specific parameters measured. In ischemia–reperfusion models, PB increases GPx activity.[24] Although its neuroprotective efficacy varies with dose and timing, several prior studies have confirmed its antioxidant effects.[23,25] Oxidative stress plays a central role in the pathogenesis of SCI.[8] Pregabalin administration has also been reported to significantly increase SOD and GPx activity and reduce MDA levels within 24 hours in an experimental traumatic brain injury model.[26] This finding indicates that pregabalin enhances antioxidant defense and mitigates oxidative stress during the early phase of traumatic injury, which is consistent with the GPx elevation observed in our spinal cord injury model. Pregabalin selectively strengthened postural resilience, improving inclined-plane resistance without restoring locomotor scores, indicating a partial rather than global neuromotor benefit. However, this functional gain did not translate into measurable histological protection, as no significant differences were detected in structural injury scores ($p>0.05$). This suggests that pregabalin exerts its early neuroprotective effects through metabolic and biochemical modulation rather than overt tissue preservation within the acute 72-hour period.

In the present study, PB partially improved GPx levels after SCI; however, its effects on antioxidant enzymes were less pronounced than those previously reported.[20,22,27] The marked increase in spinal cord GPx in the SCI group, together with the significant reduction of spinal SOD in the 40 mg PB+SCI group, confirms that oxidative stress is a major driver of secondary injury. Notably, these alterations were not consistently reflected in serum measurements, suggesting that systemic antioxidant levels may not accurately mirror local spinal cord redox status due to pharmacokinetic and compartmentalization differences. Differences between serum and spinal cord enzyme levels likely reflect pharmacokinetic and physiological factors, such as barrier permeability and local drug distribution.[28-30]

Our serum and spinal cord SOD/GPx findings alternately aligned with and diverged from those of previous reports, primarily owing to differences in experimental models, timing, and dosing. In previous studies using reversible SCI models, no significant changes in SOD or GPx levels were observed at 1, 4, or 24 hours, whereas in our study, marked increases were detected at 72 hours, suggesting that antioxidant responses may only be measurable after the acute phase.[31] Model-specific differences were also critical. Although GPx activity has been reported to decrease in ischemia–reperfusion models, the increase observed on day 3 in our contusion model likely reflects a compensatory response.[32] Differences in treatment protocols and dosing further contributed to these variations. For example, minocycline enhanced SOD/GPx activity, whereas the short-term, moderate-dose administration of PB and MP in our study produced limited systemic changes.[33] In summary, injury type, severity, timing, and treatment conditions collectively account for the variability observed in SOD/GPx outcomes across studies.

Discrepancies between histopathological findings and functional or biochemical improvements are expected in experimental models of acute SCI. Structural repair requires weeks to months to complete, whereas motor scores and biochemical markers may improve within a few days. This early recovery is attributed to reductions in edema, restoration of metabolic balance, and modulation of cellular signaling pathways.[34] Structural regeneration occurs during the subacute and

chronic phases, and short follow-up periods are insufficient to demonstrate histological recovery. Routine hematoxylin–eosin (H&E) staining is limited in detecting early microstructural changes, whereas immunohistochemical markers, such as glial fibrillary acidic protein (GFAP), can reveal astrocytic activation and repair processes beginning on day 7.[35] Therefore, the absence of histopathological improvement in the acute phase should not be interpreted as treatment failure, but rather as a reflection of the delayed nature of structural repair. The fact that functional and biochemical recovery precedes histological changes indicates that acute-phase treatments primarily exert their effects through neuroprotective mechanisms.[34,35] Although this study was conducted in a rodent model, the results provide a mechanistic foundation for future translational studies. The established clinical use and safety of pregabalin in neuropathic pain management make it a promising candidate for repurposing in acute spinal cord injury. Nevertheless, interspecies differences in pharmacokinetics, metabolism, and dosing should be carefully addressed before clinical application.

Translation of experimental SCI models into clinical practice remains challenging due to interspecies biological, pharmacokinetic, and methodological discrepancies. Rodent models cannot fully reproduce the heterogeneous and chronic nature of human SCI, and drug doses proven safe in animals may yield different efficacy or adverse effects in humans. Therefore, preclinical benefits must be interpreted cautiously and validated through well-designed clinical trials.[36,37] To enhance translational value, large animal models with anatomical and physiological features closer to those of humans (e.g., pigs) have been recommended.[38] For PB, appropriate dose conversion, comprehensive safety analyses, and well-designed phase studies are all required to establish its clinical validity.

This study has certain limitations. The short follow-up period and small sample size may restrict the generalizability of the findings, and electron microscopy or confirmatory imaging (e.g., micro-computed tomography [micro-CT]) was not performed to validate structural injury. The rodent model cannot fully replicate human SCI, and interspecies pharmacokinetic differences may limit dose translation. Although sample size imbalance could increase the risk of type II errors, post hoc power analysis confirmed adequate statistical strength for key biochemical outcomes. Finally, the exclusive use of male rats and potential inter-observer variability should be considered when interpreting the results.

CONCLUSION

In the present study, PB demonstrated antioxidant activity in an experimental spinal cord injury model by normalizing spinal cord GPx levels and partially improving functional outcomes. Its neuroprotective effects appear to be mediated primarily by a reduction in oxidative stress. However, the precise mechanisms underlying these effects remain unclear, and further experimental studies are warranted to confirm them.

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DENEYSEL ÇALIŞMA - *ÖZ*

Deneysel spinal kord yaralanmasında pregabalinin nöroprotektif etkisi: Kanda ve nöral dokuda antioksidan enzimlerin oksidatif stres açısındandan incelenmesi

AMAÇ: Bu çalışma, oksidatif stres belirteçleri olan süperoksit dismutaz (SOD) ve glutatyon peroksidaz'ın (GPx) serum ve omurilik düzeylerini ile nörolojik iyileşme sonuçlarını değerlendirerek, sıçan omurilik yaralanması (SKY) modelinde pregabalin (PB) ve metilprednizolonun (MP) nöroprotektif potansiyelini araştırmayı amaçladı.
GEREÇ VE YÖNTEM: Kırk dört sıçan altı gruba randomize edildi: Sham, PB kontrol (40 mg/kg), yalnızca SKY, MP ile tedavi edilen SKY (30 mg/kg) ve PB ile tedavi edilen SKY (40 ve 80 mg/kg). SKY, Allen ağırlık düşürme yöntemi kullanılarak T10 seviyesinde oluşturuldu. PB ve MP, yaralanma sonrası üç gün boyunca intraperitoneal olarak uygulandı. Nörolojik iyileşme, Tarlov skoru ve eğik düzlem testi kullanılarak değerlendirildi. Başlangıçta 44 sıçan ayrılmış olsa da, mortalite ve teknik kayıplar nedeniyle nihai çalışma kohortu 35 hayvanla sınırlanmıştır; buna rağmen temel biyokimyasal sonuçlar için post-hoc güç analizi %90'ın üzerinde kalmıştır.
BULGULAR: MP+SKY grubunda SOD düzeyleri, sham (p=0.006), SKY (p=0.015), 40 PB (p=0.004) ve 80 PB+SKY (p=0.028) gruplarına kıyasla anlamlı derecede azalmıştı. Ayrıca SKY grubunda SOD aktivitesi, 40 PB grubuna göre daha düşüktü (p=0.007). Serum glutatyon peroksidaz (GPx) düzeyleri, hem SKY (p=0.018) hem de 80 PB+SKY (p = 0,009) gruplarında sham grubuna kıyasla anlamlı derecede daha düşüktü; buna karşın 40 PB grubunda GPx aktivitesi, SKY (p=0.010) ve 80 PB+SKY (p=0.006) gruplarına göre daha yüksekti. Omurilik dokusunda, 40 PB+SKY grubunda SOD aktivitesi SKY grubuna göre anlamlı derecede daha düşük bulundu (p=0.007). Ek olarak SKY grubundaki SOD aktivitesi, 40 PB grubuna kıyasla anlamlı derecede daha yüksekti (p=0.007). Omurilik GPx düzeyleri, SKY grubunda sham (p=0.007), MP+SKY (p=0.010), 40 PB (p=0.003), 40 PB+SKY (p=0.003) ve 80 PB+SKY (p=0.028) gruplarına kıyasla anlamlı derecede artmıştı. Ayrıca MP+SKY grubunda GPx aktivitesi sham grubuna göre daha yüksekti (p=0.045). Pregabalin, eğik düzlem performansını iyileştirdi ancak Tarlov motor skorlarında anlamlı bir değişiklik oluşturmadı; bu durum tam bir lokomotor iyileşmeden ziyade postüral stabilitenin seçici olarak arttığını düşündürdü. Histopatolojik analizde ise travma grupları arasında anlamlı bir fark saptanmadı.
SONUÇ: Pregabalin, deneysel omurilik yaralanmasında oksidatif stresi azalttı ve fonksiyonel stabiliteyi kısmen iyileştirdi; bu durum, ileri doğrulama çalışmalarının ardından klinik uygulamaya uygun olabileceğini düşündürmektedir.
Anahtar sözcükler: Antioksidan; glutatyon peroksidaz; metilprednizolon; omurilik yaralanması; pregabalin; süperoksit dismutaz.

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EXPERIMENTAL STUDY

The effect of quercetin on ischemia-reperfusion injury in skeletal muscle in rats

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ABSTRACT

BACKGROUND: Ischemia-reperfusion (I/R) injury of the lower limbs is a significant clinical challenge that can arise due to surgical procedures, thrombotic events, embolism, or traumatic vascular damage. This study aimed to evaluate the antioxidative and histopathological protective effects of quercetin, a potent flavonoid antioxidant, on skeletal muscle subjected to I/R injury.

METHODS: Eighteen Wistar Albino rats were randomly assigned into three groups: Control (sham laparotomy), Ischemia-Reperfusion (IR) group (2 hours of ischemia followed by 2 hours of reperfusion), and Ischemia-Reperfusion plus quercetin treatment (IR-Q) group, receiving 20 mg/kg quercetin intraperitoneally 30 minutes before ischemia induction. After the experimental protocols, skeletal muscle samples were collected for biochemical assays measuring malondialdehyde (MDA) levels and superoxide dismutase (SOD) activity, as well as for histopathological examination.

RESULTS: The IR group demonstrated a significant increase in MDA concentration compared to controls ($p<0.0001$), whereas administration of quercetin in the IR-Q group significantly attenuated MDA levels relative to the untreated IR group ($p=0.012$). SOD activity was markedly diminished in the IR group ($p<0.0001$) but was significantly restored in the IR-Q group compared to IR alone ($p=0.012$). Histological analyses revealed pronounced muscle atrophy, degeneration, leukocyte infiltration, and fiber fragmentation/hyalinization in the IR group, which were significantly alleviated by quercetin treatment ($p<0.05$).

CONCLUSION: These findings indicate that quercetin exerts a protective effect against oxidative stress and structural damage induced by ischemia-reperfusion in skeletal muscle, potentially through enhancement of endogenous antioxidant defenses. Quercetin thus holds promise as a therapeutic agent in mitigating I/R injury; however, further studies are needed to elucidate its precise mechanisms and clinical applicability.

Keywords: Ischemia-reperfusion; quercetin; oxidative stress; superoxide dismutase; malondialdehyde; skeletal muscle.

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INTRODUCTION

Ischemia occurs when blood flow to tissues is insufficient, causing a lack of oxygen delivery that disrupts normal cellular activities and metabolism.[1] The subsequent restoration of blood flow, termed reperfusion, paradoxically may lead to further damage known as ischemia-reperfusion (I/R) injury. This injury involves complex biochemical and cellular events such as oxidative stress, inflammation, and tissue destruction. During ischemia, reduced ATP synthesis, accumulation of metabolic byproducts, and disruption of ionic balance impair cellular function. When oxygen supply is suddenly reinstated during reperfusion, excessive production of reactive oxygen species (ROS) is triggered, initiating oxidative damage and activating inflammatory pathways.[2,3] These processes cause oxidative modifications, including lipid membrane degradation, protein oxidation, and DNA strand breaks, which collectively contribute to cell death and exacerbate tissue injury.[4]

I/R injury of the lower extremities can be caused by a range of clinical conditions, including atherosclerosis, thrombotic or embolic arterial occlusions, traumatic vascular injuries, and surgical interventions. Thrombus or embolus formation leads to vascular blockage, while direct trauma to blood vessels may similarly result in ischemia. Clinically, I/R injury is often observed during procedures such as aortic aneurysm repair requiring cross-clamping, peripheral vascular surgeries, free flap tissue transfers, orthopedic operations, and shock states with compromised circulation.[5,6] Moreover, prolonged external pressure or the use of tourniquets can also precipitate ischemic conditions.

Ischemia-reperfusion (I/R) injury is not confined to local tissue damage but can also trigger systemic effects impacting vital organs such as the heart, lungs, kidneys, and brain.[7] The reperfusion phase initiates a cascade of harmful events, including the overproduction of reactive oxygen species (ROS), disruption of endothelial function, infiltration of inflammatory leukocytes, and secretion of proinflammatory cytokines, collectively intensifying tissue damage.[8] Central to these processes are key mediators such as tumor necrosis factor-alpha (TNF-α) and interleukin-1 beta (IL-1β), as well as adhesion molecules including intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1). These molecules facilitate leukocyte adhesion and extravasation, elevate vascular permeability, promote edema development, and drive cellular apoptosis and necrosis in affected tissues.[9]

Antioxidants serve as crucial modulators in counteracting the harmful effects of I/R injury.[10] Among them, quercetin-a flavonoid compound naturally found in many plants-has garnered attention due to its strong antioxidant and anti-inflammatory effects.[11] It protects cells by reducing lipid peroxidation, boosting endogenous antioxidant enzyme activities, and suppressing the release of proinflammatory mediators such as TNF-α and IL-1β.[12,13] At the cellular level, quercetin supports mitochondrial function, sustains energy metabolism, and inhibits pathways leading to apoptosis. Additionally, it impedes neutrophil infiltration by modulating interactions between neutrophils and endothelial cells.[14] Other compounds such as melatonin, mannitol, allopurinol, and N-acetylcysteine have also shown efficacy in limiting oxidative damage in various I/R experimental setups.[15-20]

Quercetin is widely present in numerous fruits and vegetables, including onion (Allium cepa), apple (Malus domestica), grape (Vitis vinifera), cherry (Prunus avium), green tea (Camellia sinensis), and broccoli (Brassica oleracea).[21]

This study aims to investigate the protective role of quercetin against ischemia-reperfusion injury in rat skeletal muscle by evaluating biochemical oxidative stress parameters, inflammatory responses, and histopathological alterations.

MATERIALS AND METHODS

Ethical Approval and Experimental Animals

Approval for this research was granted by the Local Ethics Committee for Animal Experiments at Gazi University (Protocol No: GÜET-16.066; approved on July 13, 2016). All experimental protocols were carried out in accordance with the guidelines provided by the U.S. National Institutes of Health regarding the care and use of laboratory animals and conformed to the ethical standards outlined in the Declaration of Helsinki.

Eighteen adult male Wistar Albino rats weighing between 200 and 250 grams were housed under standardized laboratory conditions, maintained at 20-21°C with a 12-hour light/dark cycle. Animals had unrestricted access to standard chow and water, except for a fasting period of two hours prior to anesthesia. The rats were randomly divided into three groups of six animals each. Anesthesia was induced by intramuscular administration of ketamine (100 mg/kg) before surgical procedures.

Experimental Design

The study groups were organized as follows:

- **Group K (Control):** Rats underwent only midline laparotomy without any additional intervention. After a 4-hour observation period, skeletal muscle samples were collected, and the animals were euthanized.

- **Group IR (Ischemia-Reperfusion):** Following laparotomy, ischemia was induced by clamping the infrarenal abdominal aorta for two hours, followed by two hours of reperfusion. Skeletal muscle tissues were harvested after reperfusion, and the animals were sacrificed.

- **Group IR-Q (Ischemia-Reperfusion + Quercetin):** This group underwent the same ischemia-reperfusion protocol as Group IR. Additionally, quercetin (20mg/kg; Sigma–Aldrich, Q4951-10G) was administered intraperitoneally 30 minutes before ischemia onset. Tissue collection was performed after the reperfusion period.

At the conclusion of the experiments, intracardiac blood samples (up to 10mL) and skeletal muscle specimens were obtained for subsequent biochemical and histological analyses.[22]

Aortic Occlusion and Ischemia-Reperfusion Procedure

Anesthesia was induced with ketamine hydrochloride (50mg/kg, intramuscular; Ketalar, Parke-Davis Eczacıbaşı, Istanbul, Türkiye) combined with xylazine hydrochloride (2%, intramuscular; Alfazyne, Ege Vet, Izmir, Türkiye), with supplemental doses administered as needed.

Rats were placed in a supine position beneath a warming lamp. After shaving and aseptic preparation of the abdominal area, a midline laparotomy was performed. The abdominal aorta was carefully exposed and occluded using a non-traumatic microvascular clamp. Successful occlusion was verified by the absence of a palpable distal arterial pulse. To preserve body temperature and fluid homeostasis, the incision was covered with sterile plastic.

Following 120 minutes of ischemia, the clamp was removed, allowing reperfusion for an additional 120 minutes. Animals were euthanized under deep anesthesia at the end of reperfusion, and skeletal muscle samples were collected.

Biochemical Analyses

Skeletal muscle samples were rinsed with cold (4°C) deionized water to eliminate blood residues, then homogenized at 1000rpm for three minutes using a Heidolph Diax 900 homogenizer (Germany). Homogenates were centrifuged at 10,000×g for 60 minutes, and the resulting supernatant was used for assays.

• **Superoxide Dismutase (SOD) Activity:** Evaluated by monitoring the inhibition of nitroblue tetrazolium (NBT) reduction at an absorbance of 560nm, following the method described in.[23] One unit of SOD activity is defined as the amount of enzyme that inhibits 50% of the NBT reduction. Results are presented as units per milligram of protein (U/mg protein).

• **Malondialdehyde (MDA) Levels:** Quantified using the thiobarbituric acid reactive substances (TBARS) assay, according to Van Ye et al.[24] Tissue homogenates were precipitated with 20% trichloroacetic acid and centrifuged. The resulting supernatant was incubated with 0.6% thiobarbituric acid, boiled for 30 minutes, and then cooled. Absorbance was measured at 532nm using a Shimadzu UV/VIS-1601 spectrophotometer (Japan). MDA concentrations were determined in nmol/mg protein, calculated against a standard curve generated from 1,1,3,3-tetramethoxypropane. Protein content was measured via the Lowry method, employing bovine serum albumin as the standard.[25]

Histopathological Evaluation

Twenty-five skeletal muscle samples were fixed in 10% neutral-buffered formalin, subjected to dehydration and clearing using xylene, and subsequently embedded in paraffin blocks. Serial sections, each 4µm thick, were prepared and stained with hematoxylin and eosin (H&E).

The histological assessment targeted features including muscle fiber atrophy and hypertrophy, degeneration, vascular congestion, nuclear internalization, leukocyte infiltration, as well as fiber fragmentation and hyalinization. The standard H&E staining protocol involved hematoxylin application for 3 minutes, rinsing with tap water, differentiation in acid-alcohol solution, eosin staining for 10 minutes, followed by dehydration and mounting of the slides.

Statistical Analysis

Data analysis was conducted using SPSS software version 20.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was set at $p<0.05$. Biochemical results are presented as mean±standard deviation (SD), whereas histopathological data are reported as median (25th–75th percentile). The normality of data distribution was evaluated using the Shapiro-Wilk test. Group comparisons were performed using the Kruskal-Wallis test, with post hoc pairwise comparisons conducted using Bonferroni-adjusted Mann–Whitney U tests.

RESULTS

Histopathological Evaluation

The histopathological parameters-including muscle atrophy/hypertrophy, muscle degeneration/congestion, nuclear internalization (oval or central nuclei), leukocyte infiltration, and fiber fragmentation/hyalinization-showed statistically significant differences among the groups ($p=0.012$, $p<0.0001$, $p=0.001$, $p=0.002$, and $p=0.020$, respectively) (Table 1, Figures 1-6).

Table 1. Histopathological findings of rat skeletal muscle tissue [Mean±SD]

Histopathological Parameters	Control Group (K) (n=6)	Ischemia-Reperfusion Group (IR) (n=6)	Ischemia-Reperfusion + Quercetin Group (IR-Q) (n=6)	p-value
Muscle Atrophy/Hypertrophy	0.00±0.00 *	1.33±0.42	0.50±0.22 *	0.012
Muscle Degeneration/Congestion	0.33±0.21 *	2.17±0.31	0.67±0.21 *	<0.0001
Nuclear Internalization (Oval/Central Nuclei)	0.00±0.00 *	1.50±0.22	0.83±0.31 *, &	0.001
Fragmentation/Hyalinization	0.33±0.21 *	1.83±0.31	0.67±0.21 *	0.002
Leukocyte Infiltration	0.17±0.17 *	1.17±0.31	0.33±0.21 *	0.020

p: Statistical significance was determined using the Kruskal-Wallis test ($p<0.05$). *$p<0.05$:Compared to the IR group. & $p<0.05$: Compared to the Control (K) group.

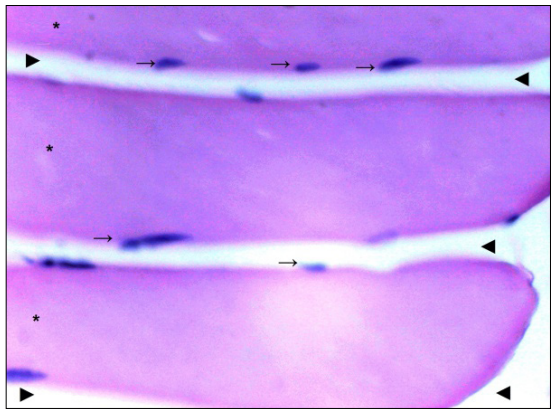

Figure 1. Longitudinal section of skeletal muscle in the Control group showing normal morphology (H&E: hematoxylin and eosin, magnification ×100). (→ peripheral flat nuclei, * muscle fibers: myofibrils, ► intercellular space).

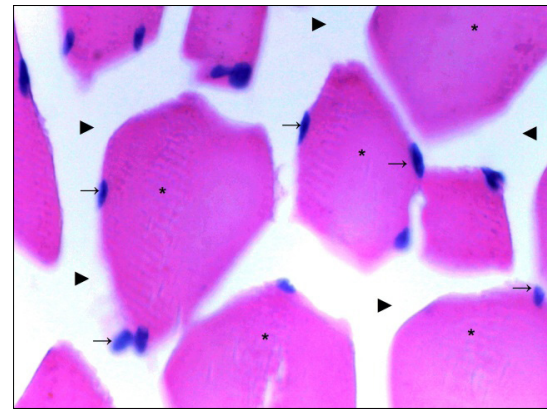

Figure 2. Cross-sectional view of skeletal muscle in the Control group demonstrating normal morphology (H&E: hematoxylin and eosin, magnification ×100). (→ peripheral flat nuclei, *muscle fibers: myofibrils, ► intercellular space).

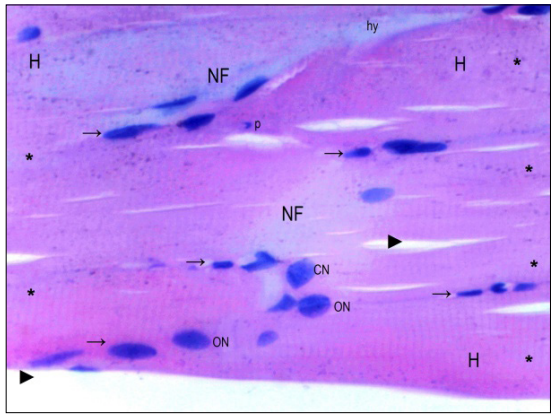

Figure 3. Longitudinal light microscopic view of skeletal muscle in the IR group (H&E: hematoxylin and eosin, magnification ×100).(→ peripheral flat nuclei, * muscle fibers: myofibrils, H: hypertrophy in muscle fibers, NF: necrotic fiber area, CN: central nucleus, ON: oval nucleus, f: fragmentation, hy: hyalinization areas, p: pyknotic nucleus).

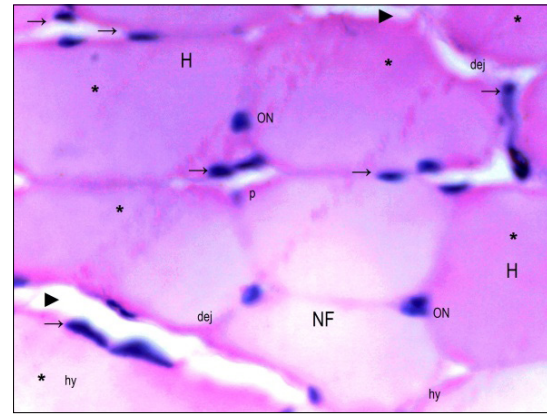

Figure 4. Transverse light microscopic view of skeletal muscle in the IR group (H&E: hematoxylin and eosin, magnification ×100). (→ peripheral flat nuclei, * muscle fibers: myofibrils, ► intercellular space; H: hypertrophy in muscle fibers, NF: necrotic fiber area, CN: central nucleus, ON: oval nucleus, f: fragmentation, hy: hyalinization areas, p: pyknotic nucleus, dej: degeneration).

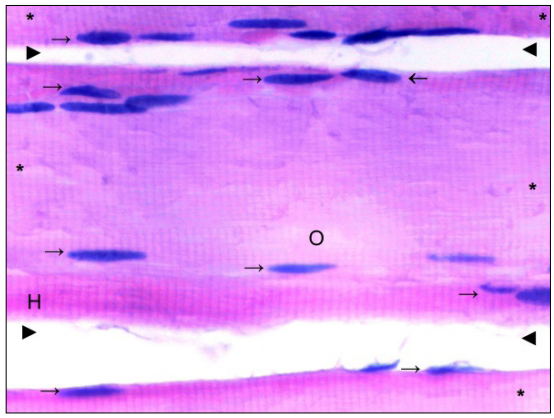

Figure 5. Longitudinal light microscopic view of skeletal muscle in the IR-Quercetin group (H&E: hematoxylin and eosin, magnification ×100). (→ peripheral flat nuclei, * muscle fibers: myofibrils, ► intercellular space; H: hypertrophy in muscle fibers, hy: hyalinization, O: edema).

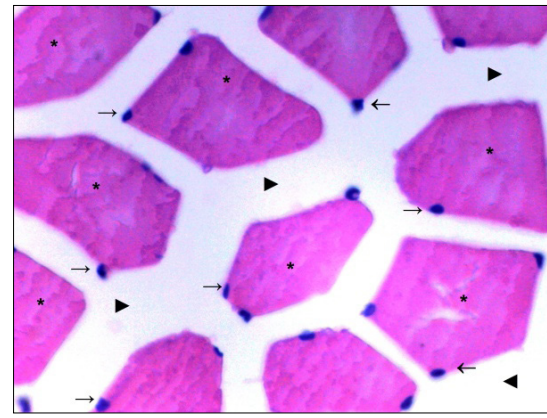

Figure 6. Transverse light microscopic view of skeletal muscle in the IR-Quercetin group (H&E: hematoxylin and eosin, magnification ×100). (→ peripheral flat nuclei, * muscle fibers: myofibrils, ► intercellular space).

Table 2. Biochemical data of skeletal muscle tissue [Mean±Standard Deviation]

Parameter	Group K (n=6)	Group IR (n=6)	Group IR-Q (n=6)	p-value **
MDA (nmol/mg protein)	21.13± 3.00	53.33±7.66*	24.11±3.19&	0.001
SOD (U/mg protein)	11.47±1.10	6.07±1.11*	10.28±0.93&	0.006

K: Control, I/R: Ischemia/Reperfusion, IR-Q: Ischemia-Reperfusion + Quercetin, MDA: Malondialdehyde, SOD: Superoxide Dismutase.

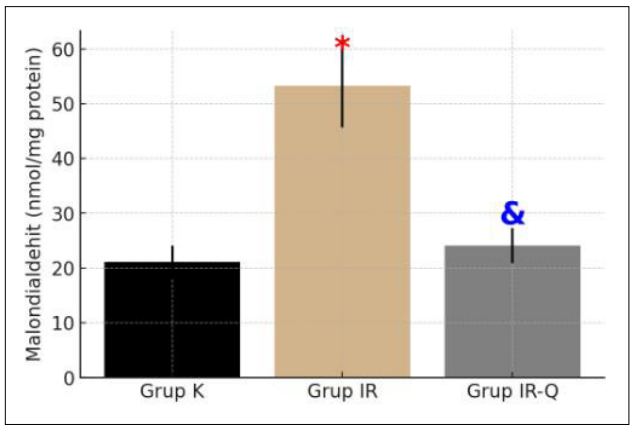

Figure 7. Malondialdehyde (MDA) levels in skeletal muscle tissue.

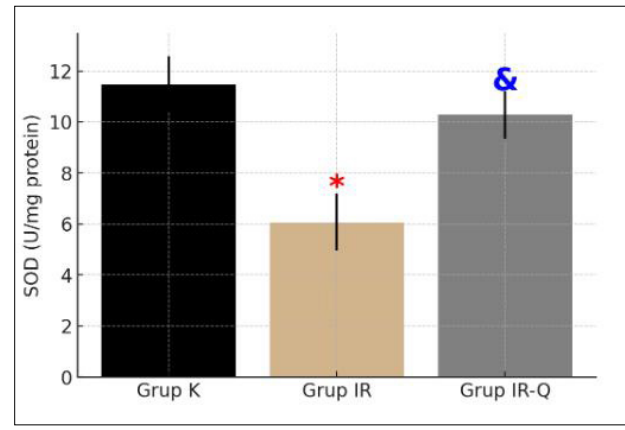

Figure 8. Superoxide dismutase (SOD) levels in skeletal muscle tissue.

Muscle atrophy/hypertrophy was significantly higher in the IR group compared to both the Control (K) and IR-Q groups (p=0.004 and p=0.049, respectively). Muscle degeneration/congestion was also significantly elevated in the IR group compared to the K and IR-Q groups (p<0.0001 and p=0.001, respectively). Nuclear internalization (oval or central nuclei) was significantly greater in the IR group compared to the K and IR-Q groups (p<0.0001 and p=0.048, respectively). Furthermore, the IR-Q group showed a significant increase in nuclear internalization compared to the K group (p=0.017). Leukocyte infiltration was significantly higher in the IR group than in the K and IR-Q groups (p=0.009 and p=0.025, respectively). Fiber fragmentation/hyalinization was significantly more pronounced in the IR group compared to the K and IR-Q groups (p=0.002 and p=0.014, respectively) (Table 1, Figures 1-6).

Biochemical Evaluation

Table 2 presents the MDA levels and SOD enzyme activities in skeletal muscle tissue across the groups. The results demonstrated that the MDA level in the IR group was significantly higher compared to the control group (p<0.0001). In the IR-Q group, the MDA level was significantly lower than in the IR group (p=0.012) (Figure 7).

SOD enzyme activity was significantly decreased in the IR group compared to the control group (p<0.0001 and p<0.001, respectively). In the IR-Q group, SOD enzyme activity was markedly higher compared to the IR group (p<0.001 and p=0.012, respectively) (Figure 8).

Malondialdehyde; SOD: Superoxide Dismutase. *p<0.05 compared to Group K; &p<0.05 compared to Group IR.)

DISCUSSION

Lower extremity ischemia may develop as a consequence of various clinical conditions, such as peripheral arterial disease, thromboembolism, traumatic vascular injury, and surgical interventions. Although the restoration of blood flow (revascularization) is vital, the reperfusion phase may exacerbate tissue injury, as it triggers a series of complex biochemical events that cause complications both in local muscle tissue and at the systemic level.[26,27] One of the main contributors to this damage is the generation of reactive oxygen species (ROS) and the subsequent inflammatory response, which can progress to multi-organ dysfunction.[28]

ROS are highly reactive molecules that initiate lipid peroxidation, disrupt cell membranes, and enhance neutrophil activation, thereby intensifying inflammation.[29] Thus, controlling oxidative stress is critical for reducing ischemia-reperfusion (I/R) injury. Enzymatic antioxidants such as superoxide dismutase (SOD) and glutathione peroxidase (GPx) constitute the first line of defense against oxidative damage in the body. Various pharmacological and immunological agents have been tested in experimental models to mitigate I/R injury. In this

study, the protective effect of quercetin-a natural flavonoid compound-was investigated in a rat skeletal muscle I/R model induced by abdominal aortic clamping.

Following ischemia, reperfusion leads to an abrupt increase in ROS production. In particular, superoxide anion (O_2^-), hydrogen peroxide (H_2O_2), and hydroxyl radicals (OH^-) target cellular structures and trigger cell death through both apoptosis and necrosis.[30] Lipid peroxidation disrupts phospholipid integrity, increases membrane permeability, and disturbs ion homeostasis. Protein oxidation weakens enzymatic functionality, while DNA damage elevates mutation risk and activates cellular stress responses.[31-33]

Oxidative stress not only initiates tissue damage but also amplifies inflammation. Lipid peroxidation products act as danger signals, promoting the release of pro-inflammatory cytokines and accelerating neutrophil migration, thereby exacerbating tissue injury. Additionally, ROS-induced mitochondrial dysfunction impairs ATP production and increases cellular vulnerability.[34-37]

Among the organism's antioxidant defense mechanisms, SOD, catalase (CAT), and GPx play major roles. SOD converts superoxide into hydrogen peroxide, thereby reducing oxidative burden. However, under I/R conditions, SOD activity decreases due to the inhibitory effects of ROS and disruptions in intracellular homeostasis.[38-39] Malondialdehyde (MDA), a reliable biochemical marker of lipid peroxidation, was used in this study to assess the degree of oxidative damage.[38,40-42]

Currently, there is no clinically effective method capable of completely preventing I/R-induced muscle injury.[43] While pharmacological treatments, hyperbaric oxygen therapy, hypothermia, and pre/post-ischemic conditioning offer partial benefits,[32,33,44] experimental studies have demonstrated protective effects of compounds such as crocin, melatonin, lycopene, and ticlopidine against lower extremity I/R injury.[45-48]

Quercetin is a polyphenolic flavonoid abundantly found in fruits and vegetables and is recognized for its potent antioxidant, anti-inflammatory, and cytoprotective properties.[49] It exerts its effects through free radical scavenging, modulation of enzymatic activities, and suppression of pro-inflammatory cytokine release.[50-52] For example, Chen et al.[53] reported that quercetin protects cardiomyocytes against I/R injury by regulating kinases such as Src, FAK, p38, and STAT3. Similarly, Sul and colleagues demonstrated that quercetin decreases ROS levels and NOX2 expression in LPS-exposed pulmonary epithelial cells, thereby reducing oxidative stress and inflammation.[54] Its antiviral, anticancer, anti-inflammatory, and metabolic regulatory properties are also well documented.[55-57] Furthermore, Lin et al.[58] showed that quercetin attenuates hepatic I/R injury by inhibiting GSDMD-mediated macrophage pyroptosis in an experimental model.

Although the protective effects of quercetin on various organ systems have been reported, its specific effects on lower extremity skeletal muscle have not been sufficiently investigated. In the present study, a significant improvement was observed in oxidative stress markers following I/R. The reduced SOD activity in the IR group increased significantly in the quercetin-treated IR-Q group, indicating enhanced antioxidant defense. Moreover, MDA levels, which were highest in the IR group, were significantly reduced in the IR-Q group, reflecting preserved membrane integrity. These findings highlight the crucial role of quercetin in ROS neutralization and the maintenance of redox balance.

Histopathological evaluations supported these biochemical findings. In the IR group, pronounced signs of muscle structure deterioration-including atrophy, hypertrophy, degeneration, congestion, and nuclear internalization-were observed, whereas quercetin treatment markedly reduced these alterations. In particular, the reduction in leukocyte infiltration, as well as decreased fiber fragmentation and hyalinization, demonstrates quercetin's tissue-protective effects through the suppression of inflammation. Considering that nuclear internalization is regarded as a marker of muscle regeneration and cellular stress, its significant reduction in the IR-Q group indicates the restorative potential of quercetin.

CONCLUSION

One of the key strengths of this study is the use of a well-established ischemia-reperfusion model under strictly controlled laboratory settings. Additionally, the combination of biochemical and histopathological analyses allowed for a comprehensive assessment of quercetin's protective effects. However, some limitations must be noted. This experimental setup focused solely on the acute phase of ischemia-reperfusion injury without exploring potential long-term outcomes. Furthermore, only a single dose of quercetin was tested, leaving the dose–response relationship unexamined.

In summary, our results demonstrate that quercetin provides significant protection against ischemia-reperfusion-induced skeletal muscle damage. Its antioxidant capabilities played an important role in reducing oxidative stress and preserving tissue structure. These findings suggest that quercetin holds promise as a therapeutic agent for preventing ischemic muscle injury. Nevertheless, further investigations involving various dosing regimens and long-term evaluations in preclinical and clinical trials are necessary before clinical application can be considered.

Ethics Committee Approval: This study was approved by the Gazi University Ethics Committee (Date: 13.07.2016, Decision No: GÜET-16.066).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: M.K., M.A.; Design: M.K., A.Ö.; Supervision: M.A., A.K.; Resource: M.K., Y.K.; Materials: Ö.E., M.Ka, A.C.B.; Data collection and/or processing: M.K., A.Ö.; Analysis and/or interpretation: A.C.B., M.Ka., Ö.E.; Literature review: L.O., G.K.; Writing: L.O., G.K.; Criti-

cal review: M.A., L.O., M.K.

Conflict of Interest: None declared.

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DENEYSEL ÇALIŞMA - *ÖZ*

Sıçanlarda iskelet kasında iskemi-reperfüzyon hasarında kuersetinin koruyucu rolü

AMAÇ: Alt ekstremite iskemi-reperfüzyon (İ/R) hasarı, cerrahi müdahaleler, tromboembolik olaylar veya travmatik vasküler lezyonlar sonrası ortaya çıkan ciddi bir patofizyolojik durumdur. Bu çalışmanın amacı, güçlü antioksidan özelliklere sahip flavonoid kuersetinin, İ/R sürecinde iskelet kasında oluşan oksidatif stres ve histopatolojik değişiklikler üzerindeki koruyucu etkilerini değerlendirmektir.
GEREÇ VE YÖNTEM: On sekiz Wistar Albino sıçan, kontrol (sahte laparotomi), iskemi-reperfüzyon (İR; 2 saat iskemi + 2 saat reperfüzyon) ve İR + kuersetin (İR-K; iskemi öncesi 30 dakika 20 mg/kg intraperitoneal kuersetin) olmak üzere üç gruba randomize edildi. Deneysel uygulamalar sonrası iskelet kası dokuları, malondialdehit (MDA) düzeyleri ve süperoksit dismutaz (SOD) aktivitesi açısından biyokimyasal olarak analiz edildi; ayrıca histopatolojik incelemeler gerçekleştirildi.
BULGULAR: İR grubunda MDA seviyeleri kontrol grubuna kıyasla anlamlı derecede artarken ($p<0.0001$), kuersetin uygulanan İR-K grubunda bu artış anlamlı ölçüde azaldı ($p=0.012$). SOD aktivitesi İR grubunda belirgin şekilde düşerken ($p<0.0001$), İR-K grubunda anlamlı bir restorasyon gözlendi ($p=0.012$). Histopatolojik değerlendirmelerde İR grubunda kas liflerinde atrofi, dejenerasyon, lökosit infiltrasyonu ve lif parçalanması/hiyalinizasyonun belirgin olduğu; kuersetin tedavisi ile bu patolojik değişikliklerin anlamlı ölçüde azaldığı tespit edildi ($p<0.05$).
SONUÇ: Kuersetin, iskemi-reperfüzyon hasarına bağlı oksidatif stres ve doku hasarını azaltarak iskelet kasında endojen antioksidan savunma mekanizmalarını güçlendirmektedir. Bu bulgular, kuersetinin İ/R kaynaklı doku hasarını önlemede potansiyel bir terapötik ajan olduğunu göstermektedir. Mekanizmalarının ayrıntılı incelenmesi ve klinik uygulama olanaklarının değerlendirilmesi için ileri preklinik araştırmalara ihtiyaç duyulmaktadır.

Anahtar sözcükler: İskemi-reperfüzyon; quercetin; oksidatif stres; süperoksit dismutaz; malondialdehit; iskelet kası.

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ORIGINAL ARTICLE

Pro-adrenomedullin: a novel diagnostic biomarker of acute appendicitis

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ABSTRACT

BACKGROUND: The objective of this study was to evaluate the diagnostic value of serum pro-adrenomedullin (pro-ADM) levels in diagnosing acute appendicitis (AA) in patients presenting to the emergency department (ED) with abdominal pain.

METHODS: This prospective clinical study included patients over the age of 18 who presented to the ED with abdominal pain and were initially suspected of having appendicitis. A venous blood sample was collected from each patient upon presentation, and serum pro-ADM levels were measured. Based on laboratory and radiological evaluations, patients were categorized into two groups: those diagnosed with AA and those without AA. The AA group was further subdivided into simple and complicated AA. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 21.0 (SPSS Inc., Chicago, IL, USA). A p-value of <0.05 was considered statistically significant.

RESULTS: This study included 83 adult patients with abdominal pain, of whom 44 were male (53.0%) and 39 were female (47.0%). The mean age of the patients was 32.28±16.10 years. Serum pro-ADM levels were higher in patients with appendicitis than in those without. Setting the cut-off value for pro-ADM at 3.375 pg/mL to identify patients with appendicitis revealed a statistically significant difference between patients with and without appendicitis (p=0.002). Additionally, there was a statistically significant difference in serum pro-ADM levels when comparing the duration of ED presentation among patients with appendicitis (p<0.001).

CONCLUSION: Serum pro-ADM levels are elevated in patients with appendicitis; however, pro-ADM is less effective in distinguishing between simple and complicated appendicitis. Serum pro-ADM levels in patients who present to the ED within the first 24 hours of abdominal pain onset may be useful for early diagnosis.

Keywords: Acute abdominal pain; acute appendicitis; emergency department; biomarker; pro-adrenomedullin.

INTRODUCTION

Acute abdominal pain accounts for 7-10% of all emergency department (ED) visits.[1] The most common cause of pain in patients presenting to the emergency department with abdominal pain is acute appendicitis.[2] The lifetime risk of developing acute appendicitis is 8.6% in males and 6.9% in females.[3] Pain associated with appendicitis typically begins around the umbilical region and migrates to the right lower quadrant as inflammation progresses.[4] Numerous scientific studies have been conducted to diagnose acute and complicated appendicitis using inflammatory biomarkers. Various biomarkers, including white blood cell (WBC) count, neutrophil count, neutrophil-to-lymphocyte ratio, immature granulocyte count,

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immature granulocyte percentage, bilirubin, C-reactive protein (CRP), procalcitonin, and D-dimer, have been utilized in these studies.[5-8]

Adrenomedullin (ADM) is a peptide hormone composed of 52 amino acids and is produced by various tissues in the body under stress conditions. It has vasodilatory, immunomodulatory, metabolic, and bactericidal properties.[9,10] ADM is released through the rapid degradation of the stable mid-region of its precursor, pro-adrenomedullin (pro-ADM). ADM exerts its vasodilatory effect by increasing cyclic adenosine monophosphate levels in vascular smooth muscle cells and enhancing nitric oxide levels in endothelial cells. During hypoxia and inflammation, serum levels of ADM rise, leading to the release of proinflammatory cytokines. The normal plasma level of ADM ranges from 1 to 10 ng/L.[11] Pro-ADM has been investigated as a biomarker for the diagnosis and prognosis of pneumonia, septic shock, early detection of renal injury, prognosis determination in patients hospitalized due to Coronavirus Disease 2019 (COVID-19), and the diagnosis of acute appendicitis (AA) in pediatric populations.[9-18] However, there are no scientific studies examining the role of ADM in the diagnosis of AA in adults. Our study aimed to evaluate whether pro-ADM could be used as a biomarker for diagnosing acute appendicitis in adult patients presenting to the ED with abdominal pain.

MATERIALS AND METHODS

Patients and Procedures

This prospective clinical study was conducted in the Adult ED of Ondokuz Mayıs University Hospital. Informed consent was obtained from all patients prior to participation. The study adhered to the principles of the Declaration of Helsinki and was approved by the local ethics committee (Ondokuz Mayıs University Clinical Research Ethics Committee; date: 06.09.2022; issue number: 2022/413). Financial support for this study was provided by the Ondokuz Mayıs University Scientific Research Project Unit (PYO.TIP.1904.23.009). The study group consisted of patients who presented to the ED with complaints of acute abdominal pain. This study included 83 adult patients (aged >18 years) who presented to the ED with abdominal pain and were suspected of having AA after initial evaluation between October 2022 and October 2023.

The exclusion criteria were as follows: (1) age under 18 years; (2) abdominal pain following abdominal trauma; (3) onset of abdominal pain more than 48 hours prior to presentation; (4) history of appendectomy; (5) abdominal surgery other than appendectomy within the past three months; (6) use of anticoagulant agents; (7) recent antibiotic and steroid therapy within the past month; (8) presence of cardiac or respiratory failure; (9) history of cerebrovascular disease; (10) pregnancy; (11) recent childbirth; and (12) presence of an existing psychiatric disorder.

All patient data were obtained from records in the automated information system and recorded on forms specially prepared for the study. These forms included patients' demographic characteristics (age and gender), abdominal examination findings (defense, rebound, tenderness, rigidity), time to presentation to the ED after the onset of abdominal pain (categorized as 0-24 hours or 24-48 hours), complete blood count results (including hemoglobin level, white blood cell count, platelet count, neutrophil count, lymphocyte count, platelet-to-lymphocyte ratio, neutrophil-to-lymphocyte ratio, and systemic immune-inflammatory index), emergency biochemical tests, CRP level, pro-ADM level, imaging methods, length of hospital stay, and final patient outcome (discharge or recovery).

Initial clinical diagnosis was made based on the patient's history, physical examination, laboratory tests, and direct abdominal radiography. Following the initial evaluation, abdominal ultrasonography and/or abdominal computed tomography were performed to confirm the diagnosis in patients suspected of having acute appendicitis. Ultrasonography examinations were conducted using a Sonolayer SSA-270A (Toshiba, Japan) sonography device with a 3.75 MHz convex probe and were performed by radiology specialists. On ultrasonography, findings such as a noncompressible appendix with a double-wall thickness greater than 6 mm, focal pain over the appendix upon compression, appendicolith, increased echogenicity of inflamed periappendiceal fat, and fluid in the right lower quadrant were considered positive signs of acute appendicitis.[19] Computed tomography (CT) examinations were carried out using a spiral CT scanner (Xpres/GX, TSX-002a, Toshiba, Japan). A scout image was obtained with the patient lying supine, and the area from the lower thoracic level to the pubic symphysis was defined as the examination field. On CT, findings such as an enlarged appendix with a double-wall thickness greater than 6 mm, appendiceal wall thickening greater than 2 mm, periappendiceal fat stranding, appendiceal wall enhancement, and appendicolith were considered positive signs of acute appendicitis.[20]

Patients who did not show any signs of AA on imaging comprised the non-appendicitis abdominal pain group (Group II, n=16). The AA group (Group I, n=67) was further divided into two subgroups: patients with simple AA (n=47) and those with complicated AA (n=20). Among the non-appendicitis abdominal pain group, 10 patients were diagnosed with nonspecific abdominal pain, four with colitis, one with ileitis, and one with mesenteric lymphadenitis.

Histopathological examination was performed on specimens from all patients who underwent surgery after presenting to the ED. Based on the extent of appendiceal involvement, patients were categorized as having either simple or complicated AA. The simple acute appendicitis group included patients with inflammation limited to the appendix and its surrounding tissues, as identified by imaging and/or histopathological examination. In contrast, the complicated AA group comprised patients who, in addition to inflammation around the appen-

dix, presented with conditions such as gangrene, phlegmon, periappendiceal abscess, free fluid, or perforation, or whose histopathological examination revealed necrotizing, suppurative, or perforated appendicitis.

Laboratory Assays

Peripheral venous blood samples were collected from patients suspected of having AA upon presentation, and emergency biochemical investigations and complete blood counts were performed. Additionally, to determine serum pro-adrenomedullin levels, a 5 mL venous blood sample was collected at the same time. The serum was separated and stored at −80°C in a deep freezer until analysis. Pro-adrenomedullin levels were measured after the serum samples were dissolved. Serum human pro-adrenomedullin levels were measured by ELISA (enzyme-linked immunosorbent assay) using an assay kit (Sunlong Biotech Co. Ltd., Cat No. SL2115Hu, Zhejiang, China). A sandwich immunoassay technique was employed for these measurements.

Statistical Analysis

The minimum number of patients required for the study was determined by power analysis. For pro-adrenomedullin, with d=0.12, σ=0.05, α=0.05, and a power of 95%, the minimum sample size was n=6.[17] All statistical calculations were performed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 21.0 (SPSS Inc., Chicago, Illinois, USA). In the statistical analyses, the conformity of measured variables to a normal distribution was assessed using the Kolmogorov-Smirnov test. Variables that did not follow a normal distribution were analyzed using the Kruskal-Wallis nonparametric test. Hourly pro-ADM levels of patients diagnosed with acute appendicitis were compared using the Mann-Whitney U test. Spearman's rank correlation coefficient was used for correlation analysis. Receiver Operating Characteristic (ROC) analysis was performed to determine optimal cut-off values. Fisher's exact probability test was used to compare categorical variables. For all statistical tests, p<0.05 was considered significant.

RESULTS

In the present study, a total of 143,767 patients visited the ED of our hospital over a 12-month period, and 12,639 of

Table 1. Pre- and post-treatment radiographic analysis data for regenerative endodontic procedure (REP) and mineral trioxide aggregate (MTA) apical plug applied groups

Variables	Acute Appendicitis (Group I, n=67)	No Acute Appendicitis (Group II, n=16)	p value
Age (years)			
	32.5±15.8	39.3±18.2	0.301
Sex*			
Female	29 (43.2%)	10 (62.5%)	0.265
Male	38 (56.7%)	6 (37.5%)	0.265
Physical examination*			
Tenderness	64 (95.5%)	14 (20.8%)	0.254
Defense	25 (37.3%)	0 (0.0%)	0.005
Rebound	22 (32.8%)	0 (0.0%)	0.010
Symptom duration, h			
0-24	37 (55.2)	10 (62.5)	0.780
24-48	30 (44.7)	6 (37.5)	0.780
Imaging methods*			
Direct radiography	62 (92.5%)	10 (62.5%)	0.016
US	52 (77.6%)	8 (50.0%)	0.058
CT	64 (95.5%)	5 (31.5%)	<0.001
Both US and CT	49 (73.13%)	3 (18.75%)	<0.001
Mean length of hospital stay (days)	1.4	2.1	<0.001
Final outcome*			
Discharged	66 (98.5)	16 (100.0)	1.000
Fatality	1 (1.4)	0 (0.0)	1.000

*Variables are presented as n (%).

these patients presented with abdominal pain. This study was conducted on 83 adult patients who presented to the ED with complaints of abdominal pain and were suspected of having AA after initial evaluation. The baseline demographic and clinical characteristics of the patients are presented in Table 1. Of the 83 patients, 44 were male (53.0%) and 39 were female (47.0%). The mean age of the patients was 35.8±17.2 years.

Patients with abdominal pain were divided into two groups: Group I included 67 patients with AA, and Group II included 16 patients without AA. The groups were compared in terms of pro-ADM, white blood cell count, neutrophil count, serum total bilirubin, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, systemic immune-inflammatory index (SII), and CRP values at the time of admission (Table 2).

While serum pro-ADM levels were elevated in patients with AA, they were lower in patients without appendicitis. The mean serum pro-ADM level was 4.118 pg/mL in patients not diagnosed with AA, 49.99 pg/mL in patients diagnosed with acute appendicitis, and 40.80 pg/mL in patients with complicated acute appendicitis. The difference between the groups was statistically significant (Fig. 1).

When serum pro-ADM levels were compared according to the time of hospital admission, a statistically significant difference was observed (p<0.001). In the 37 cases of AA presenting within the first 24 hours, the serum pro-ADM level was 63.26±58.88 pg/mL, whereas in the 30 cases presenting within 24-48 hours, the serum pro-ADM level was 26.85±46.24 pg/mL (Fig. 2). When the cut-off value of pro-ADM for diagnosing AA was set at 3.375 pg/mL, the sensitivity was 82.0%, specificity was 67.0%, positive predictive value was 80.6%, and negative predictive value was 62.5% (Table 3). According to ROC analysis, the area under the curve was 0.794 (95% confidence interval [CI], 0.682-0.905) (Fig. 3).

Using cut-off values of 3.375 pg/mL for pro-ADM and 5.4 mg/L for CRP, the sensitivity for diagnosing AA was 97.7%, specificity was 77.7%, positive predictive value was 95.6%, and negative predictive value was 87.5% (Table 4).

Using cut-off values of 3.375 pg/mL for pro-ADM and 6.60 k/µL for neutrophil count resulted in a sensitivity of 98.0%, specificity of 73.0%, positive predictive value of 94.2%, and negative predictive value of 88.8% for diagnosing AA (Table 5).

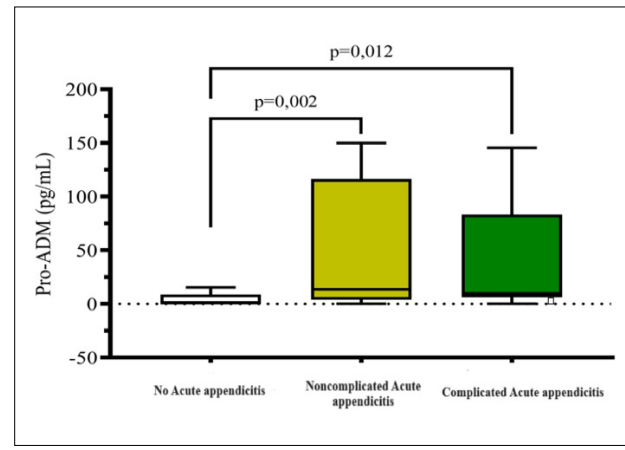

Figure 1. Pro-ADM levels of patients without appendicitis and patients with AA.

Table 2. Laboratory values of patients at the time of presentation to the Emergency Department (ED)

Variables	No Acute Appendicitis (n=16)	Noncomplicated Acute Appendicitis (n=47)	Complicated Acute Appendicitis (n=20)
Pro-adrenomedullin (pg/mL)	4.118	49.99	40.80
Hemogram (g/dL)	13.44±1.87	13.82±1.85	13.60±2.34
White blood cell count (bin/µL)	10.32±3.54	13.93±4.11**	15.15±4.38**
Neutrophil count (bin/µL)	7.25±3.40	11.00±3.88**	12.28±4.80**
Lymphocyte count (bin/µL)	1.94±0.78	1.93±0.87	1.88±0.85
Platelet count (bin/µL)	261.80±52.94	267.90±76.72	241.60±54.21
Serum total bilirubin (mg/L)	0.36±0.15	0.57±0.35*	0.72±0.29***
CRP (mg/L)	15.73±20.63	48.09±63.19*	63.60±65.90**
Neutrophil-to-lymphocyte ratio	4.24±2.73	7.42±6.67*	9.22±7.16*
Platelet-to-lymphocyte ratio	152.00±54.05	174.40±109.70	169.30±117.60
SII	1094.0±670.0	2088.0±1974.0*	2583.0±247.0*

CRP: C-reactive protein; SII: Systemic immune-inflammation index [(Platelets x Neutrophils) / Lymphocytes]. *p<0.05; **p<0.01; ***p<0.001.

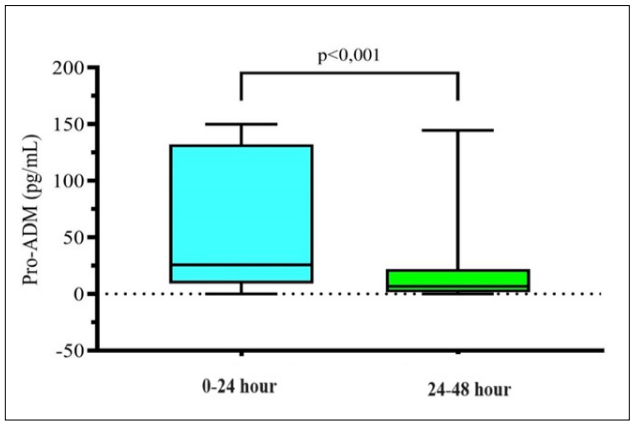

Figure 2. Comparison of serum pro-ADM levels of patients with AA according to the time of presentation.

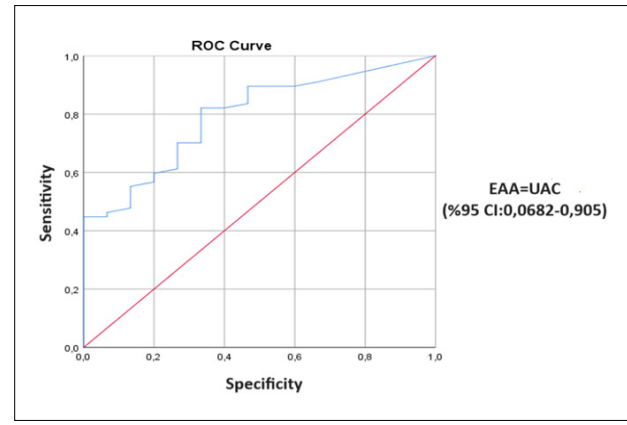

Figure 3. ROC graph of serum pro-ADM value in the diagnosis of AA. **EAA=UAC:Eğri altında kalan alan.*

Table 3. Comparison of patients' serum pro-adrenomedullin (pro-ADM) levels with radiological and pathological results

	Radiological and pathological diagnosis of acute appendicitis		
	Positive	**Negative**	**Total**
Serum pro-ADM level ≥ 3.375 pg/mL	54	6	60
Serum pro-ADM level < 3.375 pg/mL	13	10	23
Total	67	16	83

Table 4. Comparison of serum pro-adrenomedullin (pro-ADM) and C-reactive protein (CRP) levels in patients diagnosed with and without appendicitis after radiological and pathological examinations

	Radiological and pathological diagnosis of acute appendicitis		
	Positive	**Negative**	**Total**
Serum pro-ADM level ≥ 3.375 pg/mL and Serum CRP level ≥ 5.4 mg/L	44	2	46
Serum pro-ADM level < 3.375 pg/mL and Serum CRP level < 5.4 mg/L	1	7	8
Total	45	9	54

Table 5. Comparison of serum pro-adrenomedullin (pro-ADM) and neutrophil levels in patients diagnosed with and without appendicitis after radiological and pathological examinations

	Radiological and pathological diagnosis of acute appendicitis		
	Positive	**Negative**	**Total**
Serum pro-ADM level ≥ 3.375 pg/mL and Serum neutrophil level ≥ 6.60 bin/µL	49	3	52
Serum pro-ADM level < 3.375 pg/mL and Serum neutrophil level < 6.60 bin/µL	1	6	7
Total	50	9	59

DISCUSSION

When diagnosing acute appendicitis in patients presenting to the ED with abdominal pain, physicians rely not only on patient history and physical examination but also on laboratory tests and advanced diagnostic imaging methods, such as abdominal ultrasound and CT. The need for advanced diagnostic imaging arises because more than 40.0% of patients with non-appendicitis-related abdominal pain may present with signs of peritoneal irritation on physical examination.[21] Therefore, patients presenting to primary or secondary healthcare facilities with signs of peritoneal irritation can pose a diagnostic challenge for physicians, as advanced diagnostic imaging may not always be available at these centers to confirm a diagnosis of AA. As a result, physicians working in such settings often need to refer patients with peritoneal irritation to higher-level facilities for further evaluation. However, the time required to transfer patients to a higher-level center can adversely affect their clinical condition. Thus, there is a need for new biomarkers that can enable physicians at primary and secondary healthcare facilities to diagnose AA early and safely.

Biomarkers are biomolecules that are quantitatively measured and used to assess a pathogenic process or the response to treatment.[22] In our review of the literature, we observed that various biomarkers, such as WBC, CRP, interleukin-6 (IL-6), procalcitonin, bilirubin, granulocyte colony-stimulating factor (G-CSF), irisin, and others, have been evaluated in the diagnosis of AA.[5,8,23-25] The most commonly used biomarkers for diagnosing AA include neutrophil count, leukocyte count, and CRP.[26] However, none of these biomarkers alone have proven to be predictive for the early diagnosis of AA, as their sensitivity and specificity are low. Therefore, to reliably diagnose AA, these biomarkers need to be evaluated in combination. In recent years, there has been a growing trend in clinical research toward developing new biomarkers for diagnosing AA. One study conducted in children suspected of having AA evaluated multiple laboratory biomarkers together. When pro-ADM and CRP were assessed together in children suspected of AA, the sensitivity of pro-ADM was reported to be 100.0% and the specificity 61.0%; when pro-ADM was evaluated alongside neutrophil count, the sensitivity was 97.0% and the specificity 74.0%.[9] In our study, we investigated whether pro-ADM contributes to the diagnosis of AA in adults. When pro-ADM was evaluated together with CRP for the diagnosis of AA, it showed a sensitivity of 98.0%, a specificity of 78.0%, a positive predictive value of 96.0%, and a negative predictive value of 88.0% (Table 4). When pro-ADM was evaluated together with neutrophil count, the sensitivity was 98.0%, specificity was 73.0%, positive predictive value was 94.0%, and negative predictive value was 89.0% (Table 5). Our study results are consistent with the literature. Low serum levels of CRP, neutrophils, and pro-ADM are useful biomarkers for ruling out AA.

In our study, we observed that serum pro-ADM levels in venous blood samples collected from patients presenting to the ED with abdominal pain were significantly higher in those with AA compared than in those without appendicitis ($p<0.001$). However, no significant difference was observed in serum pro-ADM levels between patients with simple and complicated AA ($p>0.05$). In a study conducted on 136 pediatric patients suspected of having AA, serum pro-ADM levels were reported to be higher in patients with appendicitis than in those without.[9] In another large multicenter prospective study evaluating pro-ADM as a diagnostic biomarker for AA in 285 children with acute abdominal pain, of whom 103 were diagnosed with AA, serum pro-ADM levels were also higher in patients with appendicitis than in those without.[17] Similarly, in our study, we found that serum pro-ADM levels were higher in patients with AA compared to those without appendicitis.

Acute appendicitis typically results from obstruction of the appendiceal lumen, and the increase in intraluminal pressure can lead to ischemic necrosis (gangrene) or perforation of the appendix. Tissue gangrene or perforation paves the way for bacterial invasion. It has been reported that bacterial invasion through the portal system to the hepatic parenchyma can obstruct the excretion of bilirubin into the bile canaliculi, leading to elevated serum bilirubin levels.[27] Recent clinical studies have consistently shown that complicated appendicitis occurs in 30.4% to 34.7% of patients with AA, with an associated increase in total and/or direct bilirubin levels in the serum of these patients. This increase in bilirubin has been suggested as a noninvasive marker supporting the diagnosis of complicated AA. However, it has also been reported that elevated bilirubin levels alone are not sufficient as an independent marker for complicated AA.[7,8,24,27-30] In our study, we similarly observed increased bilirubin levels in patients with AA, with more pronounced elevations in those with complicated appendicitis.

Míguez et al.[9] reported that among 136 pediatric patients presenting to the ED with abdominal pain, 53 (38.9%) were diagnosed with AA, including nine cases of perforated appendicitis. In that study, pro-ADM levels in children with AA were compared with those in children with nonspecific abdominal pain, and a significant difference was observed between the two groups (0.54 nmol/L and 0.37 nmol/L, respectively). The study also compared pro-ADM levels in perforated and nonperforated cases of AA, finding higher levels in perforated cases (0.564 nmol/L vs. 0.492 nmol/L), although this difference was reported to have no clinical significance. In this study, pro-ADM levels were also compared according to the time of presentation to the ED, with mean serum pro-ADM levels of 0.495 nmol/L for presentations within 24 hours, 0.667 nmol/L for presentations within 24-48 hours, and 0.354 nmol/L for presentations after 72 hours.

In our study, when serum pro-ADM levels in patients with AA were compared according to the time of onset of abdominal pain, the mean serum pro-ADM level was 63.26±58.88 pg/mL for presentations within the first 24 hours and 26.85±46.24

pg/mL for presentations between 24 and 48 hours, with a statistically significant difference based on time of presentation ($p<0.001$). Míguez et al.[9] also reported that serum pro-ADM levels remained elevated for 48 hours in children with AA and then began to decline. In our study, we observed a decrease in serum pro-ADM levels when the time to presentation exceeded 24 hours. We believe this difference may be related to the age difference between the study populations. The significance of pro-ADM in predicting infection-related organ failure has been investigated, with reports indicating that pro-ADM levels increase in the early stages (within the first 24 hours) and that pro-ADM can predict sepsis up to 24 hours in advance.[31] Although our study supports the use of pro-ADM in the early diagnosis of AA, discrepancies exist in the literature regarding the elevation of serum pro-ADM levels. We believe that these discrepancies may be due to differences in patient populations and variations in measurement methodologies, and further studies are needed to clarify these inconsistencies.

Limitations

This study has several limitations. First, it was conducted at a single center with a limited number of patients. Second, blood samples for pro-ADM measurement were stored at -80°C until the day of analysis; therefore, pro-ADM was not measured concurrently with other biomarkers. Finally, although there was a plan to measure pro-ADM levels in a healthy control group, budget constraints prevented the inclusion of such a group.

CONCLUSION

Pro-ADM may be a useful biomarker for the early diagnosis of AA in adult patients. However, its ability to distinguish between simple and complicated appendicitis is limited. The combined use of biomarkers (pro-ADM, CRP, neutrophil count, bilirubin, neutrophil-to-lymphocyte ratio [NLR], and SII) enhances diagnostic accuracy in diagnosing and excluding acute appendicitis. Considering the specific limitations of this pilot study, we believe that further multicenter studies with larger sample sizes will better elucidate the role of pro-ADM in diagnosing AA.

Ethics Committee Approval: This study was approved by the Ondokuz Mayıs University Clinical Research Ethics Committee Ethics Committee (Date: 06.09.2022, Decision No: 2022/413).

Informed Consent: Written informed consent was obtained.

Peer-review: Externally peer-reviewed.

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

Conflict of Interest: None declared.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Pro-adrenomedullin: Akut apandisit için yeni bir tanı biyobelirteci

AMAÇ: Karın ağrısı şikâyetiyle acil servise (AS) başvuran hastalarda, serum pro-adrenomedullin (Pro-ADM) düzeylerinin akut apandisit (AA) tanısındaki değerini değerlendirmek.
GEREÇ VE YÖNTEM: Bu prospektif klinik çalışmaya, 18 yaş üstü ve acil servise karın ağrısı nedeniyle başvuran, başlangıçta apandisit şüphesi bulunan hastalar dâhil edildi. Her hastadan başvuru sırasında venöz kan örneği alındı ve serum Pro-ADM düzeyleri ölçüldü. Laboratuvar ve radyolojik değerlendirmelere göre hastalar iki gruba ayrıldı: AA tanısı konulanlar ve konulmayanlar. AA tanısı konulanlar ayrıca basit ve komplike AA olarak alt gruplara ayrıldı. Tüm istatistiksel analizler, SPSS for Windows sürüm 21.0 (SPSS Inc., Chicago, IL, ABD) programı kullanılarak yapıldı. $p<0.05$ değeri istatistiksel olarak anlamlı kabul edildi.
BULGULAR: Çalışmaya karın ağrısı olan toplam 83 erişkin hasta dâhil edildi; bunların 44'ü erkek (%53.0), 39'u kadındı (%47.0). Hastaların yaş ortalaması 32.28±16.10 yıl idi. Apandisit tanısı alan hastalarda serum Pro-ADM düzeyleri, tanı almayanlara göre daha yüksekti. Pro-ADM için eşik değerin 3.375 pg/mL olarak belirlenmesi, apandisit tanısı konulan ve konulmayan hastalar arasında istatistiksel olarak anlamlı bir fark ortaya koydu ($p=0.002$). Ayrıca, apandisit tanısı alan hastaların acil servise başvuru süreleriyle serum Pro-ADM düzeyleri arasında da anlamlı bir ilişki saptandı ($p<0.001$).
SONUÇ: Serum Pro-ADM düzeyleri, apandisitli hastalarda yükselmektedir ancak basit ve komplike apandisit ayrımında yeterince etkili değildir. Bununla birlikte, karın ağrısı başlangıcının ilk 24 saati içinde acil servise başvuran hastalarda Pro-ADM düzeyleri, erken tanıda faydalı olabilir.

Anahtar sözcükler: Acil servis; akut apandisit; akut karın ağrısı; biyobelirteç; pro-adrenomedullin.

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ORIGINAL ARTICLE

The role of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios in predicting the severity of acute biliary pancreatitis

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ABSTRACT

BACKGROUND: Acute biliary pancreatitis (ABP) is an acute inflammation of the pancreas that can vary in severity, potentially leading to life-threatening complications. Early identification of severe cases is crucial for effective management and improved outcomes. Traditional scoring systems, such as the Acute Physiology and Chronic Health Evaluation II (APACHE II) and Ranson, are commonly used to assess severity but can be complex and time-consuming. This study aims to assess the reliability of the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as accessible biomarkers for predicting ABP severity and to evaluate their relationship with disease severity as determined by the Balthazar grade.

METHODS: This retrospective study analyzed 161 patients diagnosed with acute biliary pancreatitis. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio values were compared with ABP severity as assessed by the Balthazar grade. The correlation between these inflammatory biomarkers and disease severity was examined. The study was approved by the Ümraniye Training and Research Hospital Clinical Research Ethics Committee (approval date: 13.03.2025, approval number: 54) and was conducted in accordance with the Declaration of Helsinki.

RESULTS: Elevated NLR and PLR values were significantly associated with increased ABP severity. Both NLR and PLR demonstrated potential as reliable biomarkers for early risk stratification, particularly in resource-limited settings.

CONCLUSION: NLR and PLR may serve as valuable biomarkers in predicting ABP severity, facilitating early clinical decision-making, particularly in settings where advanced imaging is limited. This study also highlights the clinical relevance of these biomarkers within Türkiye, potentially guiding future updates to pancreatitis management protocols.

Keywords: Acute biliary pancreatitis; neutrophil-to-lymphocyte ratio; platelet-to-lymphocyte ratio; Balthazar grade; biomarkers; severity prediction.

INTRODUCTION

Acute pancreatitis (AP) is an inflammatory condition of the pancreas with variable clinical presentations, ranging from mild to severe cases associated with substantial morbidity and mortality. Early identification of severe cases is critical to guide treatment decisions and improve patient outcomes. Severe cases often result in systemic complications such as sepsis and organ failure.[1]

Several scoring systems, including Ranson's criteria, the Acute Physiology and Chronic Health Evaluation II (APACHE II), and the Balthazar classification, are used to assess AP severity.[2]

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However, these systems are limited by their complexity, need for serial assessments, and reliance on advanced imaging. The Balthazar score was preferred in our study, as it provides an objective radiological assessment of pancreatic and peripancreatic involvement and has been shown to correlate with clinical severity. Thus, identifying simple, accessible, and cost-effective biomarkers for early severity prediction has gained clinical significance.

Inflammatory markers such as C-reactive protein (CRP) are widely used to monitor the severity of acute pancreatitis. Başak et al.[3] demonstrated that combining CRP with Ranson's score improves the accuracy of severity prediction. Additionally, D-dimer, a fibrin degradation product, has been associated with disease severity in both hyperlipidemic and biliary acute pancreatitis.[4,5] Elevated D-dimer levels reflect increased fibrin turnover and are linked to more severe disease.

Recently, the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have gained attention as simple, cost-effective markers of systemic inflammation. Due to their wide availability and low cost, these indices are particularly valuable for early risk stratification in acute pancreatitis.[6-8]

This study aimed to evaluate the reliability of NLR and PLR in predicting the severity of acute biliary pancreatitis (ABP) and to investigate their relationship with Balthazar grades, potentially optimizing early clinical management.

MATERIALS AND METHODS

Study Design and Population

This retrospective study included 161 patients diagnosed with acute biliary pancreatitis who were admitted to our hospital between 2015 and 2024. Patients were identified using electronic medical records. The study was approved by the Ümraniye Training and Research Hospital Clinical Research Ethics Committee (approval date: 13.03.2025, approval number: 54). All procedures were conducted in accordance with the principles of the Declaration of Helsinki.

Data Collection

Demographic data, CRP levels, neutrophil, lymphocyte, and platelet counts, as well as NLR and PLR values at admission and at 48 hours, were recorded. Laboratory data from complete blood count tests were analyzed.

Formulas used:

- NLR=Neutrophil count / Lymphocyte count
- PLR=Platelet count / Lymphocyte count

Radiological assessment was performed using contrast-enhanced computed tomography (CT) scans within 48 hours of admission, and disease severity was classified according to the Balthazar grade. Imaging was interpreted by an experienced abdominal radiologist.

Balthazar Grading:

- A: Normal pancreas
- B: Pancreatic enlargement
- C: Inflammatory changes in the pancreas and peripancreatic fat
- D: Single ill-defined fluid collection
- E: Two or more poorly defined fluid collections or pancreatic necrosis

Statistical Analysis

The Kruskal-Wallis test and One-Way Analysis of Variance (ANOVA) were used for group comparisons. The Pearson chi-square test was used for categorical variables. A p-value <0.05 was considered statistically significant.

RESULTS

Demographic Data

There was no significant difference in mean age between groups (p=0.797), and gender distribution was similar and not statistically significant (p=0.770) (Table 1).

Admission Data

At admission, CRP levels showed significant differences according to Balthazar grade (p=0.010), with higher levels observed in the Balthazar C and D groups. Neutrophil counts were significantly different (p=0.000), peaking in Balthazar E. Lymphocyte counts also differed significantly (p=0.036), with the lowest values in the Balthazar A and E groups. No significant difference was observed in platelet counts (p=0.225). Admission NLR values differed significantly (p=0.002), with the highest values in Balthazar E. PLR values also differed significantly (p=0.044), with the highest value in Balthazar E (238.6) (Table 2, Figs. 1 and 2).

Table 1. Demographic data comparison

Parameter	Balthazar 0	Balthazar 1	Balthazar 2	Balthazar 3	Balthazar 4	p-value
Age (mean±SD)	2.511±3.079	2.576±4.715	3.697±4.715	4.715±3.697	3.079±3.697	0.797
Gender (M/F)	0.575	0.555	0.655	0.555	1.111	0.770535

(M: Male; F: Female; SD: Standard deviation.)

Table 2. Statistical analysis of admission and 48-hour data according to Balthazar classification

Parameter	Balthazar 0	Balthazar 1	Balthazar 2	Balthazar 3	Balthazar 4	Chi-Square/ p-value
Admission CRP (mg/L)	2.3 (6)	7.15 (13)	7.8 (17)	5.15 (12)	7.5 (9)	13.297/0.010
Admission Neutrophil Count (×10³/µL)	7.3 (2.8)	8.7 (4.175)	10 (7.425)	9.55 (4.2)	13.2 (5.2)	30.161/0.000
Admission Lymphocyte Count (×10³/µL)	1.4 (1)	1.3 (0.95)	1.7 (1.15)	1.95 (1.1)	1.3 (0.6)	10.299/0.036
Admission Platelet Count (×10³/µL)	253 (96)	270 (110.3)	280 (135.5)	252.5 (96.5)	275 (104)	5.673/0.225
Admission Neutrophil-to-Lymphocyte Ratio (NLR)	5.1 (4.5)	5.3 (8.1)	6.9 (9.5)	4.75 (3.3)	12.1 (10.4)	16.712/0.002
Admission Platelet-to-Lymphocyte Ratio (PLR)	178 (85)	201.4 (156.8)	185.45 (150.7)	134.3 (90.2)	238.6 (233.9)	9.798/0.044
48-Hour CRP (mg/L)	5.3 (12.6)	35.75 (86.7)	48.85 (132.2)	29.45 (122.3)	32.2 (222.6)	40.224/0.000
48-Hour Neutrophil Count (×10³/µL)	4.8 (3.7)	5.3 (4.4)	8.6 (7.7)	6.85 (4.4)	12.5 (10.4)	34.204/0.000
48-Hour Lymphocyte Count (×10³/µL)	1.7 (1.1)	1.6 (1)	1.6 (1.3)	1.65 (0.7)	1.2 (0.7)	4.390/0.356
48-Hour Platelet Count (×10³/µL)	218 (111)	228.5 (100)	212.5 (92.8)	217 (84.5)	239 (156)	3.133/0.536
48-Hour Neutrophil-to-Lymphocyte Ratio (NLR)	3 (2.9)	3.3 (4.5)	4.9 (6.2)	4.15 (4.4)	9.7 (8.8)	30.314/0.000
48-Hour Platelet-to-Lymphocyte Ratio (PLR)	128.1 (54.9)	137.45 (66.4)	123.15 (104.9)	127 (54.9)	166.9 (169)	4.057/0.398

(CRP: C-reactive protein; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SD: Standard deviation; ×10³/µL: Thousands per microliter.)

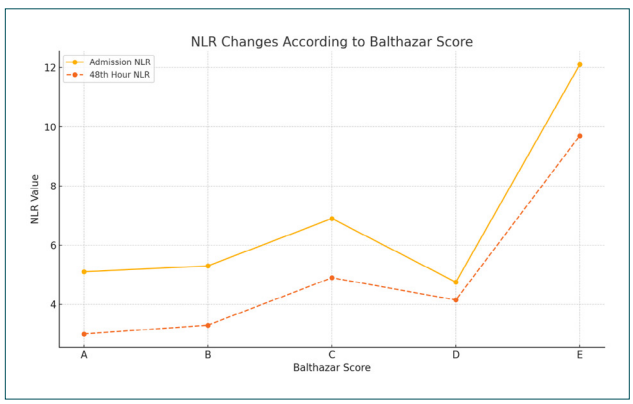

Figure 1. Changes in neutrophil-to-lymphocyte ratio (NLR) according to Balthazar score. *(NLR: Neutrophil-to-lymphocyte ratio.)*

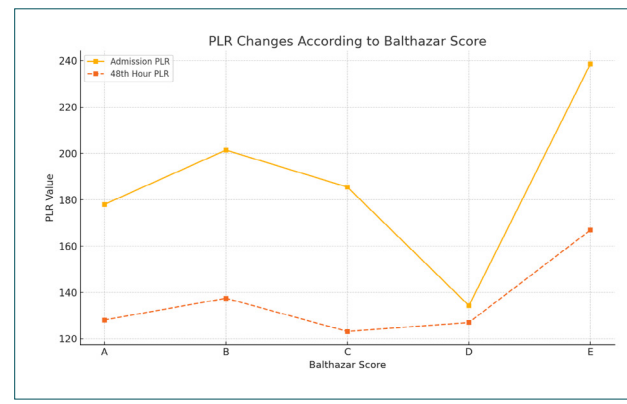

Figure 2. Changes in platelet-to-lymphocyte ratio (PLR) according to Balthazar score. *(PLR: Platelet-to-lymphocyte ratio.)*

48-Hour Data

C-reactive protein levels continued to differ significantly across groups at 48 hours (p=0.000), with the highest levels in the Balthazar C and D groups. Neutrophil counts remained significantly different (p=0.000), again peaking in Balthazar E. Lymphocyte and platelet counts showed no significant differences at 48 hours (p=0.356 and p=0.536, respectively). NLR values differed significantly at 48 hours (p=0.000), with the highest values again observed in Balthazar E. PLR values did not differ significantly at 48 hours (p=0.398) (Table 2, Figs. 1 and 2).

Overall Evaluation

Significant differences were observed in CRP, neutrophil count, NLR, and PLR at both admission and at 48 hours, with particularly elevated values in Balthazar E. No significant differences were noted for lymphocyte or platelet counts. These findings support the predictive value of laboratory markers such as NLR and PLR in assessing the severity of acute biliary pancreatitis.

DISCUSSION

Acute biliary pancreatitis is a potentially life-threatening condition requiring timely diagnosis and management. Imaging-based scoring systems, such as the Balthazar CT Severity Index, are reliable but resource-intensive.[9,10] Therefore, simpler biomarkers like NLR and PLR represent attractive alternatives.

Traditional scoring systems such as Ranson's criteria, APACHE II, and the Bedside Index for Severity in Acute Pancreatitis

(BISAP) require multiple clinical and laboratory parameters, repeated measurements, and, in some cases, advanced imaging, making them time-consuming and less practical in acute settings.[11,12] Although simpler laboratory markers such as C-reactive protein and hematocrit have been studied, their predictive value is limited. For example, CRP levels typically peak 48–72 hours after symptom onset, reducing their utility for very early risk assessment, while hematocrit can be influenced by hydration status and other comorbid conditions.[13] These limitations underline the need for easily accessible, inexpensive, and rapidly measurable markers that can aid in the early stratification of acute biliary pancreatitis severity.

Our findings demonstrate that higher NLR and PLR values are associated with increased ABP severity. Elevated inflammatory parameters corresponded with greater pancreatic and peripancreatic involvement. These results align with previous studies supporting NLR and PLR as markers of systemic inflammation.[14-16]

Advantages of NLR and PLR include cost-effectiveness, wide availability, and the ability to monitor disease progression dynamically. However, limitations include the retrospective design and reliance on imaging for Balthazar grading.[9,17] The routine use of NLR and PLR could facilitate early risk stratification and support timely management decisions in patients with acute biliary pancreatitis, particularly in resource-limited settings.

CONCLUSION

This study highlights the potential role of NLR and PLR as simple, accessible biomarkers for the early prediction of ABP severity. Their routine use could enhance clinical decision-making, especially in settings with limited imaging resources. Further large-scale validation is necessary to fully integrate these markers into clinical practice.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Akut biliyer pankreatit şiddetinin öngörülmesinde Nötrofil/Lenfosit ve Platelet/Lenfosit oranlarının rolü

AMAÇ: Akut biliyer pankreatit (ABP), pankreasın şiddeti değişkenlik gösterebilen akut inflamasyonudur ve potansiyel olarak yaşamı tehdit eden komplikasyonlara yol açabilir. Şiddetli vakaların erken tanımlanması, etkili yönetim ve daha iyi hasta sonuçları için kritik öneme sahiptir. APACHE II ve Ranson gibi geleneksel skorlama sistemleri hastalığın şiddetini değerlendirmede yaygın olarak kullanılmaktadır; ancak bu sistemler karmaşık ve zaman alıcı olabilir. Bu çalışma, nötrofil-lenfosit oranı (NLR) ve platelet-lenfosit oranının (PLR), ABP şiddetini öngörmede erişilebilir biyobelirteçler olarak güvenilirliğini değerlendirmeyi ve bu oranların Balthazar derecesi ile belirlenen hastalık şiddetiyle ilişkisini incelemeyi amaçlamaktadır.

GEREÇ VE YÖNTEM: Bu retrospektif çalışmada, akut biliyer pankreatit (ABP) tanısı alan 161 hasta incelendi. Nötrofil/lenfosit oranı (NLR) ve platelet/lenfosit oranı (PLR) değerleri, Balthazar derecesiyle değerlendirilen ABP şiddeti ile karşılaştırıldı. Bu inflamatuar biyobelirteçler ile hastalık şiddeti arasındaki korelasyon araştırıldı. Çalışma, Ümraniye Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulu tarafından onaylanmış olup (onay tarihi: 13.03.2025, onay numarası: 54), Helsinki Deklarasyonu'na uygun olarak yürütülmüştür.

BULGULAR: Yüksek NLR ve PLR değerleri, artmış ABP şiddeti ile anlamlı şekilde ilişkili bulunmuştur. NLR ve PLR'nin her ikisi de özellikle kaynakların sınırlı olduğu ortamlarda erken risk sınıflandırmasında güvenilir biyobelirteçler olarak potansiyel göstermiştir.

SONUÇ: NLR ve PLR, ABP şiddetinin öngörülmesinde değerli biyobelirteçler olarak işlev görebilir ve özellikle ileri görüntüleme yöntemlerinin sınırlı olduğu durumlarda erken klinik karar verme sürecini kolaylaştırabilir. Bu çalışma, aynı zamanda bu biyobelirteçlerin Türkiye'deki klinik uygulamadaki önemine dikkat çekmekte ve pankreatit yönetim protokollerinin gelecekteki güncellemeleri için yol gösterici olabilir.

Anahtar sözcükler: Akut biliyer pankreatit; Balthazar derecesi; biyobelirteçler; nötrofil/lenfosit oranı; platelet/lenfosit oranı; şiddet öngörüsü.

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ORIGINAL ARTICLE

Prediction of mortality in necrotizing fasciitis: comparative evaluation of established prognostic scores and a novel scoring system in a retrospective cohort

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ABSTRACT

BACKGROUND: Necrotizing fasciitis (NF) is a rare but serious surgical emergency that progresses rapidly, requires urgent operative intervention, and carries a high mortality rate. Current prognostic scoring systems may have limited predictive power for mortality across different patient groups. The aim of this study was to identify clinical, laboratory, and radiological factors associated with mortality in patients with necrotizing fasciitis. In addition, the study aimed to provide a foundation for the development of a practical prognostic scoring system that could support early risk stratification in clinical practice.

METHODS: This retrospective cohort study examined data from 65 patients diagnosed with NF between January 2021 and December 2024. A modified scoring system was created by integrating the Charlson Comorbidity Index and the total body surface area ratio (Samsun Charlson Comorbidity Index, SaCCI). Sarcopenia was assessed using the psoas muscle index. Using receiver operating characteristic (ROC) analysis, the mortality predictive performance of the modified scoring system was calculated and compared with existing systems.

RESULTS: The SaCCI score demonstrated higher prognostic accuracy than existing systems in predicting mortality, achieving the highest discriminatory power with an area under the curve (AUC) of 0.885. Higher SaCCI scores were associated with a significantly increased risk of mortality. Sarcopenia and delayed surgical intervention were also associated with mortality.

CONCLUSION: The SaCCI score shows promise as an effective tool for predicting early mortality risk in patients with necrotizing fasciitis. The validity of this scoring system, which may inform clinical decision-making, should be confirmed by further multicenter studies.

Keywords: Necrotizing fasciitis; prognosis; sarcopenia; body surface area; risk assessment.

INTRODUCTION

Necrotizing fasciitis (NF) is a rapidly progressive, serious, and life-threatening soft tissue infection characterized by widespread necrosis and systemic inflammation of the fascial tissues. It can occur in various body areas, particularly the perineal region, extremities, and abdominal wall. Despite advances in intensive care and surgical techniques, NF is still associated with high mortality rates. Recent studies have reported mortality rates between 20% and 35%.[1,2]

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Various prognostic scoring systems have been developed to support clinical decision-making and risk stratification in Fournier's gangrene (FG), a type of NF. Among the most commonly used are the Fournier's Gangrene Severity Index (FGSI), the Uludağ FGSI (UFGSI), and the Simplified FGSI (SFGSI).[3,4] The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score, originally designed to aid in diagnosis, has also been used to predict mortality in some studies.[5] These scoring systems have only been used in cases of Fournier's gangrene confined to the perineal region. Additionally, several studies have demonstrated limitations of these scoring systems regarding their prognostic performance. For example, two studies reported sensitivity and specificity for the LRINEC score ranging from 27% to 43% and 83% to 93%, respectively, while for the FGSI, these rates were 82% and 58%, respectively.[5,6] Due to their variable prognostic performance, the reliability of existing scores in identifying high-risk patients has been increasingly questioned in recent studies.[5,6]

In recent reviews and meta-analyses, sarcopenia has been significantly associated with mortality, complication rates, and length of hospital stay in necrotizing soft tissue infections, as in many surgical conditions.[7-9] Similarly, the affected total body surface area (TBSA) ratio has been identified as a prognostic variable influencing clinical outcomes and has been associated with mortality, as it quantifies the extent of infection.[10,11] However, these parameters are not systematically included in existing prognostic scoring systems.

In this context, the present study aimed to investigate clinical, laboratory, and radiological factors associated with mortality in patients diagnosed with necrotizing fasciitis who required emergency surgical intervention. In addition to identifying prognostic indicators, we also sought to construct a composite scoring system by integrating the most relevant predictors, with the goal of improving mortality risk stratification in clinical practice. This approach was designed to offer a more practical and tailored alternative to existing models.

MATERIALS AND METHODS

This retrospective cohort study was conducted at a tertiary referral center. The study protocol was reviewed and approved by the Local Ethics Committee (Approval No: GOKAEK 2024/20/13, Date: 20.11.2024). Given the retrospective design and the fact that all procedures were part of routine care, the requirement for informed consent was waived. The study was conducted in accordance with the principles of the Declaration of Helsinki.

A total of 78 patients were initially identified, of whom 13 were excluded due to incomplete clinical or radiological data. The final analysis included 65 patients diagnosed with necrotizing fasciitis. The study period was defined as January 2021 to December 2024. Electronic medical records before 2020 were not reliably accessible, and the year 2020 was excluded due to the potential confounding impact of the Coronavirus Disease 2019 (COVID-19) pandemic on emergency surgical practice. The diagnosis of necrotizing fasciitis was based on clinical suspicion (rapidly progressive soft tissue infection with systemic signs), supported by laboratory findings and imaging studies (computed tomography [CT] and/or magnetic resonance imaging [MRI]), and was definitively confirmed during emergency surgical exploration. Intraoperative findings such as fascial necrosis, grayish "dishwater" fluid, lack of bleeding of the fascia, and easy blunt dissection along tissue planes were considered diagnostic. Histopathological confirmation was obtained in all cases. All patients were started on broad-spectrum empiric antibiotic therapy upon admission, and hemodynamic stabilization was achieved. Surgical debridement was performed in all eligible patients to control infection, and repeat debridements were performed when necessary. Intensive care support was provided to patients requiring intensive care.

Patient demographics (age, gender), comorbidities, clinical findings, laboratory parameters, imaging findings, and treatment details were screened through the hospital automation system and the Turkish Ministry of Health's e-Pulse system and recorded. Patients with incomplete medical records were excluded from the study. Scores were calculated using the Charlson Comorbidity Index, Necrotizing Fasciitis Laboratory Risk Indicator (LRINEC), Fournier Gangrene Severity Index (FGSI), Uludağ FGSI (UFGSI), and Simplified FGSI (SFGSI) scoring systems. Additionally, inflammatory markers such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and lymphocyte-to-CRP ratio (LCR) were assessed.

The affected total body surface area (TBSA) was calculated based on the extent of necrotic tissue identified on contrast-enhanced computed tomography scans. Necrotic areas were manually marked on CT images to calculate the total affected surface area, and this value was then compared to the patient's total body surface area. These measurements were also verified by comparison with the extent of necrosis reported in the operative reports. TBSA was divided into two groups: <3% and ≥3%. This cutoff was determined to be the optimal cutoff value providing the highest balance of sensitivity and specificity for mortality based on receiver operating characteristic (ROC) curve analysis. Psoas muscle area (PMA) was measured on CT images at the level of the third lumbar vertebra, and the psoas muscle index (PMI) was calculated by dividing the patient's height in meters squared.

Parameters found to have a statistically significant relationship with mortality were combined with existing scoring systems to develop modified scoring systems. The performance of the modified scoring systems in predicting mortality was evaluated and compared with the original scores. Each scoring system was combined with the affected total body surface area ratio (<3%: 0 points, ≥3%: 1 point) to create composite indices. The performance of these combinations in predicting mortality was evaluated and compared with the original scores, considering the balance between specificity and sensitivity.

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 28.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize the data. The normality of distribution of continuous variables was assessed using the Shapiro–Wilk test. Normally distributed variables were expressed as mean ± standard deviation (SD), while non-normally distributed variables were expressed as median and range (minimum–maximum). Categorical variables were presented as number and percentage (%). Comparative analyses were performed according to mortality status. Multiple comparison procedures were limited to the categorical variables "etiology" and "site of infection." As no statistically significant differences were found among subgroups, post hoc analyses or correction methods (e.g., Bonferroni) were not applied. This approach was chosen to avoid unnecessary adjustment in the absence of significant findings, in line with standard statistical practice. Comparisons between two independent groups were performed using the Mann–Whitney U test for non-normally distributed data and Student's t-test for normally distributed data. Categorical variables were compared using the Chi-square test or Fisher's exact test, when appropriate. ROC curve analysis was performed to evaluate the prognostic value of various clinical and laboratory parameters in predicting mortality. The area under the curve (AUC), sensitivity, specificity, and optimal cut-off values were calculated for each score. The optimal cut-off value for the Samsun Charlson Comorbidity Index (SaCCI) score and the other scores was determined using ROC curve analysis, and a threshold of ≥3.5 was selected based on the Youden Index. In all statistical analyses, $p<0.05$ was considered significant.

RESULTS

The mean age of the study population was 59.6±13.0 years, and 53.8% of the patients (n=35) were male. The mean age of female patients was 64.8±11.4 years, while this value was 55.1±12.8 years in males (p=0.002). Of all patients, 63.1% (n=41) had diabetes mellitus, and 36.9% (n=24) had hypertension. The mortality rate was 26.8% (n=11) in diabetic patients and 20.8% (n=5) in those without diabetes. There was no significant difference in mortality rates according to the presence of diabetes (p=0.588). The mortality rate in patients with hypertension was 33.3% (n=8) and 19.5% (n=8) in those without hypertension. No significant difference was found between these two groups in terms of mortality (p=0.212). The median duration of hospital stay was 17 days (range: 1-95). While the median length of stay in patients who died was 20.5 days (range: 5-95), it was 15 days (range: 1-58) in survivors (p=0.092). The most common etiological factor was spontaneous onset of the disease (87.7%, n=57). The proportion of postoperative and trauma-related cases was 6.2% (n=4) each. Sixty patients (92.3%) had at least one comorbid disease, while only 7.7% (n=5) had no comorbid disease. The perianal region was the most commonly affected infection site (52.3%, n=34), followed by the lower abdomen (10.8%, n=7), genital area (13.8%, n=9), gluteal region (9.2%, n=6), upper abdomen (4.6%, n=3), upper thigh (6.2%, n=4) and back (3.1%, n=2). The positivity rate in microbiological cultures was 50.8% (n=33). The sepsis rate was 36.9% (n=24). The overall mortality rate was 24.6% (n=16), while the survival rate was 75.4% (n=49) (Table 1).

Table 1. Clinical characteristics of the study population

Variable	N	%
Etiology		
Spontaneous	57	87.7
Postoperative	4	6.2
Trauma	4	6.2
Comorbidities		
Yes	60	92.3
No	5	7.7
Site of Infection		
Genital	9	13.8
Gluteal	6	9.2
Lower abdomen	7	10.8
Perianal	34	52.3
Upper abdomen	3	4.6
Upper back	2	3.1
Upper thigh	4	6.2
Microbiology culture		
Positive	33	50.8
Negative	32	49.2
Sepsis		
Yes	24	36.9
No	41	63.1
Mortality		
Yes	16	24.6
No	49	75.4

Right and left psoas muscle area measurements were found to be significantly lower in deceased patients. The mean right psoas muscle area was 6.0±1.9 cm^2 in deceased patients and 7.7±2.5 cm^2 in survivors (p=0.015). The left psoas muscle area was 5.5±1.9 cm^2 in deceased patients and 7.1±2.6 cm^2 in survivors (p=0.032). Similarly, the total psoas muscle index was found to be significantly lower in deceased patients (434.8±148.6 vs. 524.9±140.2, p=0.031). However, the Charlson Comorbidity Index (median 5 [1-9] vs. 2.5 [0-10], p<0.001), LRINEC score (9 [6-13] vs. 7 [1-11], p=0.001), FGSI score (6 [1-18] vs. 3 [0-15], p=0.003), UFGSI score (8 [4-23] vs. 5 [1-16], p=0.001), and SFGSI score (3.5 [0-10] vs. 2 [0-6], p=0.003) were significantly higher in patients who died compared to survivors (Table 2).

In the total body surface area analysis, 75.0% of patients with

Table 2. Comparison of laboratory and clinical parameters according to mortality

	Mean±SD or Median (Min-Max)		P Value
	Mortality	**No Mortality**	
CRP	260.9±90.5	221.3±113.6	0.209
PMA Right	6.0±1.9	7.7±2.5	0.015*
PMA Left	5.5±1.9	7.1±2.6	0.032*
Total PMI	434.8±148.6	524.9±140.2	0.031*
CCI5 (1-9)	2.5 (0-10)	<0.001*	
LRINEC	9 (6-13)	7 (1-11)	0.001*
FGSI	6 (1-18)	3 (0-15)	0.003*
UFGSI	8 (4-23)	5 (1-16)	0.001*
SFGSI	3.5 (0-10)	2 (0-6)	0.003*
NLR	13.7 (6.0-61.0)	10.2 (2.0-64.2)	0.157
LCR	0.005 (0.001-0.041)	0.006 (0.001-0.073)	0.157
SII	2057 (310-25193)	2334 (982-22177)	0.493
PLR	177.1 (16.0-1376.7)	226.4 (75.8-687.0)	0.185
Categorical Parameters	**n** **%**	**n** **%**	
Sex			
Male	7 43.8	28 57.1	
Female	9 56.3	21 42.9	0.351
Total BSA (%)			
<3	4 25.0	38 77.6	
>3	2 75.0	11 22.4	<0.001*
Sepsis			
Yes	12 75.0	12 24.5	
No	4 25.0	37 75.5	<0.001*
CKD			
Yes	13 81.3	49 100.0	
No	2 18.8	0 0.0	0.013*
Malignancy			
Yes	10 62.5	44 89.8	
No	6 37.5	5 10.2	0.020*

PMI: Psoas muscle index; CCI: Charlson Comorbidity Index; LRINEC: Laboratory Risk Indicator for Necrotizing Fasciitis; FGSI: Fournier's Gangrene Severity Index; UFGSI: Uludag Fournier's Gangrene Severity Index; SFGSI: Simplified Fournier's Gangrene Severity Index; NLR: Neutrophil-to-lymphocyte ratio; LCR: Lymphocyte-to-C-reactive protein ratio; SII: Systemic immune-inflammation index; PLR: Platelet-to-lymphocyte ratio; BSA: Body surface area; CKD: Chronic kidney disease. *Statistically significant at p<0.05.

an involvement rate above 3% died, compared with 22.4% of patients with a TBSA rate below 3% (p<0.001). Furthermore, the incidence of sepsis was significantly higher in patients who died. Sepsis was present in 75.0% of patients who died, compared to 24.5% of surviving patients (p<0.001). Chronic kidney disease (CKD) was also significantly more common in patients who died compared to survivors (81.3% vs. 0.0%, p=0.013). Similarly, the presence of malignancy was significantly associated with mortality. Malignancy was present in 62.5% of patients who died and in 10.2% of survivors (p=0.020) (Table 2).

Among the parameters evaluated, the Charlson Comorbidity Index showed the highest discriminatory power in predicting mortality, with an AUC of 0.794, 81.3% sensitivity, and 66.6% specificity at a cut-off value of 3.5 (p<0.001). The UFGSI score also demonstrated strong predictive performance,

reaching an AUC of 0.768 with 88.0% sensitivity and 63.0% specificity at a cut-off value of 5.5 (p=0.001). The LRINEC score had an AUC of 0.760 at a cut-off value of 7.5, providing 81.3% sensitivity and 54.2% specificity (p=0.002). Similarly, the FGSI (cut-off: 4.5) and SFGSI (cut-off: 1.5) scores were also statistically significant predictors of mortality, with AUCs of 0.746 for FGSI (p=0.003) and 0.742 for SFGSI (p=0.004).

Notably, the PMI score was also significant. However, at a cut-off value of 369, the AUC was 0.682 (p=0.029). This finding indicated an inverse relationship, meaning that lower PMA values were associated with a higher risk of mortality. Although sensitivity was high (87.8%), specificity was quite low (31.3%) (Table 3, Fig. 1).

By integrating the total body surface area involvement ratio into scoring systems, the predictive performance of some parameters was improved. The combination of the Charlson Comorbidity Index and the TBSA score showed the highest discriminatory power in predicting mortality. This combination achieved an AUC of 0.885, with 100.0% sensitivity and 70.3% specificity at a cut-off value of 3.5 (p=0.012). The combination of the LRINEC score and the TBSA score also demonstrated strong predictive ability, achieving an AUC of 0.838 with 100.0% sensitivity and 54.1% specificity at a cut-off value of 7.5 (p=0.028). The combination of the UFGSI and the TBSA score was also significant, with an AUC of 0.795, sensitivity of 93.8%, and specificity of 40.0% at a cut-off value of 4.5 (p<0.001). In contrast, the combination of the FGSI and TBSA score had a moderate AUC of 0.730 but did not reach statistical significance (p=0.135) (Table 4). The dashed line in the graph indicates the baseline representing no discriminatory power (AUC=0.5) (Fig. 2).

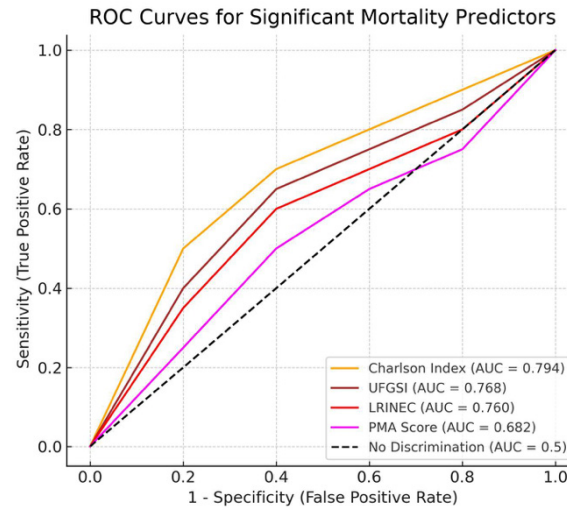

Figure 1. ROC curves of significant mortality predictors (CCI, LRINEC, FGSI, UFGSI, SFGSI, PMI). The dashed line indicates the reference (AUC=0.5).

In our study, a modified prognostic scoring system combining the Charlson Comorbidity Index and the TBSA score was developed and named the Samsun Charlson Comorbidity Index. ROC analysis revealed an AUC of 0.885 for the SaCCI score in predicting mortality (p=0.012). The optimal cut-off value was 3.5, providing high accuracy in predicting mortality with 100% sensitivity and 70.3% specificity. Accordingly, patients with a SaCCI score of ≥3.5 were considered high risk.

DISCUSSION

In this study, a modified prognostic scoring system, the SaC-

Table 3. Receiver operating characteristic (ROC) analysis of potential mortality predictors in patients

Parameter	Value	Sensitivity %	Specificity %	95% CI	AUC/p
CCI	3.5	81.3	66.6	0.672–0.916	0.794/<0.001*
LRINEC	7.5	81.3	54.2	0.637–0.882	0.760/0.002*
FGSI	4.5	75.0	69.0	0.607–0.885	0.746/0.003*
UFGSI	5.5	88.0	63.0	0.644–0.892	0.768/0.001*
SFGSI	1.5	81.3	50.0	0.596–0.888	0.742/0.004*
NLR	17.3	50.0	75.0	0.463–0.779	0.621/0.149
LCR	0.005	43.8	41.7	0.231–0.535	0.383/0.163
SII	2345.6	43.8	50.0	0.244–0.638	0.441/0.485
PLR	229.5	43.8	50.0	0.202–0.569	0.384/0.172
PMI	369	87.8	31.3	0.155–0.472	0.682/0.029
Hemoglobin	10.5	75.0	53.1	0.457–0.760	0.612/0.183
CRP	228	75.0	51.0	0.468–0.772	0.621/0.148

CCI: Charlson Comorbidity Index; PMI: Psoas muscle index; LRINEC: Laboratory Risk Indicator for Necrotizing Fasciitis; FGSI: Fournier's Gangrene Severity Index; UFGSI: Uludag Fournier's Gangrene Severity Index; SFGSI: Simplified Fournier's Gangrene Severity Index; NLR: Neutrophil-to-lymphocyte ratio; LCR: Lymphocyte-to-C-reactive protein ratio; SII: Systemic immune-inflammation index; PLR: Platelet-to-lymphocyte ratio. *Statistically significant at p<0.05.

Table 4. Receiver operating characteristic (ROC) analysis of combined mortality predictors including total body surface area (BSA)

Parameter	Value	Sensitivity %	Specificity %	95% CI	AUC/p
CCI+Total BSA	3.5	100.0	70.3	0.724-0.936	0.885/0.012*
LRINEC+Total BSA	7.5	100.0	54.1	0.716-0.922	0.838/0.028*
FGSI+Total BSA	3.5	75.0	51.4	0.648-0.912	0.730/0.135
UFGSI+Total BSA	4.5	93.8	40.0	0.680-0.911	0.795/<0.001*

CCI: Charlson Comorbidity Index; LRINEC: Laboratory Risk Indicator for Necrotizing Fasciitis; FGSI: Fournier's Gangrene Severity Index; UFGSI: Uludag Fournier's Gangrene Severity Index; BSA: Body surface area. *Statistically significant at p<0.05.

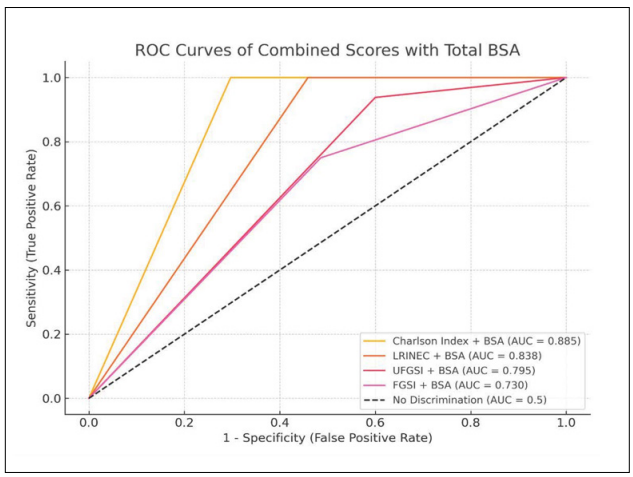

Figure 2. ROC curves of combined predictors including TBSA (CCI+TBSA, LRINEC+TBSA, UFGSI+TBSA, FGSI+TBSA), demonstrating improved discrimination in several combinations.

CI, was developed based on the combination of the Charlson Comorbidity Index and total body surface area to more accurately predict mortality in patients with necrotizing fasciitis, a surgical emergency in which delays in operative management can have fatal consequences. ROC analyses revealed that, with an AUC of 0.885, the SaCCI score demonstrated better prognostic accuracy than other scores.

In recent years, several studies have raised concerns about the limited discriminative power of traditional scoring systems in predicting mortality in necrotizing fasciitis. For example, Tran et al.[12] emphasized the variability in LRINEC performance and highlighted the need for more integrated models. Similarly, Bestari et al.[13] showed that both FGSI and quick Sequential Organ Failure Assessment (qSOFA) had moderate prognostic value in Fournier's gangrene. These findings support the rationale for developing composite tools such as the SaCCI that incorporate comorbidities and anatomical extent.

Among these traditional scoring systems, the LRINEC score, introduced by Wong et al.,[14] remains one of the most widely used tools for diagnosing and stratifying NF. However, subsequent studies have suggested that the prognostic validity of the LRINEC may be limited, particularly in heterogeneous patient groups.[6] Conversely, some studies have reported that high-risk patients can be better identified when the LRINEC score is ≥7.[15] Similarly, other scoring systems such as the FGSI, UFGSI, and SFGSI have also been used, particularly in Fournier's gangrene, which involves the perineal region in NF, and significant differences in their performance have been observed.[4] In the present study, the AUC values of these systems ranged from 0.742 to 0.768, and the SaCCI score appeared to perform better than all of these scores.

The impact of the TBSA parameter on the performance of the SaCCI score is noteworthy. In the literature, Morais et al.[10] reported a significant increase in mortality rates in patients with an affected body surface area ratio of more than 3.25%. The same study also emphasized that the combination of LRINEC and TBSA significantly increased its predictive power. The SaCCI score is one of the few systems in which this parameter is integrated into clinical scoring.

In the present study, mortality was also associated with clinical factors such as sarcopenia, age, and timing of surgery. Sarcopenia, particularly when assessed using the psoas muscle index, was associated with an increased risk of mortality in necrotizing soft tissue infections. Castillo-Angeles et al.[7] reported that sarcopenia significantly increased mortality in this patient group. In our study, PMI was found to be significantly lower in patients who died. Although sarcopenia showed a statistically significant association with mortality, it was not included in the SaCCI score for several reasons. First, the measurement of sarcopenia using the psoas muscle index requires radiological analysis and manual tracing on CT images, which limits its routine applicability in emergency settings. Second, in our ROC analyses, sarcopenia did not demonstrate sufficient discriminative power to enhance the performance of the composite model. Therefore, it was deliberately excluded in favor of a more pragmatic scoring tool that could be applied universally without reliance on imaging-based muscle metrics.

Multicenter analyses have also demonstrated that easily accessible demographic parameters such as age have a strong impact on mortality. For example, a study by Gebran et al.[16] reported a 3.36-fold increased risk of mortality in individuals aged 80 years and older. Furthermore, a study by Jabbour

et al.[2] identified age as an independent prognostic factor in necrotizing soft tissue infections. As the Charlson Comorbidity Index reflects age-related comorbidity burden, the SaCCI score indirectly represents this effect.

In addition to its predictive performance, the SaCCI score offers several practical advantages in clinical application. It is calculated using only two parameters that are routinely available during the initial evaluation: the Charlson Comorbidity Index and the total body surface area affected. These values require no laboratory testing, advanced imaging, or special software, making the SaCCI both time-efficient and cost-effective. Its simplicity enables rapid bedside calculation, which is particularly beneficial in high-acuity emergency settings where early risk stratification is crucial.

This is especially relevant considering that the timing of surgical intervention is another critical factor influencing mortality. Systematic reviews have shown that debriding infected tissue within the first six hours can reduce mortality by up to 19%, whereas surgical delays can increase this rate by as much as 32%.[17,18] We believe that the SaCCI score, along with other established scoring systems, can contribute to the early identification of patients requiring urgent intervention.

Strengths and Limitations

This study has several limitations. First, its single-center, retrospective design may introduce selection bias and limit generalizability. Second, 13 of 78 patients (16.6%) were excluded due to missing data, which may affect the representativeness of the cohort. Third, the relatively small sample size (n=65) and low number of mortality events (n=16) reduce the power of subgroup analyses.

Additionally, TBSA assessment, although supported by intraoperative findings, may still carry interobserver variability. Prior studies have noted that common TBSA calculation methods often overlook individual differences such as age, sex, and body composition.[19] Finally, although sarcopenia was statistically associated with mortality, it was not included in the SaCCI score due to its limited practicality and insufficient contribution to model performance.

Nonetheless, this study also presents important strengths. To our knowledge, it is one of the few studies to propose a modified scoring system that combines both comorbidity burden and anatomical disease extent in necrotizing fasciitis. The SaCCI score uses only two routinely obtainable clinical parameters and demonstrated superior predictive performance compared to existing models. The incorporation of intraoperative findings to assess TBSA may also increase real-world applicability. Future multicenter prospective studies with larger cohorts are needed to validate these results and assess clinical utility in diverse settings.

CONCLUSION

The Samsun Charlson Comorbidity Index, a modified scoring system based on the Charlson Comorbidity Index (CCI) developed to predict mortality in necrotizing soft tissue infections requiring emergency surgery, demonstrated stronger predictive performance compared to existing systems. The cut-off value of 3.5, in particular, stood out as a significant threshold that allows for early identification of high-risk patients. By enabling rapid recognition of patients in need of urgent operative intervention, SaCCI could support timely surgical decision-making in emergency settings. Prospective validation of this scoring system, which has high applicability in clinical decision-support processes, through multicenter, large-sample studies is crucial for its integration into clinical practice.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Nekrotizan fasiitte mortalite öngörüsü: Mevcut prognostik skorların ve yeni bir skorlama sisteminin retrospektif kohortta karşılaştırmalı değerlendirmesi

AMAÇ: Nekrotizan fasiit (NF), hızlı ilerleyen, acil cerrahi müdahale gerektiren ve yüksek mortalite riski taşıyan nadir fakat ciddi bir cerrahi acildir. Mevcut prognostik skorlama sistemleri, farklı hasta gruplarında mortaliteyi öngörmede sınırlı kalabilmektedir. Bu çalışmanın amacı, nekrotizan fasiitli hastalarda mortalite ile ilişkili klinik, laboratuvar ve radyolojik faktörleri belirlemekti. Ayrıca, elde edilen bulgular doğrultusunda, klinik uygulamalarda erken risk sınıflamasına katkı sağlayabilecek pratik bir prognostik skorlama sistemi geliştirilmesine temel oluşturmak hedeflenmiştir.

GEREÇ VE YÖNTEM: Bu retrospektif kohort çalışmada, Ocak 2021 ile Aralık 2024 arasında, NF tanısı alan 65 hastanın verileri incelenmiştir. Charlson Komorbidite İndeksi ile total vücut yüzey alanı oranı entegre edilerek modifiye bir skorlama sistemi (Samsun Charlson Komorbidite İndeksi – SaCCI) oluşturulmuştur. Sarkopeni, psoas kas indeksi (PMI) ile değerlendirilmiştir. ROC analizi kullanılarak mortaliteyi öngörme performansı hesaplanmış ve mevcut skorlarla karşılaştırılmıştır.

BULGULAR: SaCCI skoru, mortaliteyi öngörmede mevcut sistemlere kıyasla daha yüksek prognostik doğruluk göstermiştir. ROC analizinde en yüksek ayırt edici güce ulaşarak AUC değeri 0.885 bulunmuştur. Yüksek SaCCI skorları, anlamlı şekilde artmış mortalite riski ile ilişkilendirilmiştir. Ayrıca sarkopeni ve gecikmiş cerrahi müdahale de mortalite ile ilişkili bulunmuştur.

SONUÇ: SaCCI skoru, nekrotizan fasiitli hastalarda mortalite riskini erken öngörmede etkili bir araç olma potansiyeli taşımaktadır. Klinik karar süreçlerine katkı sağlayabilecek bu skorlama sisteminin geçerliliği, çok merkezli ileri çalışmalarla teyit edilmelidir.

Anahtar sözcükler: Nekrotizan fasiit; prognostik değerlendirme; risk sınıflaması; sarkopeni; vücut yüzey alanı.

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ORIGINAL ARTICLE

Impact of traumatic lens injury on visual and anatomical prognosis following open globe injuries: an analysis from a tertiary trauma referral center

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ABSTRACT

BACKGROUND: This study aims to evaluate the impact of traumatic lens injury on visual and anatomical prognosis in open globe injuries (OGI).

METHODS: The medical charts of patients with OGIs treated at a tertiary ocular trauma referral center between November 2016 and January 2025 were retrospectively reviewed. Patients were categorized into two groups: those with lens injury (LI) and those without lens injury (NLI). Primary outcome measures were final best-corrected visual acuity (BCVA), functional visual success (BCVA ≥ 0.1 [decimal]), and globe survival. Multivariate logistic regression analyses were utilized to model independent predictors of functional visual success and globe survival. Predictor variables were selected based on clinical relevance and prior trauma literature: lens injury, Zone 3 involvement, injury type, number of surgeries, and initial retinal detachment.

RESULTS: A total of 98 eyes were included in the study; 73 eyes had LI, while 25 eyes did not. Eyes with LI had significantly poorer initial BCVA (mean logMAR 2.33 vs. 1.76; p=0.003) and more frequently sustained Zone I injuries (p<0.001). Final BCVA (logMAR 1.62 vs. 1.00; p=0.022), functional visual success (23.3% vs. 60.0%; p=0.002), and globe survival (63.0% vs. 88.0%; p=0.037) were all significantly lower in the LI group. In the multivariable analysis, lens injury independently reduced the likelihood of functional visual success (adjusted OR 0.40; 95% CI 0.11–0.81; p=0.019), whereas it was not an independent determinant of globe survival. The presence of initial retinal detachment was the strongest adverse factor for both functional visual success (adjusted OR 0.07; 95% CI 0.02-0.44; p<0.001) and globe survival (adjusted OR 0.13; 95% CI 0.04–0.40; p<0.001).

CONCLUSION: Traumatic lens injury independently predicts poorer functional visual success following OGIs. Retinal detachment at presentation remains the most influential determinant of both visual and anatomical prognosis and holds critical importance in trauma management. Incorporation of lens injury into ocular trauma prognostic scoring systems may improve their predictive accuracy.

Keywords: Globe survival; lensectomy; lens injury; open globe injury; traumatic cataract; visual prognosis.

INTRODUCTION

Ocular trauma remains one of the leading causes of visual loss and, in severe cases, irreversible globe loss worldwide.[1] The standardization of terminology in ocular trauma is crucial for accurate communication, effective counseling patients and families, reliable comparison of studies, and the development of prognostic models. Since 1996, the Birmingham Eye Trauma Terminology (BETT) has become the most widely accepted classification scheme in both clinical and research ocular trauma settings.[2] Within this classification, open globe injury (OGI) represents a severe yet relatively uncommon subset of ocular trauma, with approximately 203,000 cases reported globally each year.[3]

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The Ocular Trauma Score (OTS) system proposed by Kuhn et al.[4] has become the most widely utilized prognostic tool to assess the visual prognosis following OGI. The OTS is based on initial visual acuity and the presence of globe rupture, endophthalmitis, perforating injury, retinal detachment (RD), and relative afferent pupillary defect (RAPD). Despite being documented in 32–52% of OGI cases, lens injury has not been formally included among these parameters.[5,6]

Lens involvement in OGI may manifest as traumatic cataract with or without capsular rupture, as well as lens subluxation or lens luxation (traumatic aphakia).[7,8] These changes are frequently associated with secondary complications, including phacoanaphylaxis, increased susceptibility to infection, corneal decompensation, and increased intraocular pressure (IOP), all of which necessitate additional surgical interventions."[9,10] In this context, clarifying the prognostic role of lens injury is clinically relevant, given its potential to further compromise visual outcomes.

Although the impact of lens injury on visual prognosis after OGI has been researched in multiple studies, the reported results remain heterogeneous. Some studies reported that lens damage adversely affects visual outcomes, often due to cataract formation or subsequent aphakia.[11-13] In contrast, other studies suggest that lens injury does not independently compromise visual prognosis, particularly when timely and appropriate surgical management is provided.[14,15] Moreover, in cases with traumatic cataract, the timing of cataract extraction was not consistently associated with final visual acuity.[14,16]

Given these contradictory findings, further research is warranted to clarify whether traumatic lens injury carries independent prognostic value beyond established parameters such as OTS. Therefore, this study aims to evaluate the impact of traumatic lens injury on visual and anatomical outcomes in patients with OGI treated at a major tertiary ocular trauma referral center in Türkiye.

MATERIALS AND METHODS

Study Design and Population

This retrospective study was approved by the local institutional review and ethics board (IRB #2024-577). The study adhered to the principles of the Declaration of Helsinki. Medical charts of all consecutive patients with OGI who were treated at a tertiary ocular trauma referral center between November 2016 and January 2025 were reviewed. Patients with missing medical records; those with pre-existing or trauma-related macular or optic disc pathology that could affect visual acuity; those with a history of prior cataract surgery in the injured eye; those who presented with end-stage ocular conditions that precluded further treatment (e.g., phthisis bulbi); and those with a follow-up period of <6 months were excluded from the analysis.

Clinical Evaluation and Surgical Management

Except for three individuals, almost all patients had received primary globe repair before being referred to our center. All patients subsequently underwent comprehensive ophthalmic evaluations both before and after surgery, including visual acuity, IOP, slit lamp and fundus examination, supplemented by ocular ultrasonography and computed tomography of the orbits. The ocular injuries were categorized using the BETT system.[17] The OTS was calculated according to the methodology proposed by Kuhn et al.[4]

As a tertiary ocular trauma referral center, most cases required one or more secondary surgical procedures, including vitrectomy procedures, intraocular foreign body (IOFB) removal, and lensectomy when indicated. Primary or secondary intraocular lens (IOL) implantation was determined by capsular integrity and the extent of ocular tissue damage.

Outcome Measures

Patient demographic and clinical information were obtained from patient medical records and included age, sex, laterality, injury type (mechanism), cause of injury, zone of injury, lens injury status, associated ocular findings at initial exam (endophthalmitis and RD), time to second surgery, time to lensectomy (in eyes with lens injury), IOL implantation timing and method, number of surgeries, best-corrected visual acuity (BCVA) at initial and last follow-up, development of secondary glaucoma, functional visual success, and globe survival.

Patients were categorized into lens injury (LI) and no lens injury (NLI) groups. As primary outcomes, BCVA at last follow-up, functional visual success, and globe survival were compared between LI and NLI groups. Secondary outcomes were time to second surgery, number of surgeries, and secondary glaucoma rate.

Lens injury was defined as any traumatic structural disruption of the lens capsule, zonules, or nucleus, including traumatic cataract, lens subluxation, or lens luxation (traumatic aphakia). Best-corrected visual acuity values were expressed in logarithm of the minimum angle of resolution (logMAR) notation, as described by Ferris et al.[18] Hand movements (HM) and counting fingers (CF) vision were assigned logMAR values of 3.0 and 2.0, respectively, according to the method proposed by Holladay.[19] In this study, light perception (LP) was given a logMAR value of 4.0,[20] whereas no light perception (NLP) was not assigned a logMAR value. Functional visual success was defined as final BCVA ≥ 0.1 (decimal). This threshold corresponds to ambulatory vision and exceeds the legal definition of blindness widely used in the United States, in which visual acuity of ≤ 20/200 (approximately decimal 0.1) in the better-seeing eye constitutes legal blindness.[21] The cutoff is also consistent with the World Health Organization (WHO) classification of visual impairment, where vision worse than 20/200 is categorized as severe visual impairment.[22] Globe survival was defined as complete retinal attachment, intraocular pressure above 6 mmHg, and BCVA of LP

or better at final follow-up.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows (Version 21.0; IBM Corp., Armonk, NY, USA). A p-value of <0.05 was considered statistically significant. Continuous variables were assessed for normality using the Shapiro–Wilk test and are presented as mean ± standard deviation (SD) and median with interquartile range (IQR). Comparisons between LI and NLI groups were performed using the Mann–Whitney U test due to the non-normal distribution of most continuous variables. Categorical variables are presented as numbers (n) and percentages (%). Group comparisons were carried out using the Chi-square test or Fisher's exact test when expected cell counts were <5.

Multivariate logistic regression analyses were utilized to model independent predictors of functional visual success and globe survival. Predictor variables were selected based on clinical relevance and prior trauma literature: lens injury, Zone 3 involvement, injury type, number of surgeries, and initial RD. Effect estimates were expressed as odds ratios (ORs) with 95% confidence intervals (CIs).

RESULTS

A total of 217 patients with OGIs were identified during the study period, and 98 eyes from 84 patients met the inclusion criteria. Of these, 73 eyes (74.5%) had lens injury and 25 eyes (25.5%) had no lens injury.

Baseline Characteristics

Demographics, injury characteristics, and associated clinical findings in eyes with and without lens injury are presented in Table 1. The two groups were comparable with respect to age (median, 30 vs. 26 years; p=0.769) and sex distribution (male proportion, 95.9% vs. 96.0%; p=1.000). The distribu-

Table 1. Demographics, injury characteristics, and associated clinical findings in eyes with and without lens injury

Variable	Lens injury (n=73)	No lens injury (n=25)	p value
Age (years)	31.8±15.3; 30 [17]	30.0±10.5; 26 [11]	0.769
Sex (#males, %)	70 (95.9%)	24 (96.0%)	1.000
Injury type			
Rupture	7 (9.6%)	1 (4.0%)	0.339
Penetrating	30 (41.1%)	11 (44.0%)	
IOFB	23 (31.5%)	5 (20.0%)	
Perforating	13 (17.8%)	8 (32.0%)	
Cause of injury			
Deadly weapon-related	26 (35.6%)	7 (28.0%)	0.319
Sharp-object injury	22 (30.1%)	10 (40.0%)	
Domestic accident	13 (17.8%)	13 (17.8%)	
Blunt trauma	12 (16.4%)	12 (16.4%)	
Zone of injury			
Zone 1	50 (68.5%)	6 (24.0%)	<0.001
Zone 2	17 (23.3%)	4 (16.0%)	
Zone 3	0 (0%)	11 (44.0%)	
Zone 2 and 3	6 (8.2%)	11 (44.0%)	
Endopthalmitis	0 (%)	0 (%)	-
Initial RD	34 (46.6%)	14 (56.0%)	0.457
OTS	60.9±14.6; 59 [23]	68.6±15.9; 76 [24]	0.040
OTS category			
Category 1	11 (15.1%)	0 (0%)	0.066
Category 2	28 (38.4%)	9 (36.0%)	
Category 3	32 (43.8%)	13 (52.0%)	
Category 4	2 (2.7%)	3 (12.0%)	
Initial BCVA (LogMAR)	2.33±0.63; 2.0 [1.0]	1.76 ± 0.84; 2.0 [1.08]	0.003

BCVA: Best corrected visual acuity, IOFB: Intraocular foreign body, OTS: Ocular trauma score, RD: Retinal detachment. Values are presented as mean ± standard deviation; median [interquartile range] for continuous variables, and n (%) for categorical variables. p-values obtained using the Mann–Whitney U test (continuous variables) or Chi-square /Fisher's exact test (categorical variables).

Table 2. Surgical procedures, visual and anatomical outcomes in eyes with and without lens injury

Variable	Lens injury (n=73)	No lens injury (n=25)	p value
Time to secondary surgery (days)	23.2±24.8; 14 [20]	21.4±18.4; 17.5 [11.5]	0.709
Time to lensectomy (days)	27.0±34.2; 14 [21]	N/A	-
Total number of surgeries	3.21±1.67; 3 [2]	2.68±1.11; 2 [2]	0.202
Follow-up, months	37.8±25.3; 32 [38]	35.9±20.1; 37 [26]	0.922
Secondary glaucoma	9/73 (12.3%)	3/25 (12.0%)	1.000
Final BCVA (LogMAR)	1.62±1.04; 2.0 [1.60]	1.00±1.10; 0.30 [1.90]	0.022
Functional visual success	17/73 (23.3%)	15/25 (60.0%)	0.002
Globe survival	46/73 (63.0%)	22/25 (88.0%)	0.037

BCVA: Best corrected visual acuity. Values are presented as mean ± standard deviation; median [interquartile range] for continuous variables, and n (%) for categorical variables. p-values obtained using the Mann–Whitney U test (continuous variables) or Chi-square /Fisher's exact test (categorical variables).

tion of injury type (globe rupture, penetrating injury, IOFB, perforating injury) and the cause of trauma did not differ significantly between the groups. Injury zone differed significantly between groups, with Zone 1 injuries more common in the LI group (68.5%), while Zone 3 and combined Zone 2/3 injuries were more frequent in the NLI group (p<0.001). Endophthalmitis at presentation was not identified in either group. Initial RD rates were similar (46.6% vs. 56.0%; p = 0.457). OTS scores were significantly higher in the NLI group (mean 68.6±15.9) than in the LI group (mean 60.9±14.6), indicating less severe injury in eyes without lens involvement. Initial BCVA was significantly worse in the LI group (mean logMAR 2.33 vs. 1.76; p=0.003).

Lens Injury Characteristics and Surgical Management

Among the 73 eyes with lens injury, traumatic cataract was noted in 42 eyes (57.5%), lens subluxation in 12 eyes (16.4%), and lens luxation (traumatic aphakia) in 19 eyes (26.1%). Lensectomy varied according to the extent and morphology of the lens damage. Lensectomy was performed in the majority of eyes (50 eyes, 92.6%) with a median of 15 days after primary globe repair, whereas in 4 eyes the procedure was conducted concurrently with primary globe repair.

Of the eyes with lens injury, 49 (67.1%) received IOL implantation, while 24 eyes (32.9%) were left aphakic. Among those who underwent IOL implantation, 29 eyes (59.2%) received the IOL during the lensectomy procedure, whereas 20 eyes (40.8%) underwent secondary implantation. In terms of fixation techniques, 20 eyes (40.8%) had in-the-bag IOL placement, 17 eyes (34.7%) required scleral fixation, and 12 eyes (24.5%) received a sulcus-placed IOL.

Visual and Anatomical Outcomes

Surgical procedures, visual and anatomical outcomes in eyes with and without lens injury are summarized in Table 2. The median follow-up duration was 32 months (range: 6–85 months) in the LI group and 37 months (range: 10–80 months) in the NLI group. Regarding surgical variables, time to secondary surgery, total number of surgeries, and follow-up duration did not differ significantly between groups. Eyes without lens injury achieved significantly better final BCVA (mean logMAR 1.00 vs. 1.62; p=0.022) and significantly higher rates of functional visual success, defined as final decimal VA ≥0.1 (60.0% vs. 23.3%; p=0.002). Secondary glaucoma rates did not differ between groups. Globe survival, defined as retinal attachment with IOP > 6 mmHg and LP vision or better, was significantly higher in the NLI group (88.0% vs. 63.0%; p=0.037).

Multivariate Analysis

Multivariate logistic regression analyses were performed to identify independent predictors of functional visual success and globe survival after OGI (Table 3). Forest plot representations of the multivariate models are provided in Figure 1. Independent predictors included lens injury, Zone 3 involvement, injury type, number of surgeries, and initial RD. In the model for functional visual success, initial RD had the strongest negative impact on visual outcomes (adjusted OR 0.07; 95% CI 0.02-0.44; p<0.001). Lens injury (adjusted OR 0.40; 95% CI 0.11-0.81; p=0.019) and a higher number of surgeries (adjusted OR 0.53; 95% CI 0.31–0.91; p=0.022) were also independently associated with reduced functional visual success.

In the model for globe survival, initial RD remained the dominant independent predictor of globe survival (adjusted OR 0.13; 95% CI 0.04-0.40; p<0.001). Injury type also demonstrated a significant association with globe survival (adjusted OR 1.86; 95% CI 1.04–3.32; p=0.035), with rupture and perforating injuries showing poorer anatomical prognosis. A higher number of surgeries showed a modest but statistically significant association with poorer globe survival (adjusted OR 1.58; 95% CI 1.04–2.40; p=0.030). However, lens injury

Table 3. Multivariate logistic regression analysis of functional visual success and globe survival after open globe injury.

	Functional visual success			Globe survival		
Predictor	**Adjusted OR**	**95% CI**	**p value**	**Adjusted OR**	**95% CI**	**p value**
Lens injury	0.40	0.11-0.81	0.019	0.24	0.06-1.01	0.050
Zone 3 (vs Zone I-2)	1.41	0.26-5.33	0.620	1.23	0.08-17.91	0.881
Injury type	1.03	0.35-1.87	0.617	1.86	1.04-3.32	0.035
Number of surgeries	0.53	0.31-0.91	0.022	1.58	1.04-2.40	0.030
Initial RD	0.07	0.02-0.44	<0.001	0.13	0.04-0.40	<0.001

BCVA: Best corrected visual acuity; CI: Confidence interval; IOFB: Intraoculer foreign body; OR: Odd ratio; OTS: Ocular trauma score; RD: Retinal detachment.

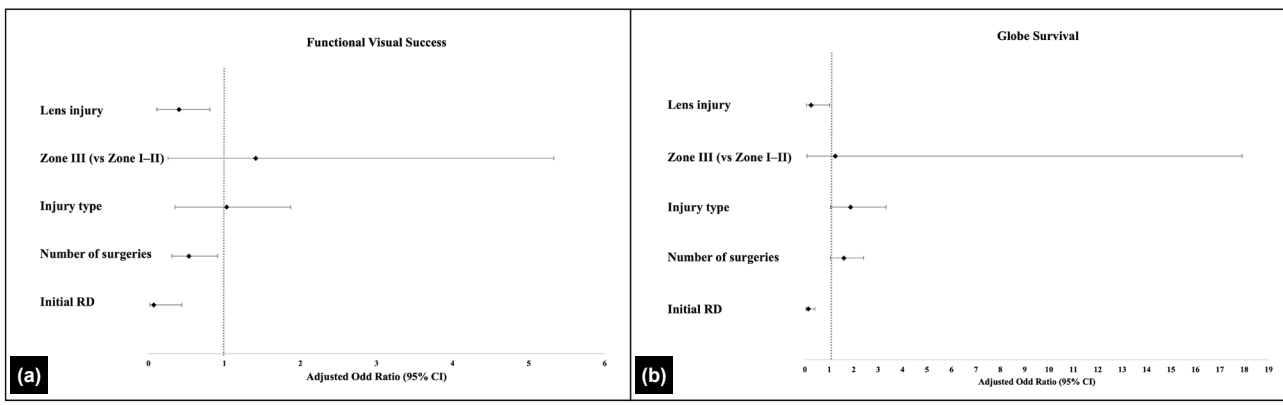

Figure 1. Forest plots showing adjusted odds ratios (ORs) for predictors of **(a)** functional visual success and (**b)** globe survival after open globe injury. Lens injury, initial retinal detachment, and the number of surgeries significantly influenced functional outcomes, while globe survival was primarily determined by initial retinal detachment, injury type, and surgical burden. Error bars indicate 95% confidence intervals.

demonstrated a borderline association (adjusted OR 0.24; 95% CI 0.06–1.01; p=0.051).

DISCUSSION

The present study evaluates the prognostic role of traumatic lens injury in OGI by comparing demographic features, surgical approaches, and visual and anatomical outcomes. Our findings indicate a distinct divergence between functional visual recovery and anatomical globe survival, revealing that lens involvement is associated with poorer functional outcomes, but it does not independently determine anatomical prognosis after adjusting for injury severity markers.

The high rate of lens injury observed in our cohort (74.5%) lies within the higher spectrum of rates reported by major tertiary ocular trauma referral centers, where lens involvement has been documented in approximately 32% to 52% of OGIs.[5,6] Studies focusing on referral populations and high-energy trauma mechanisms have reported particularly elevated rates of lens damage, reflecting greater injury severity. As a tertiary referral center, our institution predominantly manages complex cases following primary globe repair, which likely contributes to the higher prevalence of lens injury observed in this study.

In line with our results, multiple studies have demonstrated that traumatic lens injury is associated with worse visual outcomes.[8,13,23-25] Chou et al.[8] reported that eyes with lens involvement at Zone 1–2 OGIs had significantly poorer final BCVA (median logMAR of 2.3 in the LI group compared to 1.3 in the NLI group) and a substantially higher rate of endophthalmitis, reflecting the additive inflammatory and infectious risks associated with capsule violation. In combat-related ocular trauma, Smith et al.[24] showed that lens damage, especially when caused by improvised explosive devices, commonly coexisted with severe corneal and retinal pathologies and contributed to reduced visual recovery. Likewise, in a univariate analysis of preoperative factors, Agrawal et al.[25] identified traumatic cataract as a marker of poor visual prognosis in Zone 3 injuries. Although these studies evaluated different injury subsets (focusing exclusively on Zone 1–2 or Zone 3 involvement), our findings suggest that lens injury

constitutes a significant functional burden in OGI regardless of injury zone.

Conversely, some studies have questioned whether lens injury independently predicts visual outcomes when accounting for overall trauma severity. Rodrigues et al.,[14] analyzing 102 OGI cases with and without lens damage, found that traumatic cataract was associated with poor visual outcomes but did not remain a significant predictor in multivariate analysis once RD, scleral laceration, and hyphema were included. In contrast, a previous study conducted at our ocular trauma referral center showed that, in addition to initial visual acuity (OR: 8.7) and the OTS category (OR: 5.7), the zone of injury (OR: 3.0), the need for additional surgeries (OR: 2.8), and initial lens damage (OR: 1.6) were associated with poorer visual outcomes in OGI.[13] Our current analysis, by directly comparing LI and NLI eyes within a homogeneous OGI population and modeling initial RD as an independent predictor, was able to isolate the functional impact of lens injury and demonstrate its independent prognostic contribution. These findings suggest that lens injury meaningfully influences visual outcome when posterior severity is adequately accounted for, rather than being overshadowed by it.

Another key finding of our analysis is the consistently dominant role of initial RD as an adverse prognostic factor for functional and anatomical results. In agreement with our study, Chou et al.[8] demonstrated that the presence of RD with lens injury at presentation dramatically worsened final visual outcomes in Zone 1–2 OGIs. Similarly, Rodrigues et al.[14] identified RD as the strongest independent predictor of poor final visual acuity in their OGI cohort. A military trauma cohort had comparable results, with RD present in 39.3% of cases and serving as a principal determinant of severe visual impairment and structural loss. Our results confirm this universal pattern, showing that initial RD is by far the most influential determinant of both functional visual success (OR: 0.07) and anatomical globe survival (OR: 0.13).

Interestingly, although Zone 3 injuries have consistently been associated with poor outcomes in OGI across several large studies,[13,23,26] Zone 3 involvement did not independently predict either functional visual success or globe survival in our multivariate model. Several explanations can account for this: (1) Zone 3 injuries were relatively infrequent in our sample; (2) their adverse impact may have been fully mediated through RD, which was modeled explicitly; and (3) logistic regression can exhibit quasi-separation when the number of Zone 3 cases is small. Thus, our findings should not be interpreted as conflicting with prior evidence but rather as reflecting dataset characteristics and the statistical dominance of RD as a posterior segment predictor.

In our study, the number of surgeries emerged as a significant independent predictor of both worse visual and anatomical outcomes. Consistent with the prognostic analysis by Guven et al.,[13] eyes requiring repeated interventions tend to represent more severe or complicated trauma patterns and achieve inferior visual outcomes.[27] Since the total number of surgeries did not differ significantly between LI and NLI groups in our dataset, our results reinforce the view that surgical burden serves as a surrogate for underlying trauma severity and postoperative complications.

Existing literature on IOL implantation timing and technique supports that surgical details themselves are not independent determinants of visual prognosis in traumatic cataract. Rumelt and Rehany found comparable visual recovery regardless of whether IOL implantation was performed primarily or secondarily.[28] Similarly, Chou et al.[8] demonstrated that secondary IOL implantation, regardless of IOL location, yielded functional outcomes equivalent to those of primary procedures. In our cohort, various IOL implantation timings and fixation techniques, including in-the-bag, sulcus, and scleral fixation, were used among eyes with lens injury; however, the study was not designed to statistically evaluate whether these different approaches influenced final BCVA. Therefore, no conclusions regarding the prognostic relevance of IOL timing or implantation site can be drawn from the present data.

The strengths of this study include a relatively large single-center cohort, the use of standardized injury classification systems, including BETT and OTS, together with a consistent surgical approach that reflects real-world trauma care. In addition, the use of multivariate models allowed us to distinguish functional from anatomical predictors, an approach not commonly undertaken in prior OGI studies.

Several limitations should also be acknowledged. The retrospective design and the limited number of Zone 3 injuries may have reduced statistical power in subgroup analyses. As a tertiary trauma referral center, our cohort may also be subject to referral bias.

CONCLUSION

In conclusion, traumatic lens injury is associated with poorer functional visual recovery after OGIs, while anatomical globe survival is determined predominantly by posterior segment pathology-particularly RD-and injury mechanism rather than lens status. This distinction underscores the need to consider functional and anatomical prognostic pathways separately in OGI. Lens injury may therefore be more appropriately viewed as a marker of functional prognosis and could be considered in future refinements of OTS-based assessment systems. Such an approach may aid clinical decision-making and patient counseling, particularly in complex trauma settings.

Ethics Committee Approval: This study was approved by the Health Sciences University Gülhane Sientific Researches Ethics Committee (Date: 10.12.2024, Decision No: 2024-577).

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Design: Y.S.Y., H.G., A.H.D.; Supervision: Y.S.Y., H.G., A.H.D.; Resource: Y.S.Y., H.G., A.H.D.; Materials: A.H.D.; Data collection and/or processing: Y.S.Y., H.G.; Analysis and/or interpretation: Y.S.Y., H.G., A.H.D.; Literature review: Y.S.Y., H.G.; Writing: Y.S.Y., H.G., A.H.D.; Critical review: A.H.D.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Travmatik lens hasarının açık göz yaralanmalarında görsel ve anatomik prognoza etkisi: Üçüncü basamak travma sevk merkezinden bir analiz

AMAÇ: Bu çalışmada açık göz yaralanmalarında (AGY) travmatik lens hasarının görsel ve anatomik sonuçlar üzerindeki etkisinin değerlendirilmesi amaçlanmıştır.

GEREÇ VE YÖNTEM: Kasım 2016-Ocak 2025 arasında üçüncü basamak bir oküler travma referans merkezinde tedavi edilen AGY'li olgulara ait tıbbi kayıtlar retrospektif olarak incelendi. Olgular, lens hasarı varlığına göre lens hasarı olan (LH) ve olmayan (LHO) olmak üzere 2 gruba ayrıldı. Birincil sonuçlar; son vizitteki en iyi düzeltilmiş görme keskinliği (EİDGK), fonksiyonel görsel başarı (EİDGK ≥0.1 [ondalık]) ve glob sağkalımı idi. Fonksiyonel görsel başarı ve glob sağkalımını etkileyen bağımsız faktörler çok değişkenli lojistik regresyon analizi ile değerlendirildi. Önceki literatür ve klinik önemleri temel alınarak belirlenen bağımsız faktörler; lens etkilenimi, Zon 3 tutulumu, yaralanma tipi, cerrahi sayısı ve başlangıç retina dekolmanı varlığı idi.

BULGULAR: Çalışmaya toplam 98 göz dahil edildi; 73 gözde LH mevcut iken, 25 gözde lens hasarı izlenmedi. Lens hasarlı gözlerde başlangıç EİDGK anlamlı derecede daha düşüktü (ortalama logMAR 2.33 ve 1.76; p=0.003) ve Zon 1 yaralanmaları daha sık izlenmekteydi (p<0.001). Son EİDGK (logMAR 1.62 ve 1.00; p=0.022), fonksiyonel görsel başarı (%23.3 ve %60.0; p=0.002) ve glob sağkalımı (%63.0 ve %88.0; p=0.037) LH grubunda anlamlı olarak daha düşüktü. Çok değişkenli analizde lens hasarının fonksiyonel görsel başarı olasılığını bağımsız olarak azalttığı saptandı (düzeltilmiş OR 0.40; %95 GA 0.11–0.81; p=0.019); ancak glob sağkalımında bağımsız bir belirleyici değildi. Başlangıç retina dekolman varlığı, hem fonksiyonel görsel başarı (düzeltilmiş OR 0.07; %95 GA 0.02–0.44; p<0.001) hem de glob sağkalımı için (düzeltilmiş OR 0.13; %95 GA 0.04–0.40; p<0.001) için en güçlü olumsuz faktör olarak belirlendi.

SONUÇ: Travmatik lens hasarı, AGY sonrası fonksiyonel görsel başarının bağımsız bir göstergesidir. Başlangıç retina dekolmanı ise hem görsel hem anatomik prognozu belirleyen en önemli etken olup, travma yönetiminde kritik öneme sahiptir. Lens hasarının oküler travma skorlama sistemlerine dahil edilmesi, prognozun daha doğru öngörülmesine katkı sağlayabilir.

Anahtar sözcükler: Açık göz yaralanması; glob sağkalımı; görsel prognoz; lens hasarı; lensektomi; travmatik katarakt.

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ORIGINAL ARTICLE

A retrospective study of pediatric forensic trauma: sociodemographic profiles, injury patterns, and medicolegal outcomes

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ABSTRACT

BACKGROUND: Childhood forensic traumatic injuries represent one of the foremost preventable public health concerns. This study aims to evaluate the sociodemographic characteristics, types of trauma, and the legal nature of traumatic injuries in pediatric cases subjected to forensic evaluation.

METHODS: Data from 275 pediatric cases who presented to Çankırı State Hospital between January 1, 2024 and December 31, 2024, with traumatic injuries requiring forensic notification were retrospectively analyzed.

RESULTS: Of the cases, 72.4% were male and 27.6% were female, with a mean age of 13.01±4.22 years. The most common causes of injury were physical assault (43.3%), in-vehicle traffic accidents (19.6%), and out-of-vehicle traffic accidents (17.8%). The distribution of injuries varied significantly by age and sex; physical violence (73.9%), injuries from sharp or stabbing objects (95%), and firearm injuries (100%) were more frequent among males, whereas blunt trauma was more commonly observed in females (42.9%). Soft tissue trauma was present in 92.4% of the cases, and multiple body region injuries were identified in 39.3%, with the head and neck region being particularly affected in physical assault cases (53.8%). Traffic accidents were associated with multi-region injuries and moderate to severe bone fractures.

CONCLUSION: This study demonstrates that childhood traumatic injuries vary significantly by age and gender. Enhancements in socioeconomic, environmental, and educational interventions are essential for the prevention of pediatric trauma. The findings are considered to offer valuable guidance for improving clinical and legal processes.

Keywords: Pediatric trauma; forensic medicine; trauma etiology.

INTRODUCTION

Forensic cases are typically defined as incidents that arise due to external factors, resulting in physical or psychological harm or death to an individual as a consequence of negligence, carelessness, or recklessness.[1,2] These events are a significant source of morbidity and mortality worldwide.[3] Forensic traumatic injuries can occur across all age groups. However, children, due to their incomplete physical and cognitive development, are more vulnerable to trauma and represent a higher-risk group.[4]

A substantial proportion of forensic cases in childhood are associated with traumatic incidents.[5] The most common causes of such trauma include traffic accidents, falls from heights, firearm injuries, and injuries caused by sharp or penetrating objects.[6] Globally, these traumatic injuries account for approximately 40% of childhood deaths and are among

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the leading causes of mortality in children. In Türkiye, forensic trauma-related injuries are reported to be the leading cause of child deaths, with a prevalence ranging from 18% to 43%.[7] Therefore, forensic cases involving children require special attention in terms of their characteristics, clinical management, and implications for legal processes.[8]

In Turkish law, the legal classification of forensic trauma is evaluated within the framework of wounding crimes as defined in the Turkish Penal Code (TPC). Any act that causes bodily pain or impairs a person's health or sensory perception is considered an injury. To determine the legal characteristics of an injury, it must be assessed whether the injury is minor enough to be resolved with simple medical intervention, whether it leads to permanent impairment or loss of function in any sense or organ, results in permanent speech difficulty or loss of reproductive capacity, causes a permanent facial scar or disfigurement, poses a life-threatening condition, causes premature birth or miscarriage in a pregnant woman, or results in bone fractures or dislocations.[9]

While forensic cases often present to hospital emergency departments, they can also be encountered in other outpatient clinics. Consequently, the initial evaluation of such cases is frequently conducted by physicians without specialized forensic training.[7,10] In this context, defining the types and contributing factors of pediatric forensic cases is essential to develop protocols, standards, and training programs to improve approaches and preventive strategies in Türkiye. Furthermore, identifying regional forensic case profiles and patterns will help in establishing more effective intervention frameworks.[11]

The aim of this study is to identify the types of injuries observed in pediatric forensic trauma cases, analyze their sociodemographic characteristics such as age and gender, examine the relationships between these variables to determine potential risk factors, and provide data to enhance the effectiveness of forensic procedures. The findings are expected to contribute to the prevention of child health threats, the development of public health policies, and the improvement of healthcare professionals' knowledge and awareness.

MATERIALS AND METHODS

Study Design and Participants

This study included 275 pediatric cases who presented to Çankırı State Hospital between January 1, 2024 and December 31, 2024, due to traumatic events and for whom forensic reports were officially filed. General forensic examination reports prepared for each case were retrospectively reviewed. Data on sex, age, type of forensic traumatic event, and the nature and anatomical location of traumatic injuries were evaluated. The legal classification of injuries was assessed based on the provisions of the Turkish Penal Code and according to the criteria outlined in the "Guideline for Forensic Medical Evaluation of Injuries Defined in the Turkish Penal Code."[12]

Ethics

This study was approved by the Ethics Committee of Health Sciences of Çankırı Karatekin University, (Meeting No: 20, Date: April 28, 2025). The research was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

Statistical analyses were performed using IBM SPSS version 26 software (IBM SPSS Statistics for Windows, IBM Corp., Armonk, New York, USA). The data were presented as means, standard deviations, frequencies, and percentages. Differences between categorical variables were analyzed using the chi-square test. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 275 pediatric cases were included in the analysis. Of these, 72.4% (n=199) were male and 27.6% (n=76) were female. The mean age of the patients was 13.01±4.22 years. When categorized by age groups, 3.6% (n=10) were between 0–2 years, 6.5% (n=18) were aged 3–6 years, 12% (n=33) were between 7–10 years, 16.4% (n=45) were in the 11–13 age group, and 61.5% (n=169) were 14 years and above (Fig. 1).

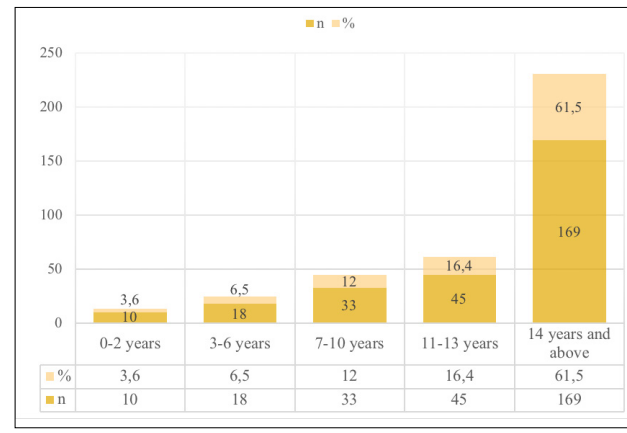

Figure 1. Distribution of cases by age groups.

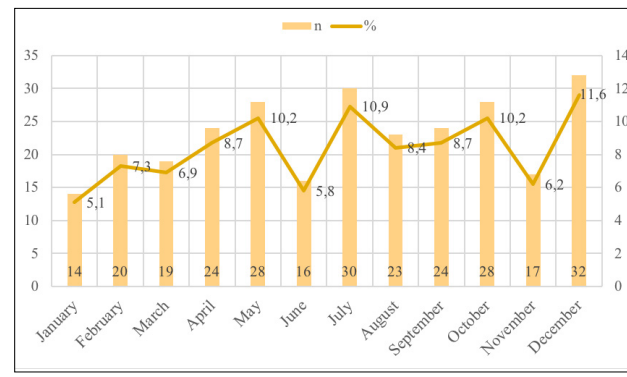

Figure 2. Distribution of cases by month.

Table 1. Distribution of origins by age groups

Age Groups	Origins						χ^2	p
	PA n (%)	IVTA n (%)	OVTA n (%)	SPBI n (%)	GSWI n (%)	Blunt Trauma n (%)		
0-2	3 (30%)	2 (20%)	3 (30%)	-	-	2 (20%)	61.06	<0.001
3-6	4 (22.2%)	5 (27.8%)	7 (38.9%)	-	-	2 (11.1%)		
7-10	10 (30.3%)	6 (18.2%)	15 (45.5%)	-	-	2 (6.1%)		
11-13	17 (37.8%)	9 (20%)	14 (31.1%)	-	-	5 (11.1%)		
14+	85 (50.3%)	32 (18.9%)	10 (5.9%)	20 (11.8%)	5 (3%)	17 (10.1%)		
Total	119 (43.3%)	54 (19.6%)	49 (17.8%)	20 (7.3%)	5 (1.8%)	28 (10.2%)	275 (100%)	

*PA: Physical assault; IVTA: In-vehicle traffic accident; OVTA: Out-of-vehicle traffic accident; SPBI: Sharp and penetrating blade injury; GSWI: Gunshot wound injury; Blunt Trauma: Blunt force injuries. χ^2: Chi-square test.

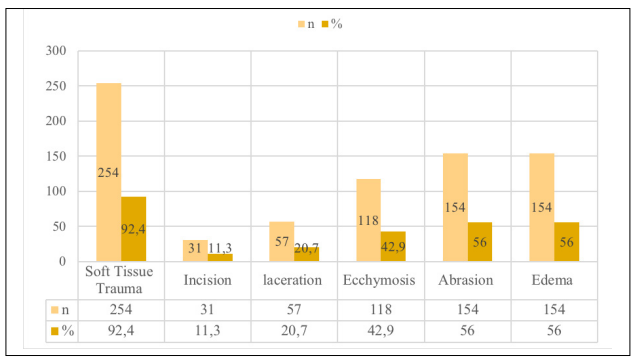

Figure 3. Evaluation of cases in terms of soft tissue trauma.

Based on seasonal distribution, traumatic events among children occurred most frequently in the spring (25.8%; n=71), followed by summer and autumn (25.1%; n=69 each), and least frequently during the winter months (24%; n=66). In terms of monthly distribution, the highest number of traumatic incidents was observed in December (11.6%; n=32), July (10.9%; n=30), May (10.2%; n=28), and October (10.2%; n=28), whereas the lowest incidence was recorded in January (5.1%; n=14) (Fig. 2).

The most common cause of trauma was physical assault, accounting for 43.3% of cases (n=119), followed by in-vehicle traffic accidents (19.6%; n=54) and out-of-vehicle traffic accidents (17.8%; n=49). Less frequently observed causes included blunt trauma (10.2%; n=28), injuries from sharp/stabbing objects (7.3%; n=20), and firearm injuries (1.8%; n=5).

When trauma etiology was examined across age groups, a statistically significant difference was observed with increasing age (χ^2=61.06; p<0.001). Assault-related injuries were most prevalent in the 14 years and above age group (50.3%), whereas out-of-vehicle traffic accidents were more commonly seen among children aged 3–10 years (ranging from 38.9% to 45.5%). Injuries from sharp/stabbing objects, firearms, and blunt force were also most frequently observed in adolescents aged 14 years and above (Table 1).

A statistically significant difference was also identified in the distribution of trauma causes by sex (χ^2=11.65; p=0.040). Physical assault (73.9%; n=88), injuries from sharp/stabbing objects (95%; n=19), and firearm-related injuries (100%; n=5) were significantly more common among male patients. In contrast, a higher proportion of blunt trauma cases involved female children (42.9%; n=12) (Table 2).

At least one soft tissue trauma was detected in 92.4% (n=254) of the cases. The most commonly observed findings were abrasions (56%; n=154) and edema (56%; n=154), followed by ecchymosis (42.9%; n=118), laceration (20.7%; n=57), and incisions (11.3%; n=31), respectively (Fig. 3).

Regarding the distribution of trauma by body regions, multiple-region injuries were the most common (39.3%; n=108), followed by head and neck injuries (33.5%; n=92), lower extremities (10.9%; n=30), and upper extremities (10.5%; n=29). The thorax (2.2%; n=6), back-waist (2.5%; n=7), and abdomen (1.1%; n=3) were less frequently affected.

Table 2. Distribution of origins by gender

Origin	Gender		χ^2	p
	Male n (%)	Female n (%)		
PA	88 (32)	31 (11.3)	11.65	0.040
IVTA	39 (14.2)	15 (5.5)		
OVTA	32 (11.6)	17 (6.2)		
SPBI	19 (6.9)	1 (0.4)		
GSWI	5 (1.8)	-		
Blunt Trauma	16 (5.8)	12 (4.4)		
Total	199 (72.4)	76 (27.6)		

*PA: Physical assault; IVTA: In-vehicle traffic accident; OVTA: Out-of-vehicle traffic accident; SPBI: Sharp and penetrating blade injury; GSWI: Gunshot wound injury; Blunt Trauma: Blunt force injuries. χ^2: Chi-square test.

Table 3. Distribution of injury regions according to origins

Origin	Injury Regions							χ^2	p
	Head-Neck n (%)	Upper Extremities n (%)	Thorax n (%)	Abdomen n (%)	Back n (%)	Lower Extremities n (%)	Multiple Regions n (%)		
IVTA	15 (5.5)	6 (2.2)	1 (0.4)	-	1 (0.4)	8 (2.9)	23 (8.4)		
OVTA	8 (2.9)	2 (0.7)	2 (0.7)	-	-	14 (5.1)	23 (8.4)		
SPBI	4 (1.5)	3 (1.1)	1 (0.4)	1 (0.4)	1 (0.4)	4 (1.5)	6 (2.2)	91.25	<0.001
GSWI	-	-	-	-	-	2 (0.7)	3 (1.1)		
PA	64 (23.3)	14 (5.1)	2 (0.7)	1 (0.4)	3 (1.1)	2 (0.7)	33 (12)		
Blunt Trauma	1 (0.4)	4 (1.5)	-	1 (0.4)	2 (0.7)	-	20 (7.3)		
Total	92 (33.6)	29 (10.6)	6 (2.2)	3 (1.2)	7 (2.6)	30 (10.9)	108 (39.4)		

*PA: Physical assault; IVTA: In-vehicle traffic accident; OVTA: Out-of-vehicle traffic accident; SPBI: Sharp and penetrating blade injury; GSWI: Gunshot wound injury; Blunt Trauma: Blunt force injuries. χ^2: Chi-square test.

Table 4. Nature of injuries according to the Turkish Penal Code (TPC)

Treatable with simple medical interventions	n (%)
Minor	184 (66.9)
Not minor	91 (33.1)
Life-threatening condition	
Present	23 (8.4)
Not present	252 (91.6)
Permanent facial scars or facial changes	
Present	4 (1.5)
Not present	248 (90.2)
Re-examination after 6 months required	23 (8.4)
Weakening or loss of sensory or organ function	
Not present	250 (90.9)
Weakening	2 (0.7)
Loss	3 (1.1)
To be evaluated at the end of treatment	20 (7.3)

A significant relationship was found between the cause of trauma and the affected body region (χ^2=91.25; p<0.001). In assault cases, the head and neck region was most commonly affected (53.8%), followed by multiple-region injuries (27.7%). In traffic accidents, multiple-region injuries were predominant (42.6% for in-vehicle and 46.9% for out-of-vehicle). Injuries caused by sharp objects and blunt trauma frequently resulted in multiple-region injuries (30.0% for sharp objects; 71.4% for blunt trauma) (Table 3).

When evaluating whether injuries were life-threatening, 91.6% of cases (n=252) did not pose a life-threatening situation, while 8.4% (n=23) were considered life-threatening. Among these, cranial fractures were found in 12 cases, comprising 4.4% of the total sample. Internal organ injuries were detected in nine cases (3.3%), with one case each of major vessel injury and blood loss (Table 4).

In 66.9% (n=184) of the cases, injuries were classified as minor and treatable with simple medical interventions; however, 33.1% (n=91) were assessed as not minor and requiring more than simple medical intervention (Table 4).

Of the cases evaluated for bone fractures or dislocations, 78.9% (n=217) had neither fractures nor dislocations, while 21.1% (n=58) had fractures or dislocations. According to the classification based on the impact of bone fractures on vital functions, injuries were assessed as mild (1 point) in 2.6% (n=7), moderate (2–3 points) in 8.6% (n=24), and severe (4–6 points) in 9.8% (n=27) (Table 5).

A statistically significant relationship was identified between the cause of trauma and the presence and severity of fractures/dislocations (χ^2=110.09; p<0.001). The type of trauma was found to be predictive of fractures/dislocations. Of the 119 physical assault cases, 108 (90.8%) had no fractures/dislocations, while 11 cases (9.2%) had mild (n=4), moderate (n=6), or severe (n=1) fractures. Fractures/dislocations were observed in 22 of 54 cases (40.7%) involving in-vehicle traffic accidents and in 20 of 49 cases (40.8%) involving out-of-vehicle traffic accidents. Moderate and severe injuries (4–6 points) were more frequent in these groups (22.2% for in-vehicle and 26.5% for out-of-vehicle). No fractures/dislocations were observed in injuries from sharp or penetrating objects. Among 28 cases of blunt trauma, moderate fractures were found in two cases (7.1%). Of the five gunshot wound injury cases, three (60%) had fractures, with two cases (40%) classified as severe and one (20%) as moderate (Table 5).

Evaluation of the 275 cases revealed traumatic injuries involving the facial region in 35.6% (n=98), whereas in 64.4%

Table 5. Distribution of bone fractures and dislocations according to origins

Origin	Bone Fractures/Dislocations				χ^2	p
	No Fracture n (%)	Mild (1) n (%)	Moderate (2–3) n (%)	Severe (4-6) n (%)		
IVTA	32 (11.6)	3 (1.1)	7 (2.5)	12 (4.4)	110.09	<0.001
OVTA	29 (10.5)	-	7 (2.5)	13 (4.7)		
SPBI	20 (7.3)	-	-	-		
GSWI	2 (0.7)	-	1 (0.4)	2 (0.7)		
PA	108 (39.3)	4 (1.5)	7 (2.5)	-		
Blunt Trauma	26 (9.5)	-	2 (0.7)	-		
Total	217 (78.9)	7 (2.6)	24 (8.6)	27 (9.8)		

*PA: Physical assault; IVTA: In-vehicle traffic accident; OVTA: Out-of-vehicle traffic accident; SPBI: Sharp and penetrating blade injury; GSWI: Gunshot wound injury; Blunt Trauma: Blunt force injuries. χ^2: Chi-square test.

(n=177) the facial region was unaffected. Regarding permanent facial scars or permanent facial changes, most cases (90.2%; n=248) showed no permanent facial scars or permanent facial changes. In 8.4% of cases (n=23), a follow-up examination after six months was recommended to reassess the possibility of permanent facial scars or permanent facial changes. Only a small fraction (1.5%; n=4) had permanent facial scars or permanent changes (Table 4).

Assessment of cases for permanent weakening or loss of sensory or organ function showed that most cases (90.9%; n=250) had neither weakening nor loss. However, permanent weakening was found in 0.7% (n=2) and permanent loss in 1.1% (n=3) of cases. Additionally, 7.3% (n=20) of cases required completion of medical treatment before a definitive evaluation could be made, indicating that they were not currently suitable for assessment (Table 4).

DISCUSSION

Trauma is one of the leading causes of mortality and morbidity during childhood, and a significant proportion of these cases have forensic implications.[13] Age-dependent anatomical characteristics, activity patterns, and physical mobility levels result in different origins and clinical presentations of trauma in children. Additionally, factors such as cultural influences, socioeconomic status, seasonality, gender, and age significantly shape the frequency of trauma exposure.[13]

In our study, among the causes of traumatic injuries in children, physical assault-related incidents accounted for the highest proportion (43.3%), followed by in-vehicle (19.6%) and out-of-vehicle (17.8%) traffic accidents. These results indicate that physical violence remains the primary source of injury in children, while traffic accidents, although relatively lower, still constitute a significant risk. The literature presents varying results according to regional, socioeconomic, and study scope differences. Some studies.[1,5,8,13-17] reported traffic accidents as the leading cause of forensic traumatic injuries, whereas others[7,18] reported assault injuries as the most prevalent. This discrepancy may result from differences in age group distributions of research populations, urban-rural residential characteristics, prevalence of traffic safety measures, and healthcare utilization patterns. For instance, children in rural areas are often in unsupervised play areas and thus may have an increased risk of exposure to violence as adult supervision decreases.[19] Conversely, in urban regions, dense traffic and inadequate pedestrian infrastructure can increase both in-vehicle and out-of-vehicle accident rates, with factors such as seatbelt usage and infrastructure modifications playing key roles in altering these rates. Hence, preventive strategies aimed at improving trauma injury profiles should thoroughly evaluate local dynamics and risk factors.

In this study, 77.9% of cases were within the 11-18 age group, with a mean age of 13.01 years. The distribution of traumatic incidents by age groups was statistically significant (χ^2=61.06; p<0.001); specifically, out-of-vehicle traffic accidents were more frequent among the 3-10 age group, whereas injuries from assault, sharp objects, and firearms were more prevalent in children aged 14 years and above. The literature generally reports an average age of forensic trauma cases ranging between 8.91 and 11.82 years, with a notable increase in traumatic injuries among adolescents.[1,3,15,18] The differentiation in trauma causes by age group is likely associated with developmental characteristics, behavioral tendencies, and environmental risk factors. For example, adolescents may be more vulnerable to violent incidents due to increased social mobility, peer influences, risk-taking behaviors, and resistance to authority. In this age group, factors such as increased time spent outdoors, school-related conflicts, and individual weapon carrying increase the risk of assault and firearm-related injuries.[5,7,8,1] Conversely, younger children have limited independent mobility and underdeveloped motor skills, making them more susceptible to accidents, particularly those involving traffic-related external factors. These children frequently face traffic exposure as pedestrians and are at increased risk

due to inadequate safe play areas and unsupervised roaming. Thus, these findings underscore the importance of developing age-specific preventive measures that consider the unique risk dynamics of childhood and adolescence. Age-targeted intervention strategies, such as violence prevention programs for school-aged children, mental health support programs for adolescents, and environmental safety measures for younger age groups, could effectively reduce trauma injury rates.

Our study found that forensic traumatic injuries predominantly occurred in males (72.4%). The distribution of injury causes by gender was statistically significant (χ^2=11.65; p=0.040), notably with injuries caused by sharp and penetrating blades (95%) and gunshot wounds (100%) almost exclusively observed in male children. This finding aligns with numerous studies in the literature. Prior research has shown that forensic traumatic incidents are significantly more frequent among male children, with males more often subjected to physically violent injuries compared to females.[13,15,16,20] Similarly, studies by Ökçesiz et al.[18] and Korkmaz et al.[21] have reported a higher incidence of physical assault, sharp and penetrating blade, and gunshot wound injuries among males, whereas non-traumatic forensic situations were more common in females. These differences can be explained within the framework of gender roles, behavioral patterns, and social expectations. Male children's greater exposure to outdoor environments, higher tendencies toward risky behaviors, and more frequent involvement in physical altercations make them more vulnerable to traumatic injuries.

In our study, the distribution of traumatic injuries throughout the year was fairly balanced across seasons (spring 25.8%; summer and autumn each 25.1%; winter 24.0%). However, the literature reports significant variations in the seasonal distribution of forensic traumatic cases. Demir et al.[16] and Kang and Kim[22] noted significant increases in cases during the summer months. Conversely, Büken and Yaşar[23] reported most cases in spring, while Ersoy et al.[5] observed peak incidences in autumn. Nevertheless, some studies, like ours, have found no statistically significant differences in seasonal distributions. These discrepancies can largely be attributed to geographic and climatic variations. For instance, increased outdoor activities and unsupervised play during summer in certain areas can elevate injury risk, while heightened school interactions during transitional seasons (spring or autumn) may increase violence-related incidents. Additionally, higher physical activity and exposure during agricultural periods in rural areas can influence case numbers.

Our research identified traumatic soft tissue injuries in 92.4% of cases, highlighting the prevalence of soft tissue injuries in pediatric forensic trauma. Literature-reported rates vary from 34% to 92%, with our study presenting a figure near the upper limit.[24] Demirel and Akpınar[20] reported soft tissue injuries in 50.6% of pediatric blunt trauma cases, rising to 92.5% in violence-related incidents. Similarly, Sever et al.[18] reported normal physical examination findings in only 12.1% of pediatric forensic cases. These findings suggest that childhood trauma predominantly involves soft tissue injuries, leaving physical marks. Our study identified abrasions (56%) and edema (56%) as the most common soft tissue injuries, consistent with previous research.[17,20,24] Abrasions and localized edema typically result from mechanical forces such as assault, falls, or blunt object impact, explaining their frequency in assault-related incidents. The prevalence of soft tissue injuries may also relate to children's physiological traits, such as weaker musculoskeletal structures and thinner subcutaneous fat, rendering them more vulnerable to traumatic impacts. Limited reflex responses and risk perception abilities in children may further increase susceptibility to soft tissue injuries. Consequently, soft tissue injuries should be considered critical diagnostic indicators in pediatric forensic evaluations, with thorough physical examinations and documentation through forensic photography as necessary.

In our study, the most frequently observed trauma pattern involved injuries affecting multiple anatomical regions (39.3%). Among isolated injuries, the most commonly affected area was the head and neck region (33.5%), followed by the lower extremities (10.9%) and upper extremities (10.5%). This distribution varied significantly based on the etiology of the trauma (χ^2=91.25; p<0.001). In cases of physical assault, the head and neck region was most commonly affected (53.8%), whereas in in-vehicle traffic accidents (42.6%) and out-of-vehicle traffic accidents (46.9%), injuries typically involved multiple anatomical regions. Similarly, multi-region involvement was frequently observed in injuries caused by sharp and penetrating objects (30.0%) and in blunt trauma cases (71.4%). These findings reflect the influence of the kinetic energy generated by different trauma mechanisms on the anatomical distribution of injuries. Data from the literature are consistent with our findings. Several studies[22,23,25] have reported that, in pediatric forensic trauma cases, the head and neck region is most commonly affected, followed by injuries to the upper and lower extremities. Sever et al.[17] demonstrated that injuries involving multiple anatomical regions were predominant in forensic cases, with the head and neck region being the most frequently affected area among localized injuries. Demirel and Akpınar[20] similarly found that the head and neck region was the most frequently targeted anatomical site in assault-related trauma, whereas traffic accidents were more commonly associated with multi-region injuries. The anatomical exposure and relatively unprotected structure of the head and neck, combined with the fact that this region is more likely to be deliberately targeted during an assault, may explain its high injury rate. Additionally, children's limited capacity to defend themselves may contribute to the increased susceptibility of this region. In high-energy trauma, such as traffic accidents, simultaneous involvement of multiple body regions is expected due to the systemic impact.

In our study, bone fractures or dislocations were identified in 21.1% of forensic trauma cases, and nearly half of these

cases (9.8%) involved severe fractures (scored 4-5-6). A statistically significant association was found between trauma etiology and fracture severity (p<0.001). Notably, both in-vehicle (40.7%) and out-of-vehicle (40.8%) traffic accidents were associated with high rates of fractures. Previous studies[3,5,15,20,22,26] have reported the presence of bone fractures or dislocations in 11.5% to 42.1% of forensic trauma cases. In the study by Basa et al.,[3] traffic accidents and falls from height were the most common causes of presentation, with most fractures resulting in moderate to severe injury. Similarly, Ersoy et al.[5] reported that 83.1% of trauma cases involving bone fractures were classified as moderate to severe. Demirel and Akpınar[21] also found a significantly higher fracture rate in cases related to traffic accidents. The relatively lower overall fracture rate in our study may be attributable to the predominance of physical assault-related cases in the sample. Nevertheless, the moderate and severe fracture rates in traffic accident-related cases align with the existing literature.

CONCLUSION

This study evaluated the sociodemographic characteristics, types of trauma, and medicolegal outcomes of pediatric cases subjected to forensic traumatic injuries. The findings revealed significant differences in childhood trauma patterns based on age and sex. Physical assault, sharp and penetrating object injuries, and firearm-related injuries were more frequently observed in male children, whereas blunt trauma was more prevalent among females. Moreover, as age increased, the proportion of violence-related injuries rose, while traffic accidents were more prominent in younger age groups.

The results also showed that most injuries consisted of soft tissue trauma, frequently involving the head and neck region or affecting multiple anatomical regions simultaneously. The high incidence of moderate-to-severe fractures in traffic accidents highlights the critical importance of traffic safety measures. Although permanent facial changes and sensory or organ function impairments were relatively rare, their clinical and legal implications remain significant.

For future research, comprehensive studies that investigate the underlying causes of trauma and explore socioeconomic and environmental risk factors in greater depth are recommended. Additionally, developing region-specific intervention strategies and educational programs aimed at preventing pediatric trauma and enhancing healthcare professionals' awareness is essential. The data presented in this study may serve as a valuable reference for improving forensic procedures and guiding the development of public health policies aimed at the prevention of childhood trauma.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Çocuklarda adli travmatik yaralanmaların retrospektif analizi: Sosyodemografik özellikler, yaralanma türleri ve adli tıbbi sonuçlar

AMAÇ: Çocukluk çağı adli travmatik yaralanmaları önlenebilir sağlık sorunlarının başta gelen sebeplerindendir. Bu çalışma adli travmatik yaralanmalara uğramış pediatrik olguların sosyodemografik özelliklerini, travma türlerini ve travmatik yaralanmaların hukuki niteliğini değerlendirmeyi amaçlamaktadır.
GEREÇ VE YÖNTEM: Çankırı Devlet Hastanesi'ne 01.01.2024 ile 31.12.2024 tarihleri arasında travmatik bir yaralanma nedeniyle başvuran ve adli bildirim yapılan 275 çocuk olguya ait veriler retrospektif olarak incelenmiştir.
BULGULAR: Olguların %72.4'ü erkek, %27.6'sı kız olup, yaş ortalaması 13.01±4.22 yıldı. En sık yaralanma nedenleri darp-cebir (%43.3), araç içi trafik kazaları (%19.6) ve araç dışı trafik kazalarıydı (%17.8). Yaralanmalar cinsiyet ve yaş ile ilişkili anlamlı farklılık göstermiştir; fiziksel şiddet (%73.9), kesici-delici alet (%95) ve ateşli silah yaralanmaları (%100) erkeklerde daha sık, künt travmalar (%42.9) ise kızlarda daha yüksek oranda izlendi. Olguların %92.4'ünde yumuşak doku travmaları, %39.3'ünde çoklu bölge yaralanmaları görülmüş, özellikle baş-boyun bölgesi darp-cebir yaralanmalarında çok sık etkilendiği bulundu (%53.8). Trafik kazaları birden fazla vücut bölgesinde yaralanmalarla birlikte orta-ağır derecede kemik kırıklarına sebep olduğu tespit edildi.
SONUÇ: Bu çalışma çocukluk çağı travmatik yaralanmalarının yaş ve cinsiyet ile önemli farklılıklar gösterdiğini ortaya koymaktadır. Pediatrik travmaların önlenmesine yönelik sosyoekonomik, çevresel ve eğitimsel süreçlerde iyileştirmeler sağlanmalıdır. Elde edilen verilerin klinik ve hukuki süreçlerin geliştirilmesinde rehber niteliği taşıyabileceği düşünülmektedir.

Anahtar sözcükler: Adli tıp; çocukluk çağı travması; travma etiyolojisi.

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ORIGINAL ARTICLE

Does the fracture line position relative to the olecranon fossa affect surgical difficulty and outcomes in pediatric supracondylar humerus fractures?

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ABSTRACT

BACKGROUND: This study aimed to investigate whether the level of the fracture line relative to the olecranon fossa influences surgical difficulty, complication rates, and radiological outcomes in pediatric supracondylar humerus fractures (PHSF).

METHODS: A retrospective review was conducted of 822 children who underwent surgical treatment for PHSF. Patients were categorized according to the location of the fracture line relative to the apex of the olecranon fossa: high-level (proximal to the fossa, n=163) and low-level (at or distal to the fossa, n=659). High-level fractures were further classified as oblique (n=40) or transverse (n=123), based on the angle between the fracture line and the transepicondylar line. Patient demographics, fracture characteristics, surgical parameters, complications, radiographic findings, and revision rates were analyzed.

RESULTS: There were no significant differences between groups in terms of patient demographics, fracture side, open versus closed fracture status, neurovascular injury, or associated trauma ($p>0.1$). High-level fractures were significantly more unstable, required longer surgical durations, and showed a greater number of K-wire cortical scars compared to low-level fractures ($p<0.05$). K-wire configuration, number, and diameter showed no significant differences. Subgroup analysis demonstrated that oblique high-level fractures more often required divergent pin configurations and had significantly higher revision rates compared with transverse high-level fractures ($p=0.049$ and $p=0.004$, respectively).

CONCLUSION: Fractures located proximal to the olecranon fossa are more unstable and technically demanding, resulting in longer operation times and more intraoperative pinning attempts. Among high-level fractures, oblique types are especially prone to technical challenges and increased revision rates, highlighting the importance of fracture morphology in surgical planning.

Keywords: Humerus fracture; elbow fracture; pediatric supracondylar humerus fracture.

INTRODUCTION

Supracondylar humerus fractures are the most common type of elbow fracture in the pediatric population, typically occurring between the ages of 5 and 7 years and usually resulting from a fall on an outstretched hand.[1] The vast majority (95–98%) are extension-type fractures, whereas flexion-type injuries are relatively uncommon.[1] The modified Gartland classification, consisting of four subtypes, is widely used for diagnostic categorization.[2] Type I fractures are nondisplaced and managed conservatively, while displaced fractures (Types II–IV) generally require surgical intervention.[3]

As the trend toward operative management of displaced fractures has increased, new clinical questions have emerged. There is ongoing debate regarding the optimal reduction method (open vs. closed), K-wire configuration, and the man-

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agement of associated neurovascular injuries.[4,5]

Some previous studies have examined the potential influence of fracture line level on clinical and radiographic outcomes in pediatric supracondylar humerus fracture (PHSF). Fayssoux et al.[6] proposed the concept of high-level fractures involving the metaphyseal-diaphyseal junction. However, their analysis included only 14 such cases, suggesting a need for further exploration. Kang et al.[7] emphasized the prognostic significance of fracture morphology, reporting that in Gartland type III fractures, a fracture line distal to the humeral isthmus correlated with poorer functional and radiological results.

The present study aims to assess whether the location of the fracture line relative to the olecranon fossa impacts surgical difficulty, complication rates, and radioclinical outcomes. By evaluating this anatomical landmark, we hope to contribute meaningful insights into the surgical planning and management of pediatric supracondylar humerus fractures.

MATERIALS AND METHODS

This retrospective study was conducted following approval from the local ethics committee (Institutional Review Board of S.B.U. İzmir Tepecik Research and Training Hospital, Date: 22/02/2021, Decision No: 2021/02-18) and in accordance with the Declaration of Helsinki. Patient data were retrieved using the Probel Hospital Automation System (Probel Software and Information Systems Inc., Izmir, Türkiye). All patients included in the study were operated on between January 2013 and December 2020 at a tertiary care center by different orthopedic surgeons.

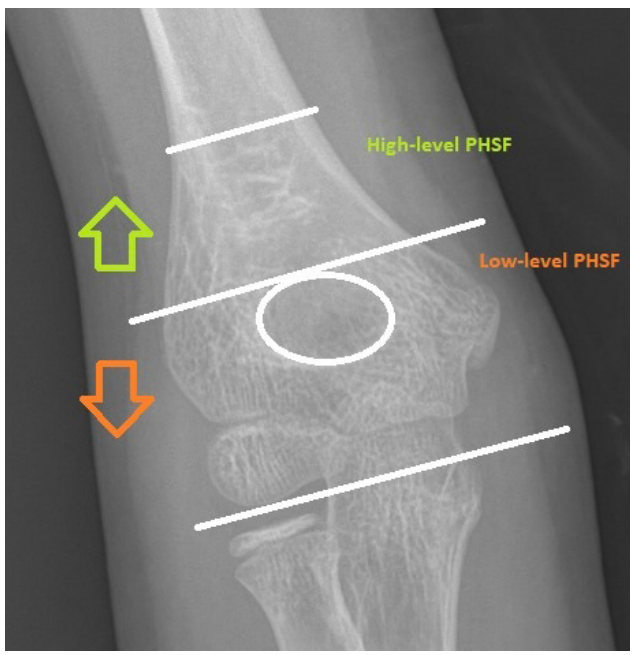

Figure 1. Fracture line in relation to the apex of the olecranon fossa.

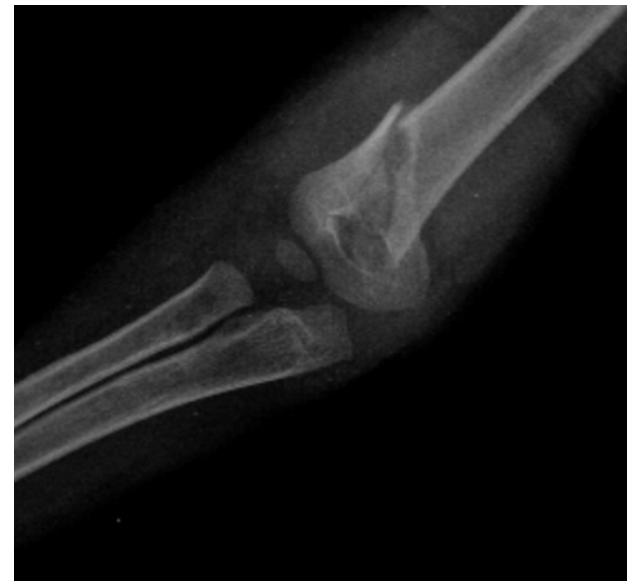

Figure 2. High-level supracondylar humerus fracture.

Inclusion Criteria:

1. Age between 1 and 13 years

2. Surgically treated supracondylar humerus fracture

3. Availability of adequate preoperative and postoperative elbow radiographs

4. Minimum follow-up until radiological bone union.

Exclusion Criteria:

1. Lateral condyle fractures coded as distal humerus fractures

2. Medial epicondyle fractures coded as distal humerus fractures

3. Miscoded fractures not involving the distal humerus.

Out of 874 screened patients, 52 were excluded (42 with lateral condyle fractures, seven with medial epicondyle fractures, and three with unrelated fracture codes). A total of 822 patients with PHSF (94% of the initial cohort) were included.

The olecranon fossa is a depression located on the posterior cortex of the distal humerus, directly proximal to the trochlea, and is the largest of the three fossae found on the humerus.[8]

Patients were categorized according to the location of the fracture line relative to the apex of the olecranon fossa (Fig. 1). Fractures proximal to the fossa were classified as high-level (n=163) (Fig. 2), while those at or distal to the fossa were classified as low-level (n=659) (Fig. 3).

The transepicondylar line was created by connecting the most extreme points of the medial and lateral epicondyles (Fig. 4). The high-level group was further subdivided based on the angle between the fracture line and the transepicondylar line into:

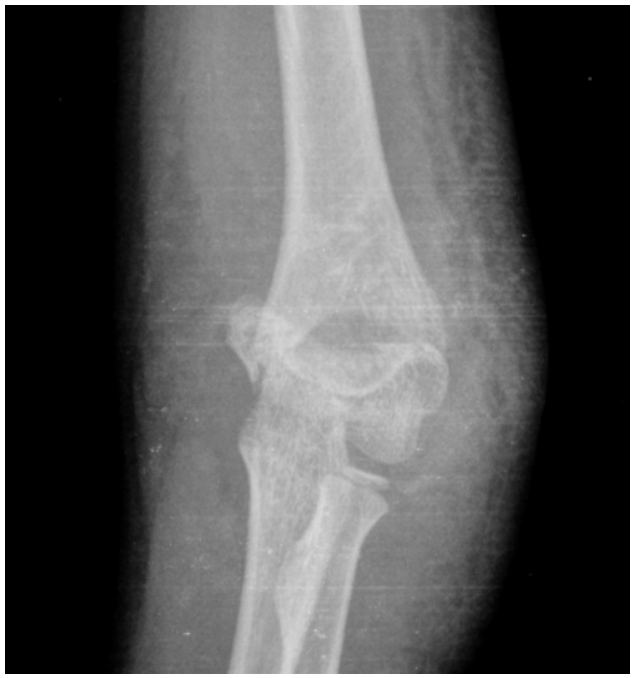

Figure 3. Low-level supracondylar humerus fracture.

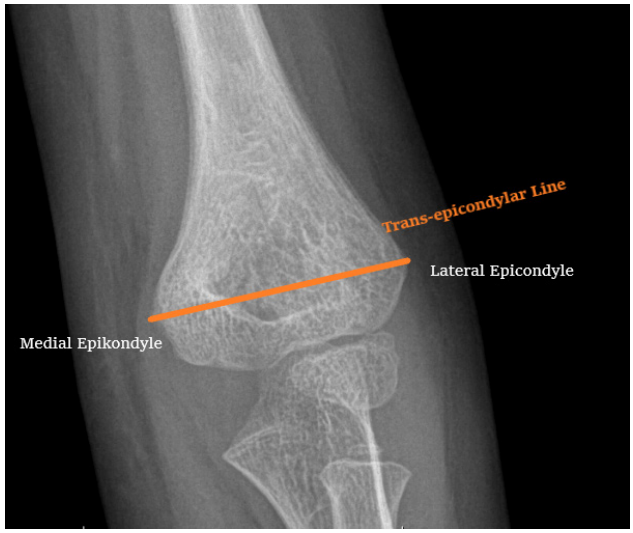

Figure 4. Transepicondylar line.

• Oblique fractures: angle >30° (n=40) (Fig. 5)

• Transverse fractures: angle ≤30° or parallel orientation (n=123) (Fig. 6).

Radiological assessments and data collection were conducted using PACS (Picture Archiving and Communication System) and the Probel database. Radiographic measurements were performed by the senior author, a pediatric orthopedic surgeon with over 15 years of experience.

Collected parameters included demographic data, fracture side, duration of surgery, method of reduction (open or

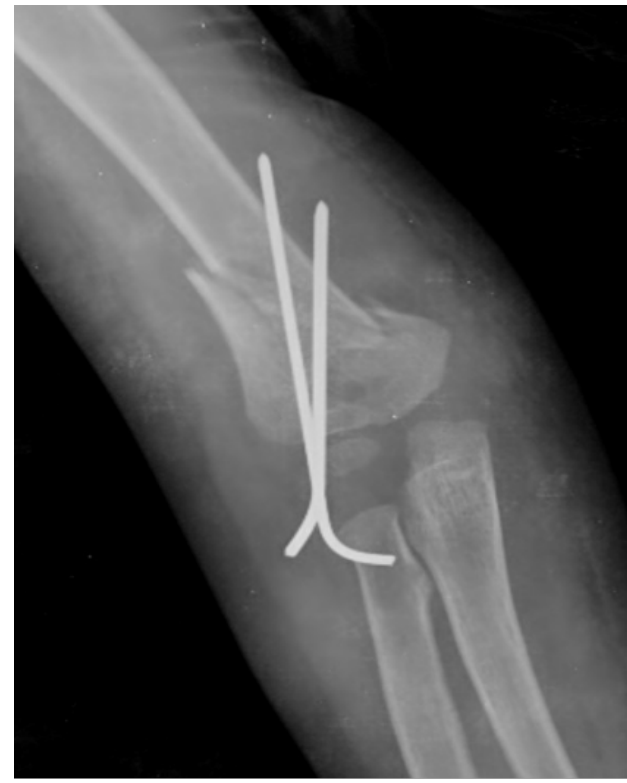

Figure 5. High-level oblique-type supracondylar humerus fracture.

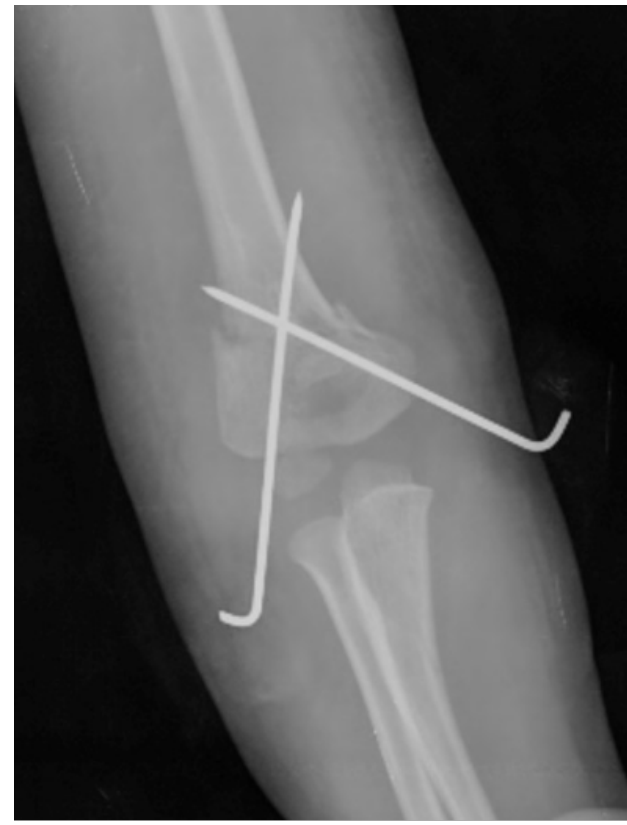

Figure 6. High-level transverse-type supracondylar humerus fracture.

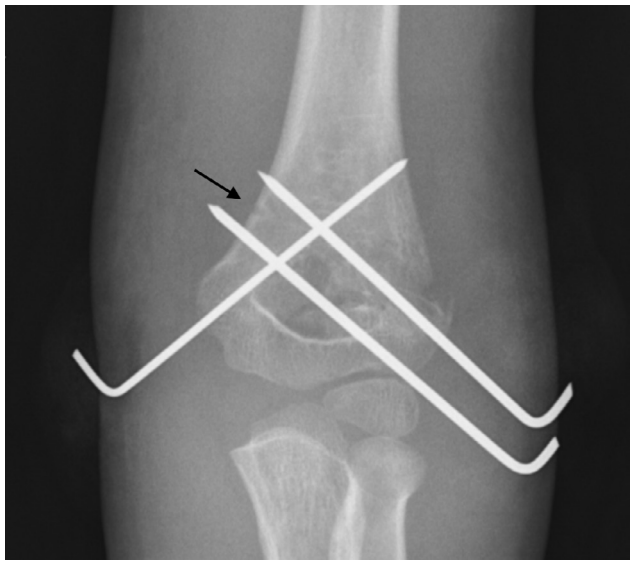

Figure 7. K-wire cortical scars.

closed), fracture type (open or closed), presence of vascular and nerve injury, systemic trauma, complications, and the requirement for revision surgery.

Radiographic analysis included fracture type (modified Gartland classification),[9] location relative to the olecranon fossa, sagittal displacement, number and diameter of K-wires, wire configuration, number of cortical scars (indicative of repeated pinning attempts) (Fig. 7), postoperative translation and rotation, anterior humeral line alignment on immediate and final radiographs, and follow-up duration.

Statistical Analysis

All statistical analyses were performed using SPSS version 24.0 (IBM Corp., Armonk, NY, USA). Normality of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed variables were compared using the independent samples t-test or analysis of variance (ANOVA), while non-normally distributed variables were compared using the Mann-Whitney U test or Kruskal-Wallis test. Chi-square or Fisher's exact tests were applied for categorical variables, depending on expected frequencies. A p-value less than 0.05 was considered statistically significant.

RESULTS

The mean age of all patients was 6.5±3 years (range, 1–13). In the low-level fracture group (n=659), the mean age was 6.5±3 years, while in the high-level group (n=163), it was 6.7±2.9 years (p=0.618). Males comprised 62% (411/659) of the low-level group and 64% (105/163) of the high-level group (p=0.348). Right-side fractures accounted for 38% (248/659) in the low-level group and 34% (55/163) in the high-level group (p=0.570) (Table 1). Of the 822 fractures, 802 (98%) were closed. Fourteen of the 20 open fractures (70%) were low-level (p=0.118). Vascular compromise was present in 49 patients (6%), with 16 showing filiform pulses, 29 having no pulse but good capillary refill, and four requiring vascular repair (p=0.102). Nerve injuries were observed in 79 patients (10%), including anterior interosseous nerve (AIN) injury in 39, ulnar nerve injury in 18, posterior interosseous nerve (PIN) injury in 11, combined ulnar and AIN injuries in six, combined ulnar and PIN injuries in four, and both AIN and PIN injuries in one (p=0.141). Additional trauma was seen in 34 patients (4%), including fractures in other regions or head trauma (p=0.221) (Table 2). Modified Gartland fracture types included 7 type 1b, 177 type 2, 441 type 3, 143 type 4, and 54 flexion-type fractures. Unstable fractures were significantly more common in the high-level group (p<0.001). Among extension-type fractures (n=768), posteromedial displacement occurred in 402 patients (49%) and posterolateral displacement in 366 patients (44%) (p=0.164) (Table 2). Mean surgery duration was 52.6±30.6 minutes for low-level fractures and 58.9±30.1 minutes for high-level fractures (p=0.006). The average number of K-wires used was similar between groups (2.7±0.6 for low-level and 2.69±0.6 for high-level; p=0.478), as was the average wire diameter (1.8±0.11 mm vs. 1.8±0.13 mm; p=0.997). High-level fractures had a significantly higher mean number of K-wire cortical scars (p=0.042). K-wire configuration showed no significant difference: cross-wire was used in 77%, divergent in 21%, and parallel in 2% of cases (p=0.58). Open reduction was required in 4% of patients, with no significant difference between groups (p=0.114) (Table 3). Postoperative translation occurred in 157 patients (120 low-level, 37 high-level; p=0.942). Rotational deformity was observed in 246 patients (193 low-level, 53 high-level;

Table 1. Demographic data of the patients

	Below Olecranon Fossa	Above Olecranon Fossa	p-value
Age mean±SD (min-max)	6.5±3 (1-13)	6.7±2.9 (1-12)	0.618
Gender (male/female)	411/248	105/58	0.348
Side (right/left)	248/411	55/108	0.570
n	659	163	

SD: Standard deviation.

Table 2. Comparison of preoperative data

	Below Olecranon Fossa	Above Olecranon Fossa	p-value
Open fracture	14	6	0.188
Vascular injury	33	16	0.102
Nerve injury	55	24	0.141
Additional trauma (fracture/head trauma/fracture+head trauma)	17/4/3	9/1/0	0.221
Fracture type (1b/2/3/4/flexion)	7/164/354/91/43	0/13/87/52/11	**<0.001**
Sagittal plane displacement direction (posteromedial/posterolateral)	316/299	86/67	0.164
N	659	163	

Table 3. Comparison of intraoperative data

	Below Olecranon Fossa	Above Olecranon Fossa	p-value
Open Surgery	23	8	0.114
Wire configuration (crossed/divergent/parallel)	505/138/16	129/32/2	0.58
Operation time (minutes) mean±SD (min-max)	52.6±30.6 (10-458)	58.9±30.1 (15-210)	**0.006**
Number of Kirschner wires mean±SD (min-max)	2.7±0.6 (1-5)	2.69±0.6 (2-5)	0.478
Number of wire scars	1±1.4 (0-6)	1.2±1.6 (0-6)	0.042
Wire thickness (mm) mean±SD (min-max)	1.8±0.11 (1.5-2)	1.8±0.13 (1-2)	0.997
N	659	163	

SD: Standard deviation.

Table 4. Comparison of postoperative data

	Below Olecranon Fossa	Above Olecranon Fossa	p-value
Complication	16	7	0.621
Revision surgery	22	6	0.492
Follow-up (months) mean±SD (min-max)	5±9.3 (1-72)	5.7±9.4 (1-65)	0.276
Translation	120	37	0.942
Rotation	193	53	0.229
Anterior humeral line (anterior/anterior 1/3/mid 1/3/posterior 1/3/posterior)	40/157/326/102/34	17/29/77/32/8	0.121
N	659	163	

SD: Standard deviation; ant: Anterior; post: Posterior.

Table 5. Comparison of peroperative data of high-level fractures

	Transverse Fracture	Oblique Fracture	p-value
Fracture type (1b/2/3/4/flexion)	13/60/43/7/0	0/27/9/4/0	0.037
Open surgery	4	4	0.064
Wire configuration (crossed/divergent/parallel)	102/19/2	27/13/0	0.049
Operation time (minutes) mean±SD (min-max)	57.9±28 (20-180)	61.8±35.9 (15-210)	0.746
Number of Kirschner wires mean±SD (min-max)	2.7±0.6 (2-5)	2.7±0.6 (2-4)	0.899
Number of wire scars	1.2±1.5 (0-6)	1.3±1.8 (0-6)	0.946
Wire thickness (mm) mean±SD (min-max)	1.8±0.1 (1-2)	1.8±0.1 (1.5-2)	0.688
Complication	6	1	0.878
Revision surgery	1	5	0.004
Translation	30	7	0.419
Rotation	38	15	0.278
Anterior humeral line (anterior/mid/posterior)	33/60/30	13/17/10	0.706
n	123	40	

SD: Standard deviation.

p=0.229). Analysis of the anterior humeral line relative to the capitellum on early postoperative radiographs showed no significant differences between groups (p=0.121). Complications occurred in 23 patients (3%), including K-wire migration, pin tract infections, loss of reduction, refracture, and iatrogenic nerve injury, with no significant difference between groups (p=0.621). Revision surgery was needed in 28 patients (3%), similarly distributed between groups (p=0.492). Mean follow-up duration was comparable (5±9.3 months for low-level and 5.7±9.4 months for high-level; p=0.276) (Table 4). Within the high-level fracture group, oblique fractures (n=40) had a higher incidence of unstable (modified Gartland) types than transverse fractures (n=123) (p=0.037). Surgery duration, number of K-wires, and wire diameter did not differ significantly between these subgroups. However, oblique fractures more frequently required divergent pin configurations (p=0.049) and had a significantly higher revision rate (p=0.004). There were no significant differences in postoperative translation, rotation, need for open reduction, or complication rates between oblique and transverse fractures (Table 5).

DISCUSSION

Most pediatric fractures can be treated conservatively; however, displaced pediatric humeral supracondylar fractures typically require surgical fixation. Among pediatric fractures, supracondylar humerus fractures are the most frequently operated on, due to the distal humerus contributing approximately 20% to longitudinal growth.[10,11] Moreover, since the elbow's flexion-extension axis lies in the sagittal plane, coronal plane deformities cannot be reliably corrected through remodeling.[12,13]

The preferred fixation technique involves the placement of divergent or crossed K-wires after achieving adequate reduction, whether open or closed.[14] Many studies have focused on the relationship between wire configuration and fixation stability in PHSF.[15] High-level fractures, located proximal to the olecranon fossa, pose challenges due to limited proximal bone stock for fixation.[16] Our study found that operation times were significantly longer in high-level fractures compared to low-level fractures (p=0.006), supporting this difficulty. Additionally, these high-level fractures were more frequently unstable based on the modified Gartland classification (p<0.001). The greater number of K-wire-induced cortical scars in high-level fractures (p=0.042) further reflects the technical challenges during fixation.

Previous literature reports the incidence of high-level PHSF (also termed distal humerus metaphyseal-diaphyseal fractures) as approximately 3.3% of all PHSF.[17,18] In contrast, our study observed a higher rate of 19.8%, likely due to inclusion criteria limited to surgically treated unstable fractures.

The narrow cross-sectional area in the metaphyseal-diaphyseal region complicates fracture reduction and fixation, increasing the risk of loss of reduction postoperatively.[19-21] Additionally, the periosteum is thinner in this region, making closed reduction more difficult and often necessitating open reduction.[19] These factors collectively contribute to prolonged surgery duration for high-level fractures, as confirmed in our study and by Fayssoux et al.[6]

Although open reduction was slightly more frequent in high-level fractures (4.9% vs. 3.5%), this difference was not statistically significant (p=0.114), possibly reflecting the surgeons' expertise. Achieving stable fixation in high-level fractures is challenging because K-wires often remain within the medullary canal rather than engaging the far cortex, reducing stability.[6,22] Additionally, the required spacing of wires at the fracture site, typically one-third of the fracture length or at least 13 mm, is difficult to maintain in high-level fractures.[6] Despite these technical challenges, the revision surgery rate and postoperative translation did not differ significantly between groups (p=0.492 and p=0.942, respectively), suggesting that with careful technique, outcomes can be comparable.

High-level fractures can be further categorized as transverse or oblique. In our cohort, 75% were transverse and 25% oblique, differing from Fayssoux et al.'s.[6] study, in which oblique fractures predominated (57%). Age distribution was similar to the known peak incidence of PHSF (5-8 years),[23] although our study showed oblique fractures presenting at a slightly higher mean age than transverse fractures (7.1 vs. 6.5 years). Operation times did not differ significantly between fracture types (p=0.746), but the need for divergent K-wire configuration was higher in oblique fractures (p=0.049). Furthermore, oblique fractures had a significantly higher revision rate (p=0.004), highlighting their increased technical complexity.

Hai Zou et al.[19] suggested that intramedullary K-wire insertion after coronal plane reduction facilitates rotational and sagittal alignment in metaphyseal-diaphyseal fractures; however, we did not utilize this technique. Postoperative rotational deformities were more common in high-level fractures, but without statistical significance (p=0.229).

Neurovascular injury rates did not differ significantly between fracture levels, although anterior interosseous nerve and ulnar nerve injuries tended to be slightly more frequent in high-level fractures (4.4% and 6.1%, respectively). The lack of significant difference in associated injuries suggests that high-level fractures do not necessarily result from higher-energy trauma.

Intraoperative multiple K-wire insertion attempts may increase cortical damage, seen radiographically as wire-induced scars. Our finding of significantly more K-wire scars in high-level fractures (p=0.042) underscores the technical difficulties encountered during fixation.

Limitations of this study include its retrospective design and the fact that surgeries were performed by multiple surgeons, which could introduce variability. However, the large sample size strengthens the validity of our findings.

CONCLUSION

This study demonstrates that pediatric supracondylar humerus fractures with a fracture line proximal to the olecranon fossa present greater surgical challenges, including increased instability, longer operative times, and a higher number of intraoperative pinning attempts. Among these, oblique high-level fractures are especially prone to technical challenges and exhibit significantly higher revision rates compared to transverse fractures.

Clinically, recognizing the fracture line's position relative to the olecranon fossa can aid surgeons in preoperative planning and patient counseling by anticipating potential difficulties and the need for more meticulous fixation strategies. This anatomical landmark should be integrated into the assessment protocol for pediatric supracondylar fractures to optimize surgical outcomes.

Our findings extend the existing literature by quantitatively establishing the olecranon fossa as a practical and relevant threshold for predicting surgical complexity and prognosis in these fractures. This contributes valuable insights that may influence decision-making and improve management strategies for pediatric supracondylar humerus fractures.

Ethics Committee Approval: This study was approved by the S.B.U. İzmir Tepecik Research and Training Hospital Ethics Committee (Date: 22.02.2021, Decision No: 2021/02-18).

Peer-review: Externally peer-reviewed.

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Authorship Contributions: Concept: E.E., A.T.; Design: E.E., A.T.; Supervision: E.E., A.T.; Resource: E.E., A.T.; Materials: E.E., A.T.; Data collection and/or processing: E.E., A.T.; Analysis and/or interpretation: E.E., A.T.; Literature review: E.E., A.T.; Writing: E.E., A.T.; Critical review: E.E., A.T.

Conflict of Interest: None declared.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Pediatrik suprakondiler humerus kırıklarında kırık hattının olekranon fossaya göre pozisyonu cerrahi zorluğu ve sonuçları etkiler mi?

AMAÇ: Bu çalışmanın amacı, pediatrik suprakondiler humerus kırıklarında (PSHK) kırık hattının olekranon fossaya göre seviyesinin, cerrahi zorluk, komplikasyon oranları ve radyolojik sonuçlar üzerindeki etkisinin araştırılmasıdır.

GEREÇ VE YÖNTEM: PSHK tanısıyla cerrahi tedavi uygulanmış 822 olgu retrospektif olarak incelendi. Kırık hattının olekranon fossa apeksine konumuna göre hastalar iki gruba ayrıldı: Yüksek seviye (fossanın proksimalinde, n=163) ve düşük seviye (fossada veya distalinde, n=659). Yüksek seviye kırıklar, kırık hattı ile trans-epikondiler çizgi arasındaki açıya göre oblik (n=40) ve transvers (n=123) olarak sınıflandırıldı. Demografik veriler, kırık özellikleri, cerrahi parametreler, komplikasyonlar, radyografik bulgular ve revizyon oranları değerlendirildi.

BULGULAR: Gruplar arasında demografik özellikler, kırık tarafı, açık-kapalı kırık durumu, nörovasküler yaralanma veya eşlik eden travma açısından anlamlı fark saptanmadı (p>0.1). Yüksek seviye kırıklar, düşük seviye kırıklara kıyasla anlamlı derecede daha instabildi, daha uzun cerrahi süreye sahipti ve daha fazla K-teli kortikal izi sergiledi (p<0.05). K-teli konfigürasyonu, sayısı ve çapı açısından anlamlı fark bulunmadı. Alt grup analizinde, oblik yüksek seviye kırıkların diverjan pin konfigürasyonuna daha sık ihtiyaç duyduğu ve transvers yüksek seviye kırıklara göre anlamlı derecede daha yüksek revizyon oranına sahip olduğu görüldü (sırasıyla, p=0.049 ve p=0.004).

SONUÇ: Olekranon fossanın proksimalinde yer alan kırıklar, daha instabil olup teknik olarak daha zorludur; bu durum daha uzun ameliyat süresi ve daha fazla intraoperatif pinleme girişimine yol açmaktadır. Yüksek seviye kırıklar arasında oblik tipler, teknik güçlükler ve artmış revizyon oranı açısından özellikle risklidir. Bu bulgular, cerrahi planlamada fraktür morfolojisinin önemini vurgulamaktadır.

Anahtar sözcükler: Dirsek kırığı; humerus kırığı; pediatrik suprakondiler humerus kırığı.

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ORIGINAL ARTICLE

The medial-first approach in unstable pediatric supracondylar humerus fractures: association with reduced need for additional exposure and improved cosmetic outcomes

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ABSTRACT

BACKGROUND: This study aimed to compare the clinical, cosmetic, and surgical outcomes of medial-first and lateral-first open reduction approaches in the treatment of unstable pediatric supracondylar humerus fractures when closed reduction fails.

METHODS: In this retrospective comparative study, 68 pediatric patients (aged 2–10 years) with Gartland Type III and IV supracondylar humerus fractures requiring open reduction were evaluated. Patients were divided into two groups based on the initial surgical approach: medial-first (n=31) and lateral-first (n=37). Demographic characteristics, surgical time, pin configuration, range of motion, Flynn's functional and cosmetic outcomes, and postoperative complications were compared between groups.

RESULTS: The medial-first group demonstrated significantly shorter surgical times (55.5±16.0 vs. 72.0±20.2 minutes, p<0.001) and superior cosmetic outcomes (excellent cosmetic Flynn's scores in 83.9% vs. 62.2%, p=0.0408). The need for an additional incision was markedly higher in the lateral-first group (0 vs. 18 patients, p<0.00001). Functional outcomes and complication rates were comparable between groups.

CONCLUSION: The medial-first approach in unstable pediatric supracondylar humerus fractures offers advantages in surgical efficiency and cosmetic outcomes while minimizing the need for secondary incisions. It represents a safe and effective option for achieving stable fixation when closed reduction is unsuccessful.

Keywords: Pediatric supracondylar humerus fracture; open reduction; Flynn's criteria; medial approach; lateral approach; cosmetic outcome.

INTRODUCTION

Pediatric supracondylar humerus fractures (SCHFs) are among the most common elbow injuries in children and typically result from a fall onto an outstretched hand.[1] While nonoperative management is appropriate for nondisplaced fractures (Gartland Type I), displaced fractures (Types II-IV) generally require surgical intervention, with closed reduction and percutaneous pinning (CRPP) being the preferred treatment method.[2] However, due to the severity of trauma, significant displacement may occur, which can also lead to soft-tissue interposition, rendering closed reduction unsuccessful in approximately 2-15% of cases according to the literature.[3] In such scenarios, open reduction is often required to restore

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anatomical alignment and achieve stable fixation.[4,5]

The surgical approach for open reduction remains a topic of ongoing debate. Although lateral pinning alone is biomechanically sufficient in many cases, bicolumnar (crossed medial-lateral) pinning provides greater rotational and varus/valgus stability, particularly in unstable fractures (Gartland Types III and IV).[6] However, medial pinning carries a risk of iatrogenic ulnar nerve injury, especially when anatomical landmarks are obscured by soft-tissue swelling.[7] To mitigate this risk, some authors recommend a small medial incision for direct visualization and protection of the nerve during pin placement.[8,9]

Given these considerations, the choice of surgical approach in cases requiring open reduction remains controversial. Furthermore, when open reduction is necessary, there is no clear consensus on the optimal surgical approach. Surgeons frequently prefer the lateral approach due to its familiarity and ease of access; however, this technique may limit visualization of the medial column, potentially resulting in malreduction[11] (e.g., cubitus varus) or suboptimal cosmetic outcomes. Eren et al.[12] reported higher patient satisfaction in the medial-open group compared to the lateral-open group in their studies. A recent study also suggests that medial or anterior approaches may provide better functional and cosmetic results with lower complication rates.[13]

Despite literature supporting surgeon-dependent approach selection,[14-16] we propose that a medial-first open approach for treating unstable SCHFs (Types III/IV) offers distinct advantages:

1. Minimizes the need for combined approaches: Lateral-first techniques often fail to adequately reduce the medial column, necessitating secondary medial exposure.

2. Enhanced safety and efficiency: Direct ulnar nerve visualization minimizes iatrogenic injury, while improved alignment reduces operative time.

3. Improved outcomes: Anatomic reduction and stable bicolumnar fixation may lower complication rates (e.g., malunion) and enhance cosmetic outcomes.

Although there are numerous studies in the literature on pediatric supracondylar humerus fractures, very few include sufficient follow-up periods to compare medial and lateral open approaches and comprehensively address their outcomes.

Therefore, in this study, we hypothesize that a medial-first strategy optimizes biomechanical stability and clinical outcomes in unstable supracondylar humerus fractures by reducing the need for combined approaches, enhancing safety through direct neurovascular visualization, and improving fracture alignment efficiency.

MATERIALS AND METHODS

Ethical approval was obtained from the Institutional Review Board (Approval No: [28/192]), and written informed consent was obtained from the legal guardians of all pediatric participants, in accordance with the principles of the Declaration of Helsinki. This research is a single-center, retrospective comparative study involving multiple surgeons. A retrospective evaluation was performed on 631 pediatric patients who were diagnosed with supracondylar humerus fractures at our hospital between 2014 and 2023. The inclusion criteria were as follows:

1. pediatric patients between the ages of 2-10 years,

2. patients who underwent open reduction after attempted closed reduction due to inadequate fracture alignment,

3. patients in whom a medial incision was used as the first incision, and

4. patients in whom a lateral incision was used as the first incision.

The indication for open reduction was the failure of closed reduction attempts, depending on the surgeon's decision and experience. Patients with concomitant fractures, open fractures, vascular injuries in the same extremity, or diagnosed compartment syndrome at presentation were excluded from the study, as were those with a history of previous fractures around the elbow joint. The minimum follow-up period in this study was two years, and patients who did not complete follow-up before this time were excluded from the study. The study flowchart is presented in Figure 1.

Patients were divided into two groups: those who underwent a medial incision (medial-first group) as the initial open approach and those who underwent a lateral incision (lateral-first group). Cases in which a secondary incision was used during surgery, such as a mini-open medial approach to protect the ulnar nerve during pin placement, were also noted.

Data Collection

The demographic, intraoperative, and follow-up data of all patients were analyzed. The collected variables included age, gender, affected side, Body Mass Index, and Gartland classification. Both intraoperative complications and early or late postoperative complications-including infection, range-of-motion limitations, nonunion, deformity, loss of reduction, and heterotopic ossification with clinical manifestations-were documented. Additionally, the pin configuration used for fixation was recorded.

Joint range of motion was assessed using a goniometer at one year postoperatively and at the final follow-up visit. Baumann's angle was measured from radiographs obtained within the first postoperative year. Pin tract infections and nerve injuries were evaluated based on outpatient follow-up records.

A standardized postoperative follow-up protocol was implemented for all patients. A long arm splint was applied immediately after surgery and removed within three weeks to allow elbow mobilization. Patients were instructed to per-

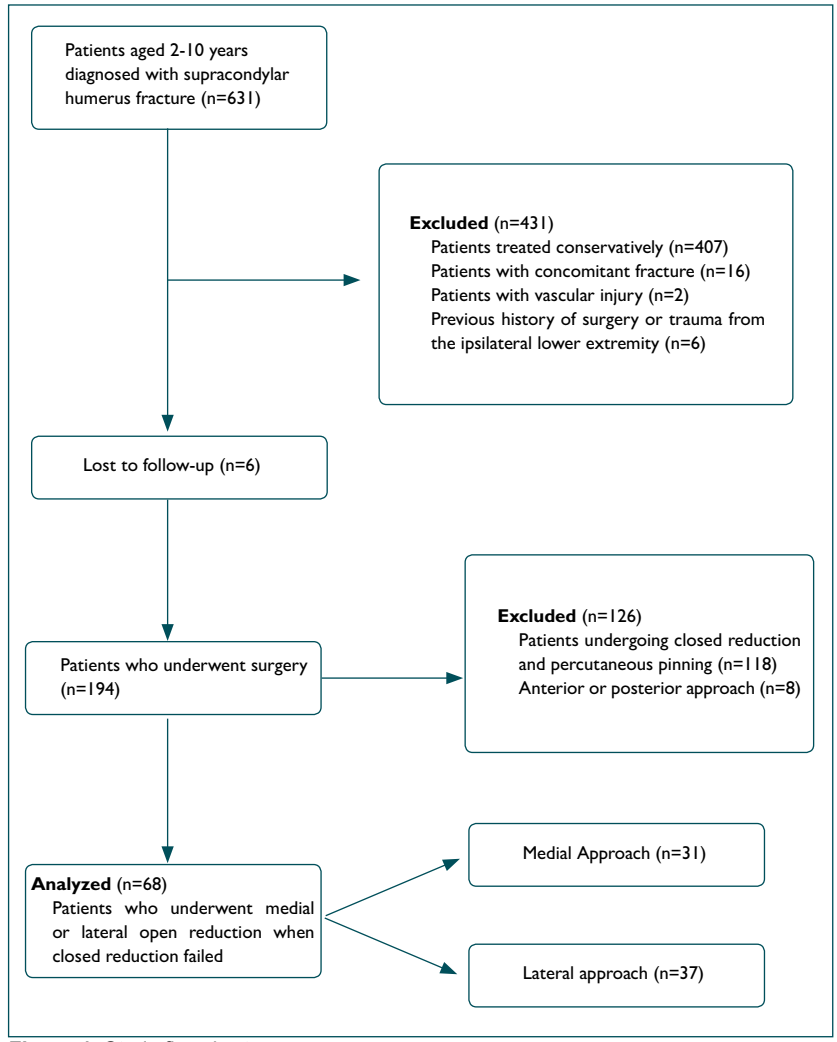

Figure 1. Study flowchart.

form daily pin care throughout the follow-up period. The pins were removed approximately four weeks postoperatively, after callus formation was confirmed on standard anteroposterior and lateral radiographs. Routine radiographic and clinical follow-up assessments were conducted at the fourth and sixth weeks, as well as at the third, sixth, and twelfth months postoperatively.

The final assessment was conducted based on Flynn's criteria, which evaluate both cosmetic and functional outcomes. Cosmetic outcomes were determined by the degree of loss in the carrying angle, while functional outcomes were assessed based on the degree of motion loss. According to Flynn's classification, a loss of 0-5° is considered excellent, 6-10° good, 11-15° fair, and ≥16° poor. The evaluations based on Flynn's criteria were performed at the 12-month postoperative follow-up. After the first year, patients were monitored for late complications and routine fracture follow-up, including poor union progression, remodeling, heterotopic ossification, or cubitus varus.

Surgical Technique

All operations were performed by experienced surgeons using lateral, medial, or combined approaches. Fluoroscopic-guided closed reduction and percutaneous pinning were initially attempted in all patients. In cases where adequate reduction could not be achieved through closed reduction, an open surgical approach was performed. All open procedures were conducted under general anesthesia with the patient positioned supine on a radiolucent table, and a sterile tourniquet was applied prior to surgery. Standard prophylaxis with a first-generation cephalosporin was administered to all patients 30 minutes preoperatively, with dosages adjusted according to age and weight.

In the medial-first group, the medial approach was initiated with a skin incision extending from 5 cm proximal to the medial epicondyle to the distal joint line. The ulnar nerve was identified and carefully protected. The incision traversed the intermuscular septum to expose the distal humerus. (Fig. 2). In the lateral-first group, a lateral approach was used, with a

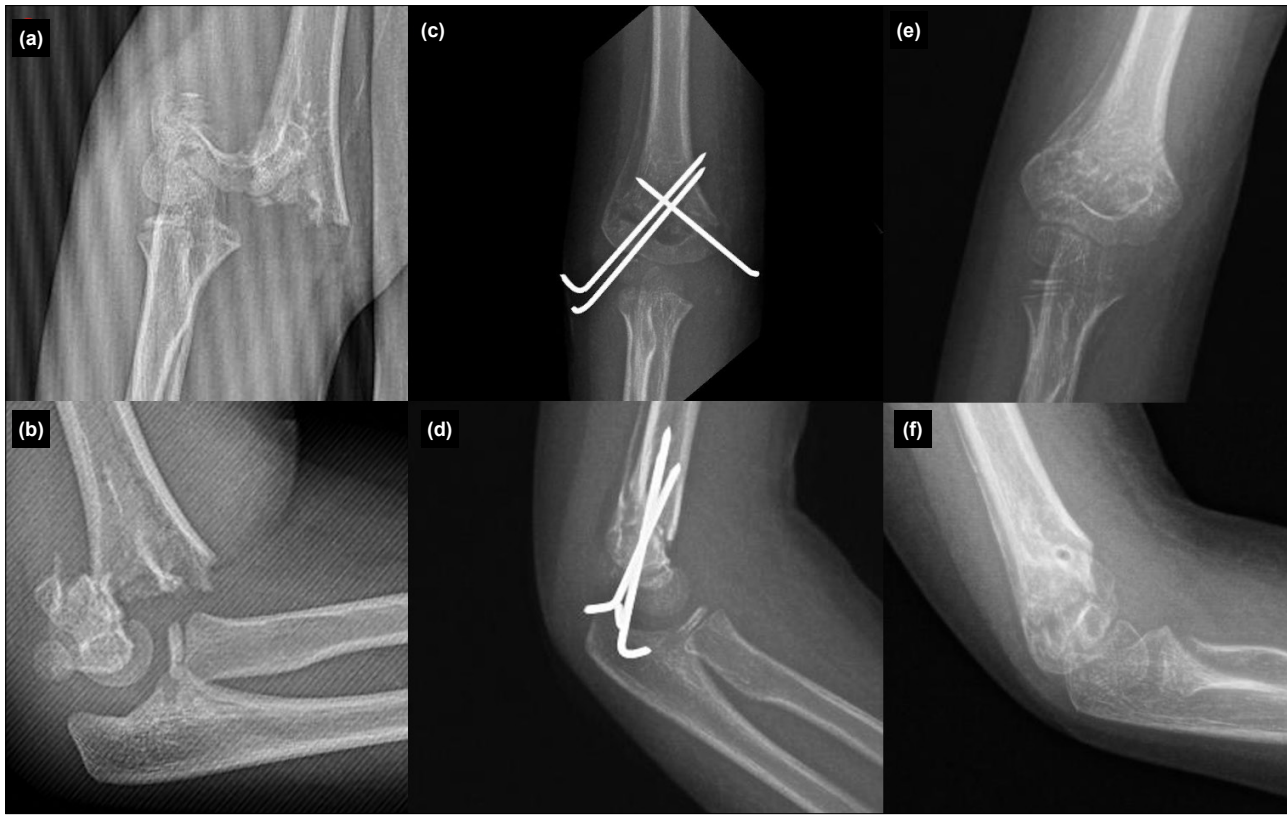

Figure 2. Preoperative, postoperative, and follow-up anteroposterior and lateral radiographs of a patient who underwent surgery using the medial-first approach.

skin incision extending from approximately 2 cm proximal to 1 cm distal to the lateral epicondyle. To visualize the lateral border of the humerus, the interval between the extensor carpi radialis longus, triceps brachii, and brachialis muscles was utilized (Fig. 3).

In the medial-first approach group, lateral pinning was performed percutaneously. In the lateral- first approach group, medial pinning was performed either percutaneously or via an additional medial incision, during which the ulnar nerve was meticulously identified and protected.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics 22 (IBM SPSS Corp., Armonk, NY, USA). The Shapiro–Wilk test was employed to assess the normality of continuous variables, which were determined to follow a normal distribution. Descriptive statistics were presented as mean ± standard deviation for continuous variables, while categorical variables were reported as frequencies and percentages.

For comparisons involving quantitative data and normally distributed variables, a one-way analysis of variance (ANOVA) was performed. Categorical data were analyzed using the chi-square test. A P-value of <0.05 was considered statistically significant.

RESULTS

Patient Demographics

A total of 68 patients were included in the study, with 31 patients in the medial-first group and 37 in the lateral-first group. Baseline demographic and clinical characteristics of the study groups are presented in Table 1. No significant differences were found in baseline demographics between the two groups. There was also no statistically significant difference between the groups in terms of displacement direction (p=1.000). The mean follow-up duration was comparable (70.2±21.0 vs. 66.4±25.2 months, p=0.631).

The mean surgical time was significantly shorter in the medial-first group compared to the lateral-first group (55.5±16.0 minutes vs. 72.0±20.2 minutes, p<0.001). Baseline demographic and clinical characteristics of the study groups are presented in Table 1.

Clinical and Functional Outcomes

Mean flexion loss was 2.7°±1.6 in the medial-first group and 3.0°±2.0 in the lateral-first group (p=0.144), while mean extension loss was 4.5°±2.3 and 5.8°±3.1, respectively (p=0.216).

According to Flynn's functional criteria, excellent or good

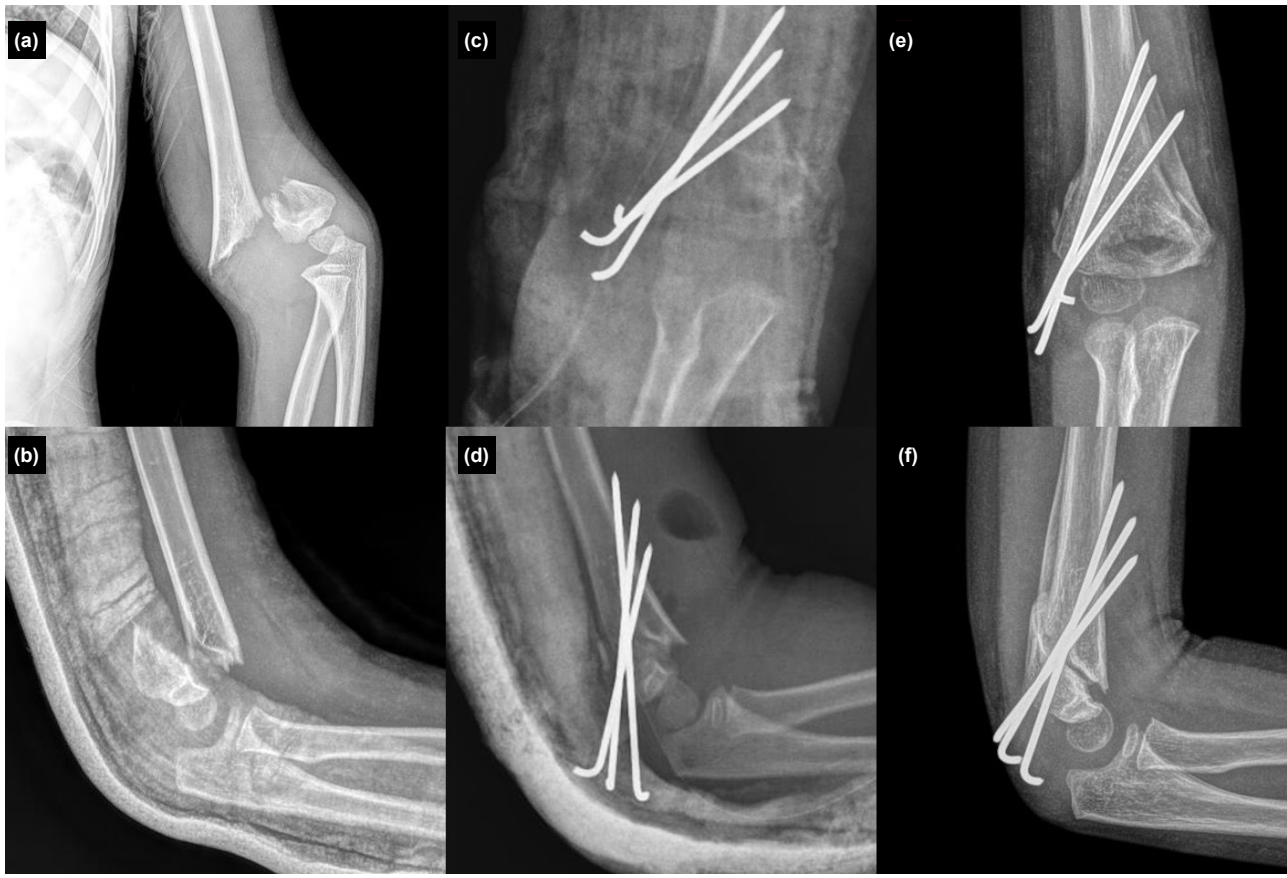

Figure 3. Preoperative, postoperative, and follow-up anteroposterior and lateral radiographs of a patient who underwent surgery using the lateral-first approach.

Table 1. Patient demographics and baseline characteristics

Variable	Medial-First Group (n=31)	Lateral-First Group (n=37)	p-value
Age (years, mean±SD)	5.3±2.6	5.6±3.4	0.0974
Sex (Male/Female)	18/13	22/15	1
BMI (mean±SD)	16.8±2.4	16.2±3.2	0.777
Side (Right/Left)	19/12	23/14	1
Gartland Type III	11 (35.5%)	14 (37.8%)	1
Gartland Type IV	20 (64.5%)	23 (62.2%)	1
Follow-up duration (mean, months)	70.2±21.0	66.4±25.2	0.631
Surgical Time (mean, minutes)	55.5±16.0	72±20.2	<0.0001

outcomes were achieved in 96.8% of the medial group and 91.9% of the lateral group (p=0.6779), with no cases classified as poor in either group.

In contrast, Flynn's cosmetic outcomes showed a statistically significant difference between groups (p=0.0408). Excellent cosmetic results were obtained in 83.9% of the medial-first group versus 62.2% of the lateral-first group, while fair cosmetic outcomes were observed only in the lateral group (16.2%) (Fig. 4).

Regarding pin configuration, all patients in the medial-first group received medial + lateral pinning (100%), whereas this configuration was used in only 56.7% of the lateral-first group.

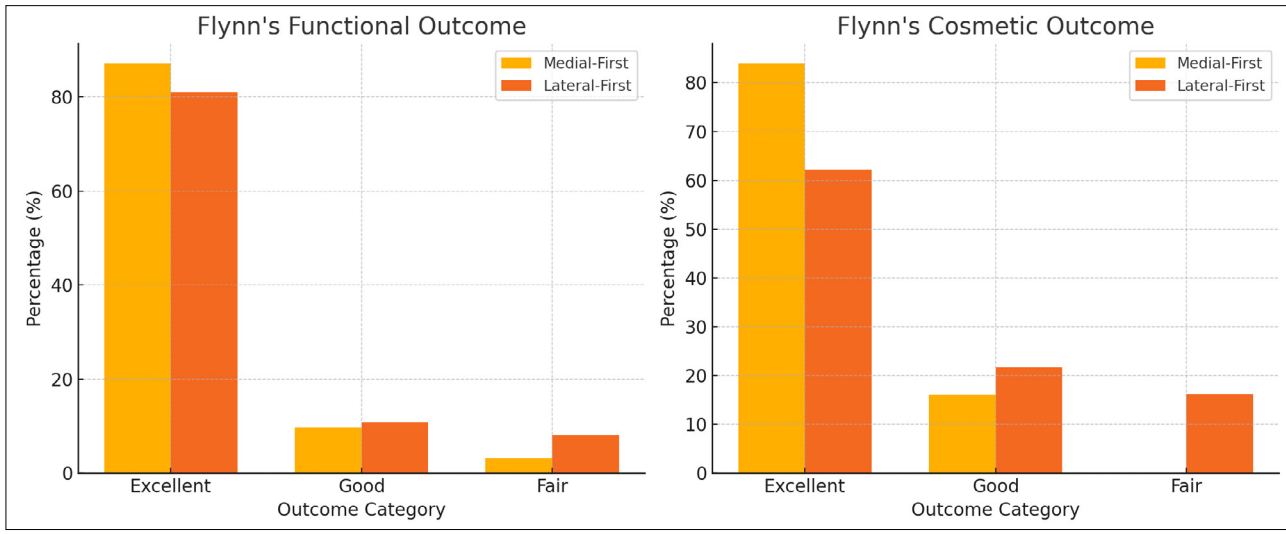

Figure 4. Distribution of functional and cosmetic outcomes according to Flynn's criteria in medial-first and lateral-first approaches.

Table 2. Clinical and functional outcomes

Outcome Measure	Medial-First Group (n=31)	Lateral-First Group (n=37)	p-value
Flexion loss (°, mean±SD)	2.7°±1.6	3.0°±2.0	0.144
Extension loss (°, mean±SD)	4.5°±2.3	5.8°±3.1	0.216
Flynn's Functional Outcome (%)			0.6779
Excellent (0-5°)	27 (87.1%)	30 (81.1%)	
Good (6-10°)	3 (9.7%)	4 (10.8%)	
Fair (11-15°)	1 (3.2%)	3 (8.1%)	
Poor (≥16°)	-	-	
Flynn's Cosmetic Outcome (%)			0.0408
Excellent (0–5°)	26 (83.9%)	23 (62.2%)	
Good (6–10°)	5 (16.1%)	8 (21.6%)	
Fair (11–15°)	-	6 (16.2%)	
Poor (≥16°)	-	-	
Pin Configuration			
Medial+Lateral	31 (100%)	21 (56.7%)	0.0002
Two Lateral Pins	0	9 (24.3%)	0.0029
Three Lateral Pins	0	7 (18.9%)	0.0133

The remaining lateral-first group patients were treated with either two (24.3%) or three (18.9%) lateral pins. The differences in pin configuration between groups were statistically significant (p=0.0002 for medial + lateral vs. others, p=0.0029 for two lateral, and p=0.0133 for three lateral pin configurations). Clinical and functional outcomes, including range of motion, Flynn's scores, and pin configuration, are summarized in Table 2.

Complications

A low overall rate of complications was observed, with specific adverse events distributed across both groups as follows: pin tract infections occurred in two patients in the medial group and one in the lateral group (p=0.588). Ulnar nerve injury was observed in two patients in the lateral-first group, while no such cases occurred in the medial-first group (p=0.496). In both patients who showed clinical signs of early

Table 3. Complications

Complication Type	Medial-First Group (n=31)	Lateral-First Group (n=37)	p-value
Pin tract infection	2	1	0.588
Ulnar nerve injury	0	2	0.496
Loss of reduction	0	2	0.496
Heterotopic ossification	1	1	1
Nonunion	0	0	1
Additional incision	0	18	<0.0001
Revision surgery	0	2	0.496

postoperative ulnar nerve impairment, open reduction had been performed via the lateral approach, and the medial pin was inserted percutaneously. On the following day, in one patient, the medial pin was removed due to signs of ulnar nerve irritation. The other patient underwent reoperation the following day for ulnar nerve exploration, during which the medial pin was replaced. Similarly, loss of reduction was reported in two patients in the lateral-first group and in none of the medial-first group (p=0.496). The medial pin was not used in either of these patients. However, no additional intervention was performed for loss of reduction, and the patients were followed throughout the remodeling process. Heterotopic ossification occurred in one patient per group (p=1.000), and there were no cases of nonunion.

The need for an additional incision during surgery was significantly more common in the lateral-first group (0 vs. 18 patients, p<0.00001). Among the patients who required an additional incision, a secondary medial incision was used to safely place the medial pin in 7 of 18 patients, while in 11 patients, an additional medial incision was necessary because reduction was not successful using the lateral approach alone. One patient in the lateral group required revision surgery, whereas no revisions were necessary in the medial group. One patient underwent revision surgery the following day due to postoperative ulnar nerve symptoms. No new complications were observed during the long-term follow-up period. The incidence and distribution of postoperative complications in both groups are detailed in Table 3.

DISCUSSION

The most important finding of our study is that the medial-first approach reduces the need for dual incisions in unstable supracondylar humerus fractures. In addition, it was observed that more medial pins were used in patients treated with the medial approach, as the concern for ulnar nerve injury was eliminated. Loss of reduction was also less frequent in the medial-first group throughout the follow-up period.

The treatment strategy for unstable supracondylar humerus fractures in which proper alignment cannot be achieved with closed reduction is controversial. Recent biomechanical studies have shown that the use of bicolumnar pins provides the most stable fixation in unstable supracondylar humerus fractures. From this perspective, the effect of medial pin use on stability in these patients is clear. When the medial-first approach is used, there is no concern about adding lateral pins or the number of medial pins. This allows the use of as many pins as needed to increase stability.

On the other hand, when the lateral-first approach is used, it is necessary either to protect the ulnar nerve with a medial incision or to accept the risk of closed medial pin placement in a swollen arm with poorly defined landmarks. The third alternative is to complete the surgery with lateral pins only, without placing a medial pin, resulting in a less stable fixation. In our series, greater loss of reduction was observed in the patient group in which only lateral pins were used.

Loss of carrying angle has been reported as the most common complication of the lateral open approach.[12,13] In the systematic review by Gonzalez-Morgado et al.,[13] the posterior and lateral approaches were associated with a higher relative risk (RR) for unsatisfactory cosmetic Flynn's scores compared to the medial approach. The medial and anterior approaches showed a lower RR for unsatisfactory cosmetic results. They reported that a possible explanation for this finding is that these approaches provide better exposure of the medial column and facilitate correction of internal rotation of the distal fragment, which contributes to loss of the carrying angle and varus deformity. In our study, we observed better cosmetic scores and less loss of carrying angle in the medial-first group.

Kizilay et al.[17] compared open approaches used when closed reduction failed in their study. They reported that the medial and lateral approaches yielded better cosmetic and functional results than the posterior approach, while the medial approach showed the best results according to the Flynn

score after closed reduction. In our study, we also observed that the medial approach was associated with better results in terms of Flynn scores compared to the lateral approach. However, the main point we want to emphasize in our study is that when the medial approach is used, there is no need for an additional incision, whereas when the lateral approach is used, an additional incision is required for both medial column reduction and medial pin placement.

Another important aspect involves the differences in the trabecular bone structure of the distal humerus. Diederichs et al.[18] found the lowest trabecular bone density in the capitellum region and reported high trabecular bone density on the medial side. Therefore, it can be predicted that medial pins will provide greater stability than lateral pins. Consequently, the medial approach facilitates medial pin placement, which is a significant advantage. In our study, we observed poorer outcomes in patients who did not receive medial pins.

Although several studies support selecting the surgical approach based on the direction of fracture displacement, a more nuanced view suggests that the incision should be made on the side of maximum soft-tissue injury rather than strictly following the displacement pattern.[13] In many cases, soft-tissue trauma does not perfectly align with the direction of the metaphyseal spike seen on radiographs. For instance, in many fractures, the medial periosteum and soft tissues are often disrupted, making a medial approach more logical and potentially facilitating reduction.[12,13] Conversely, if lateral soft-tissue injury is more severe, a lateral approach may be preferable.[19] This perspective emphasizes that surgical access through the injured side may be more physiologic and technically effective, as attempting reduction from the intact side can increase the risk of further soft-tissue damage and may complicate the procedure. However, in our study, no statistically significant difference was observed between posteromedial and posterolateral displacement patterns in terms of the chosen surgical approach. Furthermore, there was no apparent correlation between the direction of soft-tissue injury and the type of incision performed.

Eren et al.[12] reported that the medial incision was cosmetically preferred when patients were asked about their satisfaction. They concluded that the medial approach is more appropriate for displaced supracondylar humerus fractures because of the lower incidence of ulnar nerve injury and less cubitus varus deformity due to accurate evaluation of the medial column. Our results also suggest that the medial approach provides better cosmetic outcomes as well as proper postoperative alignment and stability.

Yavuz et al.,[20] in a multicenter study comparing four different surgical approaches, reported that each approach yielded similar results. They suggested that the choice of approach should be based on surgical experience. However, surgical time was not included in their analysis. In our series, the medial-first approach was statistically significantly shorter in surgical time compared to the lateral-first approach. An important reason for this was likely that no additional incision was required during surgery. In addition, percutaneous placement of lateral pins after medial pin placement may be relatively easier.

This study had some limitations. First, although the overall study population was large (631 patients), we applied strict exclusion criteria to include only unstable patients who required open reduction, resulting in a relatively small final study group of 68 patients across both groups. Second, the retrospective nature of the study introduces some selection bias. The decision regarding incision type and pin configuration was made by the treating surgeon, with potential variability between individual assessments. Third, the decision to convert from closed to open reduction was also surgeon-dependent, and it was not possible to determine which incision group had more unstable fractures. In our clinic, closed reduction and percutaneous pinning are routinely preferred as the first-line treatment for all supracondylar humerus fractures. It is standard practice to attempt closed reduction initially and proceed to open reduction only if the closed approach fails. However, we acknowledge that the threshold for converting to open reduction may vary among surgeons, and some may opt for open reduction more readily in cases where they are not fully satisfied with the alignment achieved through closed techniques. This variation in clinical decision-making may represent a limitation in the generalizability of our findings. Finally, since no surgeon in our clinic routinely uses an anterior incision in patients without vascular injury, the anterior approach is reserved only for cases with suspected vascular injury. In our study, patients with vascular injury who underwent the anterior approach were excluded; therefore, it was not possible to compare the anterior approach with other techniques. Although our study addresses some important questions despite these limitations, multicenter prospective randomized controlled trials with larger cohorts comparing different approaches are needed to validate these findings and further investigate outcomes in this challenging fracture type.

CONCLUSION

In the surgical management of unstable supracondylar humerus fractures requiring open reduction, our findings suggest that the medial-first approach offers notable clinical advantages over the lateral-first approach. This technique not only reduces the need for additional incisions but also facilitates safe and effective medial pin placement, contributing to enhanced construct stability and fewer cases of reduction loss. Moreover, better cosmetic outcomes and shorter operative times were observed in the medial-first group. These results support the preference for the medial approach in cases where closed reduction is unsuccessful, given its contribution to stable fixation, improved alignment, and patient satisfaction. Nevertheless, the potential benefits of the surgeon's experience and familiarity with a particular approach should

not be overlooked.

Ethics Committee Approval: This study was approved by the University of Health Sciences Baltalimani Bone Diseases Training and Research Hospital Ethics Committee (Date: 28.10.2024, Decision No: 28/192).

Informed Consent: Written informed consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: K.A., E.A.; Design: K.A., E.A.; Supervision: E.A., B.O.; Resource: G.K., M.B.K.; Materials: S.S., G.K.; Data collection and/or processing: G.K., B.O.; Analysis and/or interpretation: M.B.K., B.O.; Literature review: S.S., G.K.; Writing: K.A.; Critical review: B.O., E.A.

Conflict of Interest: None declared.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Stabil olmayan pediatrik suprakondiler humerus kırıklarında medial-öncelikli yaklaşım: Ek insizyon gereksiniminin azalması ve kozmetik sonuçlardaki iyileşme ile ilişkisi

AMAÇ: Kapalı redüksiyonun başarısız olduğu durumlarda, instabil pediatrik suprakondiler humerus kırıklarının tedavisinde medial-öncelikli ve lateral-öncelikli açık redüksiyon yaklaşımlarının klinik, kozmetik ve cerrahi sonuçlarını karşılaştırmak.

GEREÇ VE YÖNTEM: Bu retrospektif karşılaştırmalı çalışmada, açık redüksiyon gerektiren Gartland Tip III ve IV suprakondiler humerus kırığı tanısı almış, 2-10 yaş aralığındaki 68 pediatrik hasta değerlendirildi. Hastalar, uygulanan ilk cerrahi yaklaşıma göre iki gruba ayrıldı: Medial-öncelikli (n=31) ve lateral-öncelikli (n=37). Demografik özellikler, cerrahi süresi, pin konfigürasyonu, eklem hareket açıklığı, Flynn'ın fonksiyonel ve kozmetik sonuçları ile postoperatif komplikasyonlar gruplar arasında karşılaştırıldı.

BULGULAR: Medial-öncelikli grupta cerrahi süre anlamlı düzeyde daha kısa bulundu (55.5±16.0 dakika ve 72.0±20.2 dakika, $p<0.001$) ve kozmetik sonuçlar daha üstündü (Flynn'ın kozmetik skorunda mükemmel sonuç oranı: %83.9 ve %62.2, $p = 0.0408$). Ek bir insizyon ihtiyacı lateral-öncelikli grupta belirgin şekilde daha fazlaydı (0 ve 18 hasta, $p<0.00001$). Fonksiyonel sonuçlar ve komplikasyon oranları ise gruplar arasında benzerdi.

SONUÇ: Kapalı redüksiyonun yetersiz kaldığı instabil pediatrik suprakondiler humerus kırıklarında medial-öncelikli yaklaşım, cerrahi etkinlik ve kozmetik sonuçlar açısından avantaj sağlamakta ve ek insizyon ihtiyacını azaltmaktadır. Bu yaklaşım, stabil fiksasyon sağlamak için güvenli ve etkili bir seçenek olarak değerlendirilebilir.

Anahtar sözcükler: Açık redüksiyon; Flynn kriterleri; kozmetik sonuç; lateral yaklaşım; medial yaklaşım; pediatrik suprakondiler humerus kırığı.

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ORIGINAL ARTICLE

Is long arm splinting sufficient in the nonsurgical follow-up of pediatric Type I and Type IIa supracondylar humerus fractures?

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ABSTRACT

BACKGROUND: This study aims to compare the radiological and functional outcomes of long arm casting versus splinting in the nonsurgical treatment of pediatric supracondylar humerus fractures classified as Modified Gartland type I and IIa.

METHODS: Between January 2021 and January 2024, 112 pediatric type I and IIa supracondylar humerus fractures (SCHFs) treated nonoperatively with long arm splinting or casting were evaluated. Baumann angle and lateral capitellohumeral angle (LCHA) were measured pre-reduction, post-reduction, and at weeks 1 and 4. Outcomes were compared using Flynn's criteria.

RESULTS: Of the 112 patients, 55 had type I (49%) and 57 had type IIa (51%) fractures (mean age: 7.51 years; 69 males, 43 females). Fractures were equally distributed between the right and left sides (n=56 each). Fifty-eight patients were treated with long arm splinting and 54 with long arm casting. Follow-up durations were similar between groups. In the splint group, the mean Baumann angle was 72.1° pre-reduction and 73.2° at week 4; in the cast group, it was 70.7° and 73.4°, respectively. Mean LCHA increased from 43.9° to 50.8° with splinting and from 42.4° to 50.1° with casting. A statistically significant difference was not observed for loss of reduction between the splinting and casting groups (p=0.475). No statistically significant differences were observed in LCHA (p=0.175), Baumann angle values (p=0.485), or Flynn scores (p=0.768) pre- and post-reduction in type I and type IIa SCHFs.

CONCLUSION: Splinting and casting yielded comparable clinical and radiological outcomes in nonsurgically managed Modified Gartland type I and IIa supracondylar humerus fractures. However, splinting stands out as a strong alternative due to its ease of application and lower complication rates.

Keywords: Supracondylar humerus; fractures; elbow; reduction; pediatric.

INTRODUCTION

Supracondylar humerus fractures (SCHFs) occur primarily before 10 years of age,[1] accounting for 3% to 18% of all reported pediatric fractures.[2-5] The instability observed in cases of Modified Gartland types IIb and III SCHFs generally necessitates surgical treatment.[6-8] While there is widespread consensus on the most appropriate treatments for types I, IIb, and III SCHFs, treatment approaches for type IIa remain controversial.[9] The American Academy of Orthopaedic Surgeons published updated clinical practice guidelines in 2011 for treating pediatric SCHFs.[7,10] Treatment of type IIa SCHFs with the application of closed reduction and percutaneous pinning was moderately recommended. Nevertheless, many pediatric orthopedists would still argue that the application of closed reduction followed by immobilization is sufficient for the treatment of pediatric patients with type IIa SCHFs.[11-15] In the present study, closed reduction was first applied for

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types I and IIa fractures, and the patients were subsequently followed with long arm splinting or casting.

Immobilization of stable types I and IIa fractures for 4 weeks generally yields satisfactory functional results. As soon as the fracture has healed, movement of the limb should begin.[16] Conservatively managed fractures may be addressed with various immobilization strategies, including long arm casting or splinting. With both of these strategies, the elbow is immobilized in flexion at a 90° angle, with the forearm held in supine neutral positioning.[3,17] The most widely utilized treatment approach entails the application of a circular cast with immobilization for 3 to 4 weeks.[18,19] However, based on their review of the literature, Cuomo et al. suggested that long arm splinting may also constitute a viable treatment approach, especially for type I SCHFs.[20] No research has been reported in the literature to date comparing the effectiveness of long arm splinting and long arm casting for SCHFs of type I and type IIa. The present study is the first to be conducted on type I and especially type IIa fractures in this context. We aimed to evaluate and compare the long-term functional and radiographic results and complication rates of pediatric cases of types I and IIa SCHFs treated with long arm splinting or long arm casting.

MATERIALS AND METHODS

The study was approved by the Ethics Committee of Erzurum City Hospital (Approval No: 34926-08.01.2025) and was conducted in accordance with the principles of the Declaration of Helsinki.

A total of 112 patients who were followed with nonsurgical long arm splinting or casting between January 2021 and January 2024 were retrospectively examined in this study. All patients had a minimum of 6 months of follow-up. For patients with type I fractures, reduction was achieved without manipulation of the current positioning. For patients with type IIa fractures, closed reduction manipulations were applied before casting or splinting.

Demographic data on age, sex, and affected side were collected. The evaluated radiographic parameters comprised the Baumann angle (BA) and lateral capitellohumeral angle (LCHA) (Figure 1).[21-22] These values were measured after the injury, immediately after reduction, and on radiographs obtained at 1 and 4 weeks of follow-up. All of these radiographic measurements were made simultaneously by two experienced pediatric orthopedic surgeons. Elbow joint ranges of motion and carrying angles were measured, and functional and cosmetic evaluations were performed based on Flynn's criteria. These functional and cosmetic evaluations, along with measurements of elbow joint range of motion and carrying angle, were performed at specific follow-up intervals, primarily at 1 week, 4 weeks, and 6 months post-treatment. Although the minimum clinical follow-up was six months, radiographic evaluations were primarily performed at the first and fourth weeks, as subsequent imaging at six months did not demonstrate significant differences in fracture healing compared to earlier assessments.

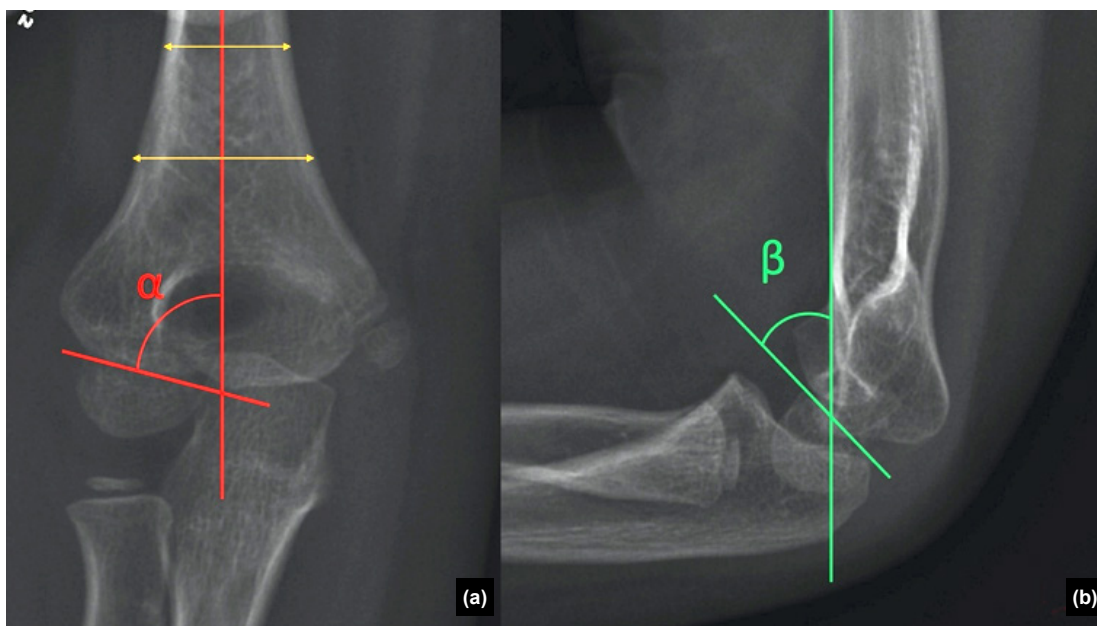

Figure 1. X-ray images show the 3-year follow-up of an 8-year-old male patient with a right elbow Type I fracture. **(a)** demonstrates the Baumann angle on an anteroposterior X-ray. The Baumann angle (α) is defined as the angle between the longitudinal axis of the humeral shaft and a line tangential to the lateral condylar physis (the red line). **(b)** shows the lateral elbow X-ray of the same patient. It demonstrates the Lateral Capitellum Humeral Angle (LCHA), (β) which is defined as the angle between the anterior axis of the humeral shaft and the proximal margin of the capitellum (the green line).

Statistical Analysis

For all obtained data, statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Variables were examined for compliance with normal distribution using both visual (probability graphs and histograms) and analytical (Shapiro–Wilk and Kolmogorov-Smirnov tests) approaches. For comparisons of qualitative variables between two independent groups, chi-square tests or Fisher's exact tests (in the event that values observed in cells did not satisfy chi-square test assumptions) were used. For comparisons between two independent groups, the independent-samples t test was utilized for parametric variables, and the Mann-Whitney U test was performed for nonparametric variables. The Wilcoxon test was applied for comparisons of nonparametric variables between two dependent groups.

Radiological measurements were repeated by two orthopedists at 2-day intervals, and the data obtained from these four measurements were graded radiologically. The agreement between the radiological gradings of the four measurements was evaluated with the kappa test, and measurements were confirmed to be consistent between the two observers ($p<0.05$). Subsequently, the mean values of the measurements of the two observers were calculated and used in the data analysis.

RESULTS

Sixty-nine of the analyzed patients were male and 43 were female. The average age was 7.51 years. Splinting was applied for 31 (63.4%) cases of type I SCHF, and casting was applied for 24 (44.4%) cases. Splinting was applied for 27 (46.6%) cases of type IIa SCHF, and casting was applied for 30 (55.6%) cases. A statistically significant difference was not observed in the distribution of Modified Gartland fracture classifications of patients with SCHFs treated with closed reduction and casting or splinting ($p=0.341$).

No statistically significant differences were detected in LCHA and BA values or Flynn scores calculated before and after reduction for type I and type IIa SCHFs followed with casting or splinting (Table 1).

Since the assumptions of normality were not met by the data, multivariate analysis of variance could not be performed. The mean differences in vertical displacement amounts immediately after reduction and at 4 weeks were compared for both groups using the Wilcoxon test, which is utilized for data that do not comply with a normal distribution. A statistically significant difference was found between LCHA values after reduction and those obtained at 4 weeks for all patients, reflecting an increase over time ($p=0.002$). When the differences in LCHA and BA values obtained after reduction and those obtained at 4 weeks were compared between the groups, no statistically significant difference was found (Table 2).

Loss of reduction was observed in 6 patients followed with splinting and 8 patients followed with casting. Eight of these patients subsequently underwent percutaneous pinning, while the other 6 once again underwent closed reduction and conservative follow-up. A statistically significant difference was not observed for loss of reduction between the splinting and casting groups ($p=0.475$). In one patient who was followed with casting, edema developed due to pressure from the cast, and in another patient, a wound developed due to pressure from the cast. In both cases, the cast was removed, and the patients continued follow-up with splint-

Table 1. Comparison of splinting and casting follow-up in terms of radiological, functional, and cosmetic outcomes

	Treatment Method		
	Splinting, n=58	**Casting, n=54**	**p**
BA before reduction (°)	72.1 (60-4.2)	70.7 (57.3-83.2)	0.6231
BA after reduction (°)	73.3 (67.3-80)	75.2 (67.1-78.1)	0.8641
BA, week 1 (°)	74.2 (68.3-80.1)	74 (66-78.9)	0.4491
BA, week 4 (°)	73.2 (68.9-80)	73.4 (69-77.1)	0.8091
LCHA before reduction (°)	43.9±11.9	42.4±12.2	0.5042
LCHA after reduction (°)	49.2 (46.8-54.7)	48 (46.6-50.4)	0.0741
LCHA, week 1 (°)	50.3 (46-55)	49.1 (47.6-51)	0.5221
LCHA, week 4 (°)	50.8 (47.8-55)	50.1 (48-53)	0.3651
Flynn elbow score - functional	4 (4-4)	4 (4-4)	0.9551
Flynn elbow score - cosmetic	4 (3-4)	4 (3-4)	0.7681

[1]: Mann-Whitney U test, with data given as median (25th-75th percentile) values. [2]: Independent samples t-test, with data given as mean ± standard deviation values.

Table 2. Comparison of changes in LCHA and BA values obtained after reduction and at the 4th week of follow-up

	Conservative follow-up of types I and IIa SCHFs after closed reduction		
	Splinting, n=58	**Casting, n=54**	**p**
BA before reduction (°)	74.2	68.36	0.6231
BA after reduction (°)	75.08	71.99	0.8641
BA, week 1 (°)	74.98	72.49	0.4491
BA, week 4 (°)	75.11	70.79	0.8091
LCHA before reduction (°)	47.31	39.24	0.5042
LCHA after reduction (°)	49.67	48.77	0.0741
LCHA, week 1 (°)	50.61	47.75	0.5221
LCHA, week 4 (°)	51.39	48.2	0.3651
Flynn score – functional	3.93	3.67	0.9551
Flynn score – cosmetic	3.85	3.49	0.7681

[1]: Mann-Whitney U test, with data given as median (25th-75th percentile) values.

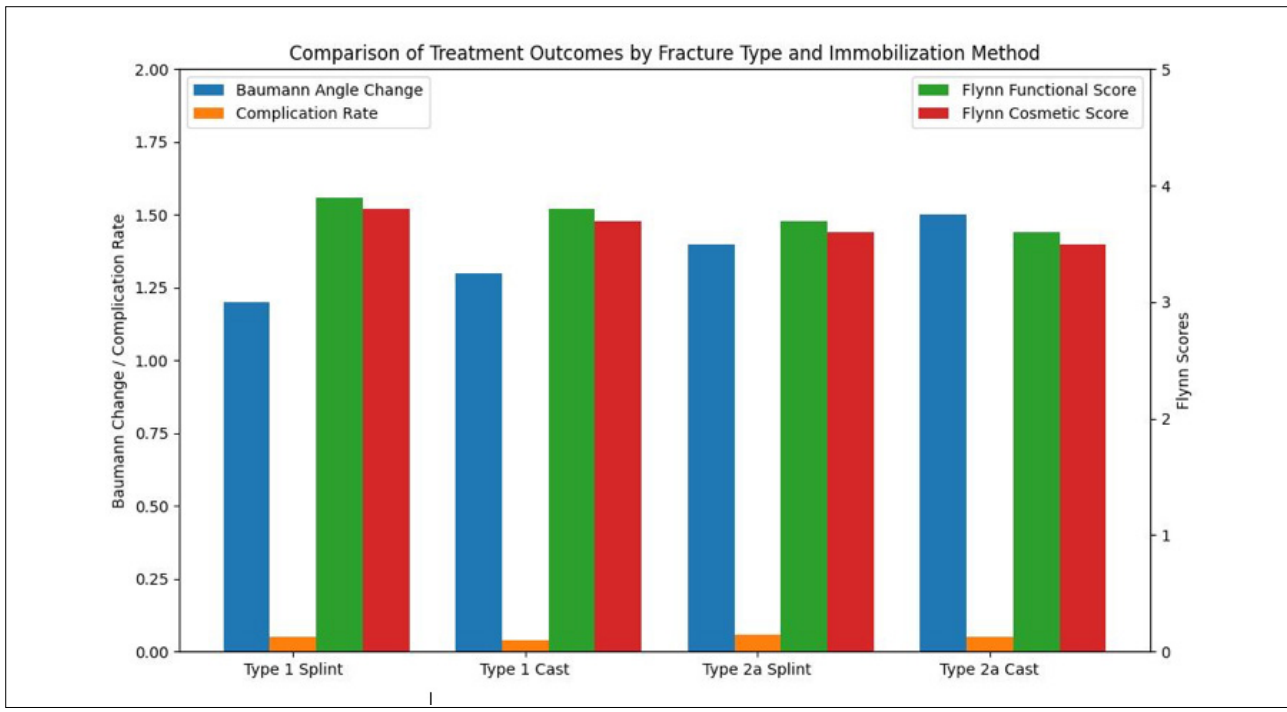

Figure 2. Treatment outcomes by fracture type and immobilization method (Type 1 Splinting, Type 1 Casting, Type 2a Splinting, Type 2a Casting). Differences in Baumann angle change, complication rates, and Flynn scores are shown. Data are mean±SD. Statistical significance indicated where applicable.

ing. Additionally, subgroup analysis dividing patients into four groups based on fracture type and immobilization method (Type I splinting, Type I casting, Type IIa splinting, Type IIa casting) was performed. This detailed subgroup comparison revealed significant differences in reduction loss and other treatment outcomes, enhancing the reliability of the results (Figure 2).

Additionally, subgroup analysis based on the Gartland classification demonstrated significant differences between type I and type IIa fractures. The post-reduction Baumann angle ($p=0.0087$), Baumann angle at the 4th week ($p=0.0157$), and pre-reduction lateral capitellohumeral angle ($p<0.0001$) were all significantly higher in patients with type I fractures compared to those with type IIa fractures (Table 3).

Table 3. Comparison of radiological and clinical parameters between Modified

Parameter	Type I Mean	Type IIa Mean	p-value
BA before reduction (°)	74.2	68.36	0.6231
BA after reduction (°)	75.08	71.99	0.8641
BA, week 1 (°)	74.98	72.49	0.4491
BA, week 4 (°)	75.11	70.79	0.8091
LCHA before reduction (°)	47.31	39.24	0.5042
LCHA after reduction (°)	49.67	48.77	0.0741
LCHA, week 1 (°)	50.61	47.75	0.5221
LCHA, week 4 (°)	51.39	48.2	0.3651
Flynn score – functional	3.93	3.67	0.9551
Flynn score – cosmetic	3.85	3.49	0.7681

Gartland type I and IIa fractures. Values are means. Mann–Whitney U test was used. BA: Bauman angle, LCHA: Lateral capitello-humeral angle. Significant results: BA after reduction (p=0.0087), BA week 4 (p=0.0157), LCHA before reduction (p<0.0001).

DISCUSSION

While there is consensus on the application of nonsurgical methods in treating type I fractures, the treatment of type IIa fractures is still debated.[9] Hadlow et al.[12] and Parikh et al.[13] both described the successful treatment of type IIa fractures with closed reduction and casting, with surgery being required in 23% and 28% of cases, respectively. In the present study, surgery was deemed necessary for 10.3% of type IIa fractures followed with splinting and 14.8% followed with casting. For both types of immobilization, the rate of progression to surgery was lower than the rates reported in the literature, and this rate was also lower for patients followed with splinting compared to casting. Akgülle et al.[23] reported that in operatively treated patients, casting was superior to splinting in preventing loss of reduction. However, in our patient cohort, there were no fractures with instability severe enough to require surgical intervention.

Children who have experienced type IIa SCHFs treated with closed reduction and long arm splinting must be monitored carefully, both clinically and radiographically, for possible loss of reduction or alignment. It has been recommended that the first follow-up evaluation in these cases be performed within 7 days after reduction.[9] Furthermore, it is crucial that the parents or guardians of children with fractures fully comply with the treatment protocol by attending all scheduled follow-up appointments. Noncompliance with follow-up X-rays can lead to malunion and possible cosmetic deformities, in association with surgery-related expenses and potential complications.[3,13] In our study, patient follow-up was carried out weekly based on radiological measurements while checking the strength and positioning of the splints and casts.

A difference of less than 5° in BA has been observed by several authors to predict less reduction loss and satisfactory cosmetic results.[24,25] In our study, it was determined that patients with loss of reduction (14/112) had differences of 6.8° to 19.7° in BA values, with these differences being higher compared to patients without loss of reduction. In this sense, there is a significant relationship between reduction loss and BA differences. However, in this study, we did not find any significant differences between the groups for the change in BA or Flynn's cosmetic criterion.

A previous study stated that surgical fixation was required for type IIa fractures if the LCHA difference was 18° or more.[25] In our study, we observed loss of reduction in two patients with respective LCHA differences of 28.2° and 27°, for whom closed reduction with percutaneous pinning was applied. The treatment of the other 17 patients with differences of ≥18° ended after closed reduction, regardless of the application of splinting or casting. These findings align with the observations of Ariyawatkul et al.,[26] who reported that surgical intervention may not be necessary in type IIa fractures with angular differences below 18°. We argue that surgery should not be directly recommended to patients solely based on LCHA values and that such patients should initially be managed with closed reduction and long arm splinting.

In this study, none of the Modified Gartland type I SCHFs treated with long arm splinting necessitated a switch in treatment to casting and/or surgical intervention. There was a loss of reduction in only one of those cases; an increase in LCHA and BA was observed, the patient underwent closed reduction again, and the treatment was completed with splinting. Among the cases of type IIa fractures, loss of reduction was observed in 8 (7.14%) of the patients followed with casting, while loss of reduction was observed in 5 (4.4%) of the patients followed with splinting. Thus, splinting had a numerically superior rate of success. These data suggest that long arm splinting is a viable alternative to long arm casting in the

conservative follow-up of both type I and type IIa SCHFs. There are increasing findings in the literature suggesting that minor pediatric fractures do not require more than a splint.[27-30] These studies have shown that splints offer better functioning and are a preferred treatment option compared to casting. Furthermore, splinting was reported to be cost-effective in treating minor ankle fractures and minimally angled distal fractures of the radius.[30]

CONCLUSION

No significant difference was observed in this study between the radiological and clinical results of splinting and casting in the nonsurgical treatment of pediatric type I and type IIa SCHFs. However, splinting offers additional benefits, such as increased ease of application, greater comfort, lower complication rates, and improved hygiene. We advocate splinting as an appropriate alternative in the nonsurgical treatment of type I and type IIa fractures.

Ethics Committee Approval: This study was approved by the Erzurum Medical Faculty Scientific Research Ethics Committee for Clinical Research Ethics Committee (Date: 08.01.2025, Decision No: 34926).

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Conflict of Interest: None declared.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Pediatrik Tip I ve Tip IIa suprakondiler humerus kırıklarının cerrahi dışı takibinde uzun kol atel uygulaması yeterli midir?

AMAÇ: Bu çalışma, pediatrik, değiştirilmiş Gartland tip I ve IIa suprakondiler humerus kırıklarının cerrahi dışı tedavisinde uzun kol alçı ve atel uygulamalarının radyolojik ve fonksiyonel sonuçlarını karşılaştırmayı amaçlamaktadır.
GEREÇ VE YÖNTEM: Ocak 2021 ile Ocak 2024 tarihleri arasında, uzun kol alçı veya atel ile cerrahi dışı olarak tedavi edilen 112 pediatrik tip I ve IIa suprakondiler humerus kırığı (SCHF) retrospektif olarak değerlendirildi. Bauman açısı ve lateral kapitellohumeral açı, redüksiyon öncesi, sonrası, 1. hafta ve 4. haftalarda ölçüldü. Klinik ve radyolojik sonuçlar Flynn kriterleri kullanılarak karşılaştırıldı.
BULGULAR: Çalışmaya dahil edilen 112 hastanın 55'inde tip I (%49), 57'sinde tip IIa (%51) kırık mevcuttu (ortalama yaş: 7.51 yıl; 69 erkek, 43 kız). Kırıklar sağ ve sol dirseklerde eşit dağılım gösterdi (n=56). Elli sekiz hasta uzun kol atel ile, 54 hasta ise uzun kol alçı ile tedavi edildi. Takip süreleri her iki grupta da benzerdi. Atel grubunda ortalama Bauman açısı redüksiyon öncesi 72.1°, 4. haftada 73.2°; alçı grubunda ise sırasıyla 70.7° ve 73.4° olarak ölçüldü. Ortalama lateral kapitellohumeral açı atel ile 43.9°'den 50.8°'ye, alçı ile 42.4°'ten 50.1°'e yükseldi. Atel ve alçı uygulanan gruplar arasında redüksiyon kaybı açısından istatistiksel olarak anlamlı bir fark gözlenmemiştir (p=0.475). Tip I ve tip IIa SCHF olgularında, redüksiyon öncesi ve sonrası LCHA (p=0.175), BA değerleri (p=0.485) ile Flynn skorları (p=0.768) arasında istatistiksel olarak anlamlı bir fark bulunmamıştır.
SONUÇ: Cerrahi dışı tedavi edilen değiştirilmiş Gartland tip I ve IIa suprakondiler humerus kırıklarında atel ve alçı uygulamaları benzer klinik ve radyolojik sonuçlar vermektedir. Ancak atel, uygulanabilirliğinin kolaylığı ve daha düşük komplikasyon oranı nedeniyle güçlü bir alternatif olarak öne çıkmaktadır.

Anahtar sözcükler: Dirsek; kırık; pediatrik; redüksiyon; suprakondiler humerus.

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CASE REPORT

Non-operative management algorithm in a case of grade II pancreatic, grade IV splenic, and renal injury due to blunt abdominal trauma

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ABSTRACT

Blunt abdominal trauma most often results from high-energy mechanisms such as motor vehicle accidents. The spleen and kidneys are the organs most commonly injured in such cases, whereas pancreatic injuries are rare. Concomitant involvement of the pancreas along with splenic and renal injuries is particularly uncommon. We report the successful non-operative management (NOM) of a 24-year-old male patient who sustained grade IV splenic and left renal injuries, a grade II pancreatic injury, and widespread pulmonary contusions following a motorcycle accident. During follow-up, expansion of the retroperitoneal hematoma, perisplenic fluid collection, and left-sided pleural effusion were observed. Interventional radiology procedures, including abdominal and thoracic drainage, were performed. The presence of high levels of amylase and lipase in the abdominal catheter output indicated the development of a pancreatic fistula, for which conservative treatment was initiated. Following catheter repositioning and administration of a somatostatin analogue, the fistula resolved spontaneously. Although left renal atrophy was detected on long-term follow-up, the patient remained clinically stable. This case highlights that even in the presence of multiple high-grade solid organ injuries, favorable outcomes may be achieved without surgical intervention through NOM. Supported by advanced imaging modalities and interventional radiology, NOM represents a safe and effective therapeutic strategy that can minimize surgical complications in hemodynamically stable patients.

Keywords: Blunt abdominal trauma; non-operative management; splenic injury; renal injury; pancreatic fistula.

INTRODUCTION

There are many causes of blunt abdominal trauma, such as falls from height, traffic accidents, motorcycle accidents, and others.[1] In recent years, due to high rates of surgical complications, there has been a shift toward non-operative management (NOM) of blunt abdominal trauma in hemodynamically stable patients.[2]

Blunt pancreatic trauma is a rare condition, accounting for less than 1% of all abdominal traumas. Blunt abdominal trauma resulting in both pancreatic and splenic injury is even rarer. These types of cases usually lead to surgical treatment and postoperative complications.[2]

In this case study, we present the successful NOM of a patient with blunt abdominal trauma due to a motorcycle accident, who sustained a grade IV splenic injury, grade IV kidney injury, and grade II pancreatic injury, as well as widespread contusions to the lungs. Informed consent was obtained from the patient after the nature of the procedures had been fully explained.

CASE REPORT

The patient was a 24-year-old male who presented with blunt abdominal trauma after crashing into a car door while riding his motorcycle. Initial evaluation showed that he was conscious and oriented to time and place, with a Glasgow Coma Scale (GCS) score of 15. His pupils were isochoric and responsive to light, all four extremities were mobile, there

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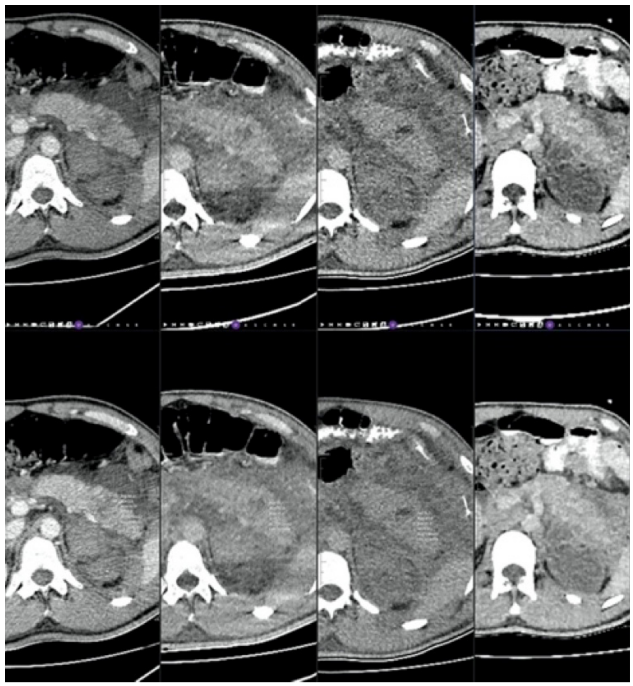

Figure 1. Serial contrast-enhanced computed tomography (CT) images of the upper abdomen obtained weekly, demonstrating a grade II laceration in the pancreatic tail. The sequence shows the lesion from the early post-trauma stage through progressive healing, with complete regression in the final image. The lower row illustrates the calculated laceration area (cm^2) at each time point.

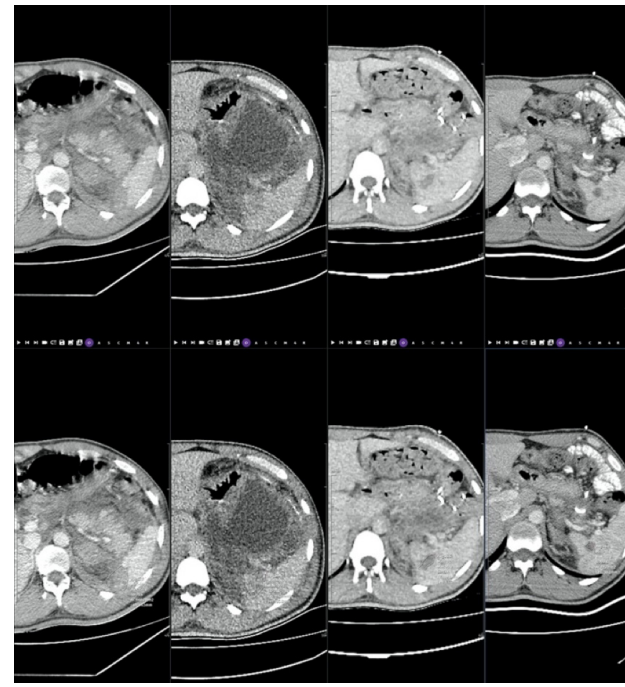

Figure 2. Serial contrast-enhanced computed tomography (CT) images showing splenic and renal injuries. A laceration in the lower medial pole of the spleen gradually decreased in size during follow-up. Renal injury is also demonstrated, with the final image revealing a cystic degenerative area. The lower row illustrates area-based quantification of injury (cm^2) at different time points.

was no spinal tenderness on palpation, and no neuromuscular deficits were detected. Bilateral lung auscultation revealed normal breath sounds, and the abdomen was nontender, with no rebound or guarding. Placement of a Foley catheter revealed 400 ml of grossly hemorrhagic urine. Vital signs were as follows: blood pressure (BP), 122/70 mmHg; oxygen saturation (SpO_2), 97%; pulse rate, 97 beats per minute (bpm). Laboratory values were as follows: white blood cell count (WBC), 27,000/mm^3; hemoglobin, 14.5 g/dL; creatinine, 1.17 mg/dL; aspartate aminotransferase (AST), 119 U/L; alanine aminotransferase (ALT), 87 U/L; amylase, 481 U/L; and lipase, 401 U/L.

A contrast-enhanced computed tomography (CT) angiogram of the abdomen and head was performed. No neurological pathology or fractures were detected. Bilateral pulmonary contusions were present, but no hemothorax or pneumothorax was detected. A hematoma was observed in the splenic area, and a laceration extending from the superior to the posterior pole of the spleen, reaching the hilar area and resulting in >25% devascularization. According to the American Association for the Surgery of Trauma (AAST) classification, this splenic injury was classified as grade IV. A 3 cm retroperitoneal hematoma was noted adjacent to the left adrenal gland. The left renal parenchyma showed no contrast enhancement, and the upper and middle branches of the left renal artery were not visualized; only the lower branch was patent, supplying approximately 10% of the renal parenchyma. This renal injury was classified as grade IV according to AAST criteria. In addition, a laceration of the pancreatic tail was detected, with preservation of the Wirsung duct and no parenchymal tissue loss, corresponding to a grade II pancreatic injury according to the AAST classification (Figs. 1 and 2).

Intravenous fluid resuscitation was initiated in the emergency department, and the patient was subsequently admitted to the intensive care unit (ICU). Two hours after admission, his hemoglobin level was 12.1 g/dl; BP was 180/77 mmHg; SpO_2 was 97%; and he reported left flank pain radiating to the left upper quadrant. His pulse rate ranged between 104-107 bpm. During the three-day ICU stay, his pulse rate remained between 97-107 bpm, and he required transfusion of 5 units of packed red blood cells (PRBC), bringing the total to 8 units within 82 hours. During this period, the lowest recorded hemoglobin value was 9.8 g/dl. No fresh frozen plasma was administered during the course of treatment.

In the following days, a repeat CT scan demonstrated enlargement of the hematoma in the left retroperitoneal space. Minimal fluid was noted in the perihepatic region and pelvis, and no free intraperitoneal air was detected. The patient did not develop signs of an acute abdomen. Daily urologic examinations showed that the urine had become clear by the 28th hour after admission. His daily urine output was approximately 2000 ml, and serum creatinine was 1.44 mg/dL.

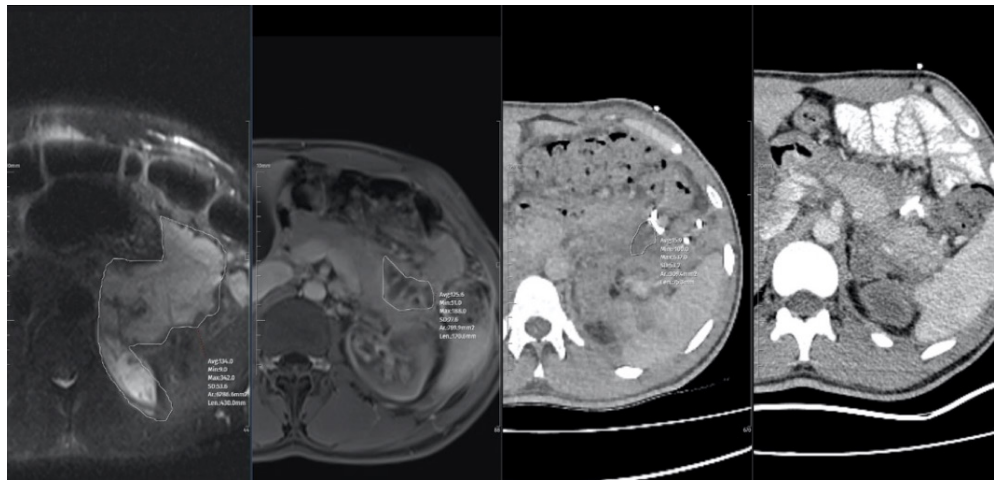

Figure 3. Imaging findings of a pancreatic fistula-associated loculated cystic fluid collection. On fat-suppressed T2-weighted magnetic resonance imaging (MRI), the collection appears hyperintense. Following placement of a drainage catheter, contrast-enhanced fat-suppressed T1-weighted MRI demonstrates a reduction in the size of the rim-enhancing loculated collection. Subsequent serial follow-up contrast-enhanced abdominal computed tomography (CT) scans (third and fourth images) show further decrease in the size of the collection, with complete regression in the final image. The drainage catheter is visible as a hyperdense tubular structure on CT.

BP measurements were typically within the range of 180/60-80 mmHg. From the first day of treatment, serum amylase and lipase levels remained between 400 and 500 U/L, WBC count between 22,000 and 26,000 mm^3, and C-reactive protein (CRP) levels between 300 and 370 mg/L. After three days of treatment, his pulse rate was 95 bpm and BP was 160/80 mmHg. A subsequent CT scan revealed a fluid collection measuring 122×121 mm between the stomach and spleen. In addition, pleural effusion measuring 6 cm on the left side and 1 cm on the right side was identified. The patient was consulted by infectious disease specialists, cardiothoracic and vascular surgeons, and pulmonologists, and low-molecular-weight heparin (LMWH) therapy was initiated. A pleural drainage catheter was placed in the left pleural space, yielding 800 ml of clear fluid. It was removed after five days when the effusion had completely resolved. An abdominal drainage catheter was also inserted to evacuate the perisplenic fluid located between the stomach and spleen.

The abdominal catheter drained 1100 ml of light brown, non-purulent fluid during the first 24 hours. After seven days, the daily drainage volume had decreased to approximately 200 ml, and the fluid had become completely clear. Laboratory parameters also improved, with a WBC count of 14,000 mm^3 and a CRP level of 82 mg/L. Analysis of the catheter fluid revealed markedly elevated amylase (42,000 U/L) and lipase (13,000 U/L) levels, while urea and creatinine values were within normal limits. These findings were interpreted as consistent with a pancreatic fistula.

The patient was initially kept nil per os for four days, after which he was able to tolerate a clear liquid diet, followed by puréed foods and soups, all of which were well tolerated. After 10 days of ICU stay, his vital signs and ultrasound findings were stable, and his condition had improved sufficiently to allow transfer to the surgical ward. During the ICU stay, the patient developed fever on only two occasions.

On the second day in the surgical ward, repeat CT imaging demonstrated a significant reduction of the left adrenal/retroperitoneal hematoma to 12 mm, non-enhancement of approximately 90% of the left kidney, and a decrease in the perisplenic fluid collection between the stomach and spleen. The patient was discharged with his abdominal catheter in place, which was draining approximately 200 ml of clear fluid daily. Renal artery Doppler ultrasonography and renal scintigraphy confirmed left kidney atrophy with only 5% residual functional. Prior to discharge, the patient was evaluated by the urology, cardiothoracic, and vascular surgery teams, all of whom recommended continued outpatient observation.

During outpatient follow-up, abdominal magnetic resonance imaging (MRI) demonstrated a minimal fluid collection at the pancreatic tail (Fig. 3). The abdominal catheter was draining approximately 100 ml of clear fluid daily, which was considered higher than expected. The patient was readmitted to the surgical ward, and the catheter was repositioned to avoid direct contact with the pancreatic tail in order to minimize local irritation. Octreotide was initiated at a dose of 0.1 mg three times daily, and dietary adjustments were made. Within 24 hours, the drainage decreased to 70 ml/day, and by the third day it had further declined to 30 ml/day.

On the fourth day, no fluid was collected from the catheter, and abdominal ultrasonography confirmed the absence of free fluid in the peritoneal cavity. The catheter was removed. Laboratory results at that time were as follows: WBC, 7,000/

mm^3; AST, 42 U/L; ALT, 34 U/L; CRP, 8 mg/L; amylase, 216 U/L; and lipase, 372 U/L.

The patient was discharged the following day with instructions to return for a repeat abdominal ultrasound after three days. Follow-up ultrasonography demonstrated no free intra-abdominal fluid, and serum amylase and lipase levels were within the normal range. Urologists recommended outpatient follow-up. Imaging showed left renal atrophy, and serum creatinine levels ranged between 1.2 and 1.44 mg/dL. At the two-month follow-up, abdominal MRI revealed no pathological findings in the pancreas or spleen (Figs. 1-3). At the eight-month follow-up, the patient was found to have a 4 cm cystic lesion in the pancreatic tail, consistent with post-traumatic sequelae. Serum amylase and lipase levels ranged between 200–300 U/L during follow-up. The left kidney remained atrophic, with only 5% residual renal function on static renal scintigraphy, while the spleen demonstrated a homogeneous parenchymal structure without new pathology.

DISCUSSION

Simultaneous injury to multiple organs in blunt abdominal trauma is not uncommon; however, concomitant injuries to the spleen, pancreas, and kidneys are relatively rare. Such injuries typically result from high-energy mechanisms, including motor vehicle accidents, falls from significant heights, or severe blunt force trauma. Among intra-abdominal organs, the liver and spleen are the most frequently injured, followed by the small intestine. Less commonly injured organs include the kidneys, stomach, gallbladder, urinary bladder, and pancreas.[3]

Precise statistics on the frequency of simultaneous injuries to the spleen, pancreas, and kidney are lacking in the literature; however, available studies suggest that the incidence of such cases is low, estimated at less than 1%.[2] In the management of these trauma patients, surgical intervention is often associated with serious morbidity and complications, prompting the development of alternative strategies. The high rate of surgical complications observed in hemodynamically stable trauma patients has led to a paradigm shift from operative management toward non-operative management.[4-5] Over the past two decades, numerous successful case reports have been published, and NOM has become an accepted treatment protocol for hemodynamically stable solid organ injuries. Several studies have also demonstrated that the NOM approach provides a significant reduction in hospital stay and morbidity compared to operative treatment.[6]

The widespread availability of high-resolution CT imaging and interventional radiology, together with the capacity for close patient monitoring in specialized centers such as the ICU, has facilitated the establishment of NOM as a widely accepted management protocol for solid organ injuries in hemodynamically stable patients with blunt abdominal trauma.[7-8]

With the publication of many successful case reports over the last 20 years, NOM has been accepted as one of the standard management protocols for hemodynamically stable solid organ injuries. In this context, Raza et al.[7] reported on 1,071 hemodynamically stable patients with blunt trauma to the liver, spleen, kidney, and pancreas who were treated non-operatively regardless of the severity of single or multiple blunt injuries; 89.98% of these patients were successfully managed with NOM. Lu et al.[9] recently reported that in 98 patients with blunt pancreatic injury, outcomes were comparable between those treated operatively and those managed non-operatively, further supporting the safety of NOM in selected patients.

In a study on blunt abdominal trauma, it was reported that hemodynamically stable splenic injuries can be managed conservatively regardless of injury grade, and that NOM is successful in more than 90% of cases of renal trauma.[10-11] Similarly, Raza et al.[7] showed that radiological severity and injury grade are not contraindications to NOM. Podda et al.[12] also demonstrated that NOM can be applied even in high-grade (III-IV) splenic lesions. On the other hand, several researchers have identified risk factors for NOM failure in splenic trauma, including age >55 years, associated liver injury, arterial-phase contrast extravasation, and the need for ≥4 units of erythrocyte suspension transfusion.[13,14]

The findings of Vanderviles et al.[6] are consistent with those of Raza et al.,[7] supporting our case report by demonstrating that NOM can be successfully implemented in centers equipped with advanced imaging methods, an ICU, and interventional radiology, thereby preventing unnecessary laparotomies. Furthermore, Feng Jian et al.[15] highlighted the role of percutaneous catheter drainage as an effective minimally invasive strategy in the initial conservative treatment of grade III–IV blunt pancreatic injuries, underscoring the importance of interventional radiology techniques in pancreatic trauma management. In our case, which involved grade IV splenic and renal injuries according to AAST, a grade II pancreatic injury, and diffuse pulmonary contusions, management was continued using multimodal imaging and minimally invasive drainage procedures performed by interventional radiologists. Subsequent follow-up of the pancreatic injury and fistula was conducted with serial ultrasonography and MRI.

According to the literature, the complication rate after pancreatic trauma ranges from 20% to 40%, with pancreatic fistula (10-35%), pancreatic abscess (10-25%), hemorrhage (10%), pseudocyst formation (5%), and pancreatitis being the most frequently reported sequelae.[16-17] In our case, a pancreatic fistula developed secondary to pancreatitis and was successfully managed with our treatment strategy. Although pseudocyst formation was anticipated during long-term follow-up, this complication was not observed on subsequent MRI examinations.

In the literature, external drainage methods have been emphasized as the standard approach for pancreatic contusions or minor parenchymal injuries. Conversely, surgical resection

should be considered in cases of pancreatic duct injury. In situations where the integrity of the pancreatic duct is shown to be intact by endoscopic retrograde cholangiopancreatography (ERCP), surgical treatment is not required.[18-19] In our case, MRI revealed a grade II injury in the distal pancreas without evidence of pancreatic duct injury. The volume of pancreatic fluid drained through the catheter progressively decreased and ultimately resolved after the catheter was retracted by 2 cm. We attributed this improvement to relief of local irritation caused by direct contact between the catheter tip and pancreatic tissue. Had the fluid output not decreased with this strategy, our next step would have been ERCP to confirm ductal integrity and, if necessary, perform stent placement. Surgical intervention was reserved as a last resort.

CONCLUSION

Non-operative management is a safe and effective treatment strategy for patients with blunt abdominal trauma who are hemodynamically stable and exhibit no signs of peritonitis. Excluding definitive indications for laparotomy, NOM can be applied regardless of the degree of solid organ trauma, provided that appropriate radiological imaging and interventional procedures are available and the patient remains hemodynamically stable. This approach protects patients from the risks associated with surgical complications. In our case, successful recovery was achieved through NOM in a patient who, according to AAST classification, presented with diffuse pulmonary contusions, grade IV splenic and renal injuries, and a grade II pancreatic injury.

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OLGU SUNUMU - *ÖZ*

Künt batın travması nedenli pankreas grade 2, dalak ve böbrek grade 4 hasarlı hastada non-operatif tedavi algoritmamız

Künt abdominal travma, motorlu taşıt kazaları gibi yüksek enerjili olaylardan kaynaklanabilir. Dalak ve böbrekler, künt abdominal travmada sıklıkla yaralanan organlar olmakla birlikte, pankreas yaralanmaları nadirdir, özellikle pankreasın dalak ve böbrek yaralanmalarıyla birlikte oluşması daha da nadirdir. Bu olgu sunumu, bir motosiklet kazası sonucu grade 4 dalak ve böbrek yaralanmaları, grade 2 pankreas yaralanması ve yaygın akciğer kontüzyonları yaşayan 24 yaşındaki bir erkeğin başarılı nonoperatif yönetimini (NOM) sunmaktadır. Takip sürecinde, retroperitoneal hematomun büyüdüğü, dalak etrafında sıvı koleksiyonu geliştiği ve sol plevral efüzyon oluştuğu izlenmiştir. Girişimsel radyoloji tarafından abdominal ve plevral kateterler yerleştirilmiş; plevral sıvı başarıyla drene edilmiştir. Abdominal kateterden yüksek amilaz ve lipaz düzeylerine sahip sıvı gelmesi üzerine pankreatik fistül geliştiği değerlendirilmiş ve hastaya konservatif tedavi uygulanmıştır. Kateterin pozisyonunun düzeltilmesi ve somatostatin analoğu ile tedavi sonrası fistül spontan olarak kapanmıştır. Sol böbrekte uzun dönem takiplerde atrofi saptanmış; ancak hasta stabil seyretmiştir. Pankreatik fistül ve plevral effüzyonun drenajı dahil konservatif yönetimle, hastanın tedavisi başarılı olmuştur. Batın içi solid organ travması çoklu olması ve tomografide yüksek derecede sınıflandırılmasına rahmen hastanın yönetiminde ilk planda cerrahi yerine NOM tercih edilerek bu hastanın tedavisi yönetilmiştir. Bu vaka, NOM'un, ileri görüntüleme ve girişimsel radyolojiyle desteklendiğinde, hemodinamik olarak stabil hastalarda cerrahi gereksinimi önleyerek komplikasyonları azaltan etkili bir strateji olduğunu vurgulamaktadır.

Anahtar sözcükler: Künt abdominal travma; non-operatif yönetim; dalak yaralanması; böbrek yaralanması;s pankreatik fistül.

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CASE REPORT

Emergency Whipple procedure for traumatic pancreas–duodenum separation in a patient with multiorgan injury: a case report and review

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ABSTRACT

Although pancreaticoduodenal injuries are rare, they represent complex surgical conditions associated with high risks of morbidity and mortality. This case report presents an emergency pancreaticoduodenectomy (Whipple procedure) performed on a 17-year-old male patient who was admitted to the emergency department following a non-vehicular traffic accident. Imaging studies revealed free intraperitoneal air and fluid, as well as multiorgan injury, including right renal perfusion loss. Emergency surgical exploration revealed a Grade V pancreatic head avulsion, distal bile duct injury, duodenal laceration, a laceration in the proximal one-third of the transverse colon, and right renal devascularization. Considering the patient's intraoperative hemodynamic stability, a Whipple procedure, segmental colectomy with primary anastomosis, and right nephrectomy were performed. On postoperative day 11, a leak developed at the colocolonic anastomosis site, and the patient underwent emergency surgery involving a right hemicolectomy and end ileostomy. During the follow-up period, no additional emergency surgical intervention was required from a general surgery perspective. This case highlights the importance of multidisciplinary team collaboration and individualized surgical decision-making in the management of high-risk trauma based on the patient's clinical condition. In the presence of complex anatomical injuries, determining appropriate surgical timing, selecting optimal techniques, and managing complications play decisive roles in treatment success. In this context, the surgical approach and timing are discussed in light of the current literature and evaluated in comparison with similar cases.

Keywords: Duodenal injury; emergency surgery; multiorgan injury; pancreatic trauma; Whipple procedure.

INTRODUCTION

The retroperitoneal position of the pancreas provides a degree of anatomical protection in cases of blunt abdominal trauma, rendering isolated pancreatic injuries a rare clinical entity.[1] Motor vehicle collisions account for nearly 80% of all blunt pancreatic trauma cases.[2] Injuries to adjacent organs may also occur in association with pancreatic trauma.[3] Although pancreatic injuries resulting from abdominal trauma are rare, they are associated with a mortality rate ranging from 10% to 30%.[4] The definitive diagnosis of pancreatic injuries is established through computed tomography (CT) imaging or, in hemodynamically unstable patients, during exploratory laparotomy.[5] The timely diagnosis of such injuries depends on both the extent of pancreatic damage and the patient's hemodynamic stability, guiding a spectrum of therapeutic strategies from non-operative management to urgent surgical intervention. To standardize the assessment of clinical severity and management strategies for pancreatic injuries, the American Association for the Surgery of Trauma (AAST) developed a five-grade classification system. According to the AAST pancreatic injury scale, Grade I-II injuries typically involve contusions or superficial lacerations without disruption of the pancreatic duct, whereas Grade III-V injuries represent more severe trauma, including distal or proximal transection of the pancreatic parenchyma, disruption of the pancreatic duct, or fragmentation

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of the pancreatic head (Fig. 1). This classification plays a critical role in guiding the decision-making process between surgical and conservative management and constitutes a cornerstone of the clinical approach in trauma care.[6]

This case report presents a patient who sustained pancreatic head avulsion accompanied by bile duct injury and multiorgan trauma following blunt abdominal injury. Through this case, we aim to highlight the various challenges encountered in the surgical management of complex multiorgan injuries involving the pancreas.

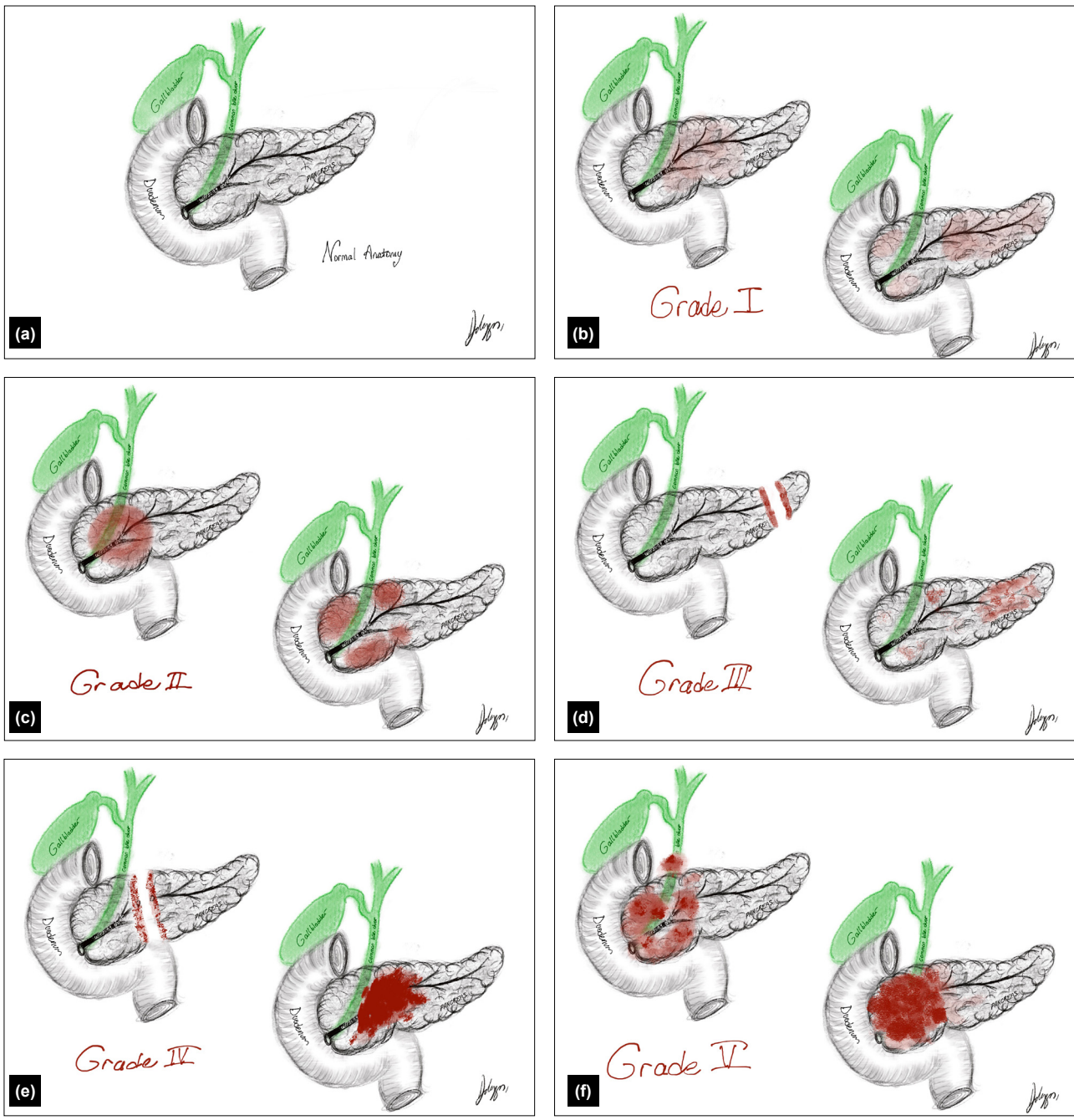

Figure 1. AAST (American Association for the Surgery of Trauma) Pancreatic Injury Scale – visual overview. **(a)** Normal anatomical structure of the pancreas. **(b)** Grade I – Mild bruising or superficial tear without involvement of the main duct or loss of pancreatic tissue. **(c)** Grade II – Hematoma affecting more than one segment or a laceration involving less than half the circumference of the pancreatic tissue, without ductal damage. **(d)** Grade III – Injury to the distal pancreas involving disruption of the main pancreatic duct. **(e)** Grade IV – Laceration or complete transection in the proximal pancreas (to the right of the superior mesenteric vein) accompanied by ductal injury. **(f)** Grade V – Extensive destruction of the pancreatic head with severe structural damage.

CASE REPORT

A 17-year-old male patient presented to the emergency department approximately seven hours after a non-vehicular traffic accident. Upon admission, he was spontaneously breathing but exhibited hypotension and tachycardia. Physical examination revealed an ecchymotic area in the right upper quadrant, along with generalized abdominal tenderness, guarding, and rebound tenderness. Laboratory investigations showed the following results: leukocyte count $10.8\times10^3/\mu L$ (reference: 4-10.5), hemoglobin 12.4 g/dL (12.5-16.1), hematocrit 38.1% (36-47), platelet count $378\times10^3/\mu L$ (150-450), alanine aminotransferase (ALT) 226 U/L (13-45), amylase 345 U/L (22-80), and lipase 830 U/L (7-39).

Abdominal computed tomography revealed a Grade 3 laceration in segment 4B of the liver, loss of perfusion in the right kidney, and a large abdominal wall defect in the right quadrant. Colonic and small bowel loops were observed within the defect area, consistent with herniation of these structures. Free intraperitoneal air measuring up to 8 cm in its deepest location was detected around the duodenum, along with a defect distal to the duodenal bulb and an abnormal tract extending superiorly from the defect-findings suggestive of duodenal perforation. Additionally, free intraperitoneal fluid was observed in the perigastric and perihepatic regions, measuring up to 4 cm at its deepest point (Figs. 2 and 3).

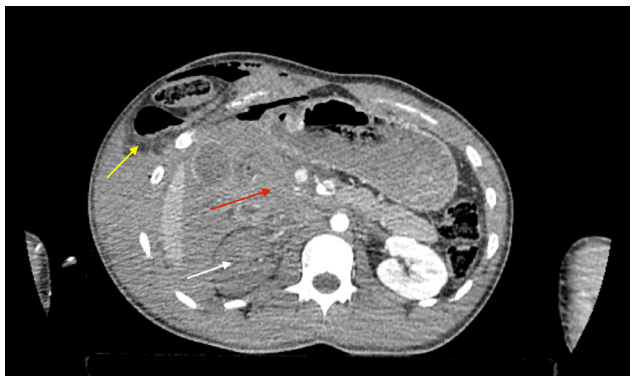

Figure 2. Preoperative axial computed tomography (CT) image. *White arrow: hypoperfused right kidney; red arrow: high-grade pancreatic injury; yellow arrow: trauma-related abdominal wall herniation.*

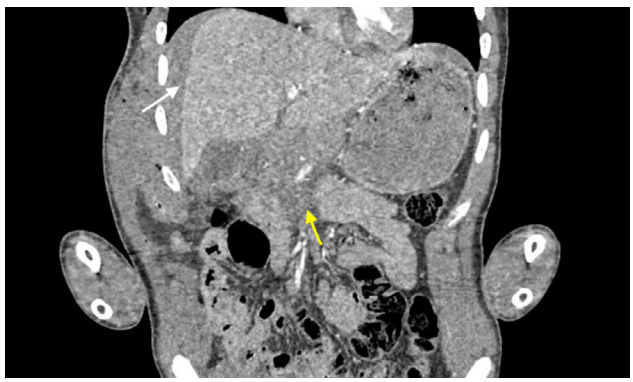

Figure 3. Preoperative coronal computed tomography (CT) image. *Yellow arrow: severe pancreatic injury; white arrow: free intraperitoneal fluid.*

Based on the clinical findings, the patient was taken for emergency surgery. During exploration, hemorrhagic fluid was identified within the abdominal cavity. Following copious irrigation with warm saline, detailed exploration revealed fractured ribs in the right upper quadrant and a superficial liver laceration approximately 5 cm in length without active bleeding. Avulsion of the pancreatic head accompanied by injury to the distal bile duct was identified, consistent with an AAST Grade V pancreatic injury (Fig. 4). Additionally, lacerations consistent with an AAST Grade III injury were observed in the duodenum and the proximal one-third of the transverse colon. The right kidney demonstrated absence of perfusion, consistent with devascularization. Given the patient's hemodynamic stability, emergency pancreaticoduodenectomy (Whipple procedure, EPD), segmental colectomy with primary anastomosis, and right nephrectomy were performed by the hepatobiliary surgery team at our institution. Following the operation, the patient was transferred to the intensive care unit (ICU) under intubation. During the 21-day ICU stay, the patient was extubated; however, on postoperative day 11, he required reoperation due to an anastomotic leak. Surgical exploration revealed a leak at the colonic anastomosis site, while the other anastomoses were found to be intact. A right hemicolectomy was performed, and an end ileosto-

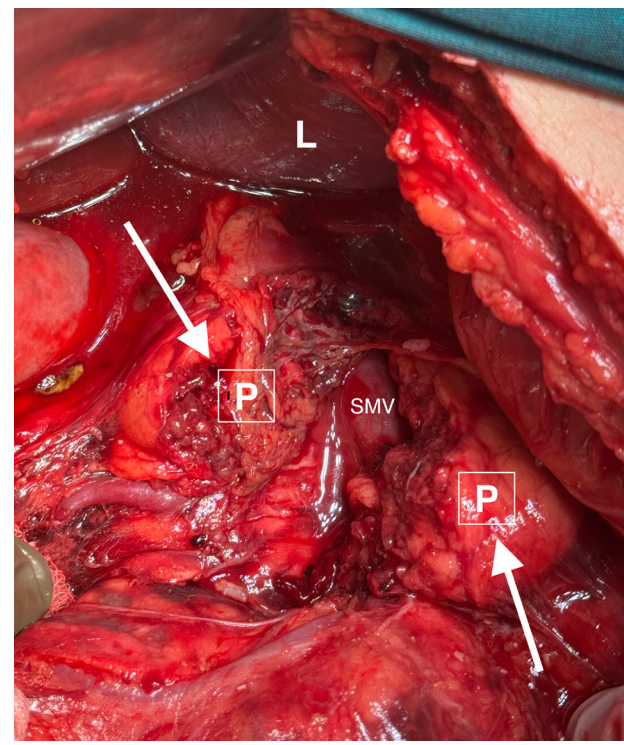

Figure 4. Intraoperative view of a Grade V pancreatic head injury. *L: liver; P: pancreas; SMV: superior mesenteric vein.*

my was created. During the ICU stay, the orthopedic team performed multiple surgical interventions due to extremity fractures. Following stabilization, the patient was transferred to the orthopedic ward. After the second surgery, no additional pathology requiring urgent surgical intervention from a general surgery perspective was observed. During postoperative follow-up, the patient was discharged and scheduled for outpatient follow-up for evaluation and planning of ileostomy closure.

DISCUSSION

Pancreatic injuries are rare in cases of blunt abdominal trauma and are frequently accompanied by injuries to adjacent organs.[3,7] In the literature, only a limited number of case reports address the diagnosis and management of such injuries.[8] This case report aimed to discuss the outcomes of EPD for pancreatic head trauma accompanied by multiorgan injury in the context of the current literature.

Diagnosis of pancreatic injuries is particularly challenging in the early phase. Serum amylase and lipase levels have limited diagnostic value, and computed tomography may also be insufficient for the detection of pancreatic duct injury. Therefore, in cases with high clinical suspicion, diagnostic laparotomy may be warranted.[9] Surgical intervention is often required for high-grade pancreatic injuries. EPD may serve as a life-saving option in hemodynamically stable patients, particularly in those with pancreatic head and duodenal injuries accompanied by biliary tract damage.[10] However, this procedure is associated with a high risk of morbidity and mortality. Therefore, the decision to perform surgical intervention requires a multidisciplinary approach.[11,12] In cases of high-grade pancreatic injuries accompanied by multiorgan trauma, initial hemodynamic stabilization followed by the application of damage control surgery principles is recommended.[13] In hemodynamically unstable patients, the primary goal in managing severe pancreaticoduodenal trauma is the rapid correction of life-threatening hypovolemia, coagulopathy, acidosis, and hypothermia. The damage control surgery (DCS) approach applied for this purpose includes intra-abdominal hemorrhage control, temporary closure of gastrointestinal perforations, and containment of retroperitoneal contamination. During the initial surgical intervention, limited procedures-such as abdominal packing, drainage, and temporary abdominal closure-are preferred over definitive resections. After this stage, patients are transferred to the intensive care unit for physiological stabilization. Following this initial phase, a second-look surgery is typically performed within 48-72 hours, during which gastrointestinal reconstruction and, if necessary, pancreaticoduodenectomy are performed. This two-stage approach may be lifesaving and can reduce morbidity, particularly in cases involving concomitant vascular injuries and a high risk of mortality.[14] In this case, considering the patient's intraoperative hemodynamic stability, EPD was performed by a surgical team experienced in hepatopancreatobiliary procedures. During the same session, segmental colectomy with primary anastomosis was performed due to the presence of colonic laceration. No complications related to EPD occurred in the postoperative period. However, on postoperative day 11, a leak developed at the colocolonic anastomosis site, necessitating right hemicolectomy and end ileostomy creation. Pancreatic injuries are frequently accompanied by multiorgan trauma, highlighting the importance of a multidisciplinary approach in surgical planning for such cases. In this context, the presence of colonic injuries may warrant avoiding simultaneous anastomosis.[15] The surgical approach may vary depending on the patient's clinical status, intraoperative findings, degree of intra-abdominal contamination, and the surgeon's experience.

EPD is associated with significant risks, including coagulopathy, massive hemorrhage, prolonged operative times, and pancreatic fistula. According to the literature, patient-related factors such as advanced age, male sex, jaundice, and malnutrition, along with technical factors such as a soft pancreatic parenchyma, narrow duct diameter, and limited surgical experience, have been shown to increase the risk of postoperative complications.[16] However, in the present case, the decision to perform EPD was primarily guided by several favorable factors, including the patient's young age, preserved hemodynamic stability, absence of accompanying acidosis or coagulopathy, and the surgical team's expertise in hepatopancreatobiliary surgery.

CONCLUSION

Although rare, severe pancreaticoduodenal trauma is a complex clinical condition characterized by a high risk of complications and the need for advanced surgical management. In treating such cases, the patient's hemodynamic status, the presence of concomitant organ injuries, and the surgical team's experience play a critical role in shaping the therapeutic strategy. EPD may be considered a viable option in selected patients who require a multidisciplinary approach and high-level surgical expertise. This case underscores the importance of individualized decision-making and team-based management in the context of complex abdominal trauma.

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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.

Peer-review: Externally peer-reviewed.

Authorship Contributions: CConcept: B.S., N.B.K., D.D., K.E., A.A.; Design: B.S., N.B.K., D.D., K.E., A.A.; Supervision: B.S., N.B.K., D.D., K.E., A.A.; Resource: B.S.; Materials: B.S., K.E.; Data collection and/or processing: B.S., N.B.K.; Analysis and/or interpretation: B.S., D.D.; Literature review: B.S., N.B.K.; Writing: B.K., N.B.K., K.E.; Critical review: B.S., K.E.

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OLGU SUNUMU - *ÖZ*

Çoklu organ yaralanması olan hastada travmatik Pankreas-Duodenum ayrılması için acil Whipple prosedürü: Bir olgu sunumu ve derleme

Pankreatikoduodenal travmalar nadir görülmekle birlikte, yüksek morbidite ve mortalite riski taşıyan komplike cerrahi durumlar arasında yer almaktadır. Bu olgu sunumunda, acil servise araç dışı trafik kazası nedeniyle getirilen ve yapılan görüntülemelerinde batın içinde serbest hava ve serbest sıvı ile birlikte sağ böbrekte perfüzyon kaybı dahil çoklu organ yaralanması saptanan 17 yaşındaki erkek hastaya uygulanan acil pankreatikoduodenektomi (Whipple prosedürü) sunulmaktadır. Hastaya yapılan acil cerrahi eksplorasyonda; Grade V düzeyinde pankreas başı avülsiyonu, distal safra yolu hasarı, duodenal laserasyon, transvers kolonun proksimal üçte birlik kısmında laserasyon ve sağ böbrek devaskülarizasyonu tespit edilmiştir. Hastanın intraoperatif hemodinamik stabilitesi göz önünde bulundurularak Whipple prosedürü, segmenter kolon rezeksiyonu ve anastomoz ile birlikte sağ nefrektomi gerçekleştirilmiştir. Ameliyat sonrası 11. günde hastada kolokolonik anastomoz hattında kaçak gelişmiş olup, acil cerrahi girişimle sağ hemikolektomi ve uç ileostomi uygulanmıştır. Takip süresince hastada genel cerrahi açısından ek bir acil cerrahi müdahale gereksinimi olmamıştır. Bu olgu, yüksek riskli travmalarda multidisipliner ekip çalışması ve hastanın klinik durumuna göre bireyselleştirilmiş cerrahi kararların önemini vurgulamaktadır. Kompleks anatomik hasarların varlığında, uygun cerrahi zamanlamanın belirlenmesi, doğru teknik seçimi ve komplikasyonların yönetimi, tedavi başarısında belirleyici rol oynamaktadır. Bu kapsamda, cerrahi yaklaşım ve zamanlama, güncel literatür eşliğinde tartışılmış ve benzer olgularla karşılaştırmalı olarak değerlendirilmiştir.

Anahtar sözcükler: Acil cerrahi; duodenum yaralanması; çoklu organ yaralanma; pankreas travması; Whipple prosedürü.

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CASE REPORT

Aortoesophageal fistula from an ingested large hand needle in a nonverbal adult with autism

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ABSTRACT

Aortoesophageal fistula (AEF) is a rare and life-threatening condition that can result from foreign body ingestion, particularly in vulnerable populations with impaired communication, where diagnosis may be delayed. A 26-year-old male with severe autism and limited expressive ability presented to the emergency department with a two-day history of fever and melena. Two hours prior to arrival, hematemesis occurred during an attempt at oral intake. Caregivers reported behavioral changes and a deterioration in his general condition over the preceding 10 days. Diagnostic imaging revealed a large, curved metallic foreign body that had perforated the esophageal wall, traversed the prevertebral space, and appeared to penetrate the thoracic aorta with its tip, leading to mediastinitis and AEF. Despite emergency surgery with cardiopulmonary bypass, the patient succumbed to sepsis and multi-organ failure within 24 hours postoperatively. This case highlights the importance of clinicians considering the possibility of an asymptomatic period following sharp metallic foreign body ingestion, which can lead to severe complications, particularly in patients with communication impairments. The asymptomatic interval can result in significant complications, including luminal erosion, rupture, or the development of a fistula with adjacent structures. Emergency physicians must suspect AEF, especially in patients with a history of foreign body ingestion, when gastrointestinal bleeding is accompanied by signs of severe infection. Timely use of computed tomography (CT) imaging is critical for confirming the diagnosis and determining the need for emergency surgical intervention. This case underscores the necessity of thorough evaluation in managing potentially life-threatening foreign body ingestion.

Keywords: Foreign body ingestion; aortoesophageal fistula; mediastinitis; autism.

INTRODUCTION

Aortoesophageal fistula (AEF) is a rare but life-threatening condition that typically results from esophageal perforation, often due to foreign body ingestion. Early recognition of foreign body ingestion is crucial to prevent progression to AEF and severe complications such as mediastinitis, sepsis, and multi-organ failure.[1,2] In patients suffering from dysphagia, chest pain, a history of problematic ingestion, and vomiting of a small amount of blood, AEF should be considered.[2] However, the clinical presentation of AEF can be subtle, especially in patients with communication impairments, where diagnosis may be delayed and the clinical course can deteriorate rapidly. This case report describes an adult patient with severe autism who ingested a sharp foreign body, leading to a delayed diagnosis of AEF and subsequent fatal sepsis despite emergency surgical intervention.

CASE REPORT

A 26-year-old male with severe autism and limited expressive capacity presented to the emergency department with a two-day history of fever and melena. Two hours prior to arrival, hematemesis occurred while attempting oral intake. Given his profound communication limitations, he was un-

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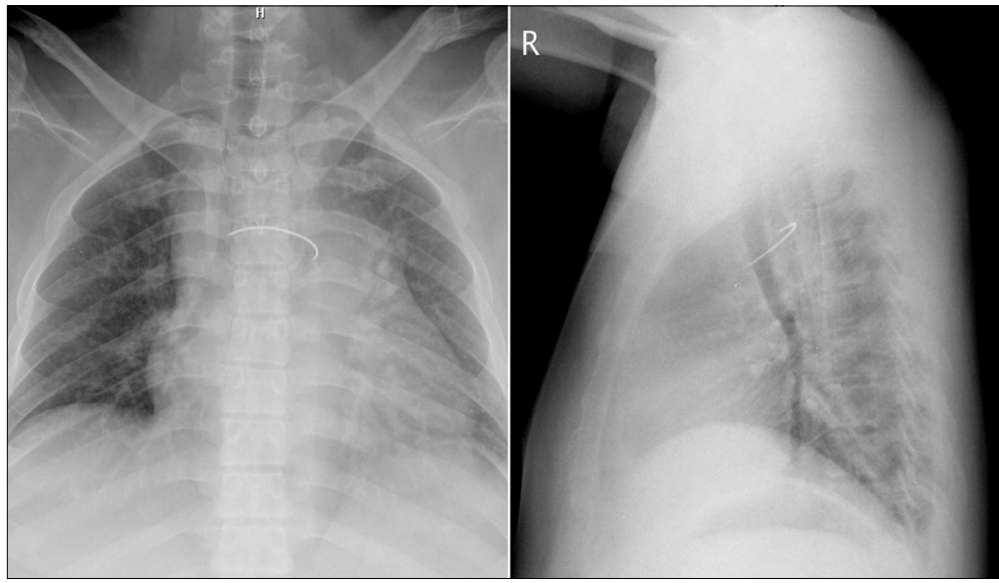

Figure 1. Chest radiograph showing a large semicircular metallic foreign body projected over the mid-thoracic region.

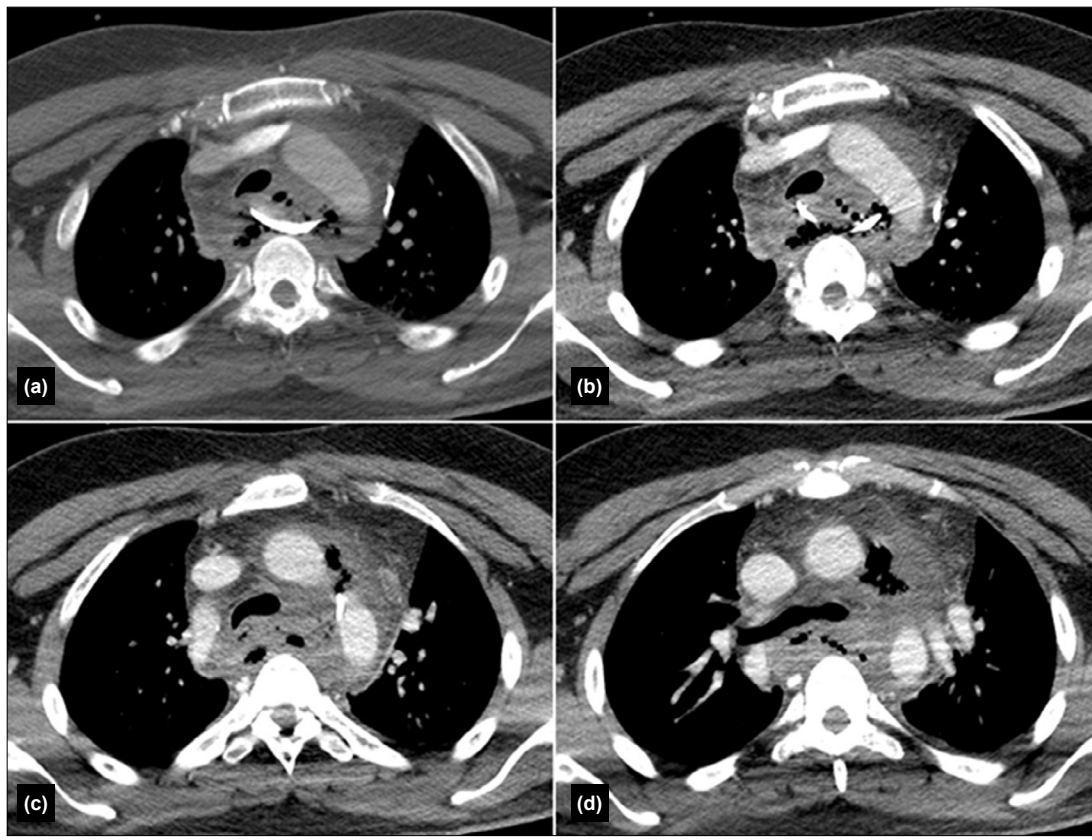

Figure 2. Contrast-enhanced chest computed tomography (CT) showing a large semicircular metallic foreign body perforating the esophageal wall and penetrating the posterior wall of the thoracic aorta, with surrounding mediastinal fluid accumulation and gas formation consistent with abscess formation.

able to clearly express pain or other symptoms in the days before presentation, but caregivers noted behavioral changes and deterioration in his general condition over the preceding 10 days. On presentation, his body temperature was 39.3°C, blood pressure was 100/60 mmHg, and heart rate was 110 beats per minute. His hemoglobin was 7.8 g/dL (previously 14 g/dL one year earlier), C-reactive protein was 22.08 mg/dL, and erythrocyte sedimentation rate was 52 mm/h. The white

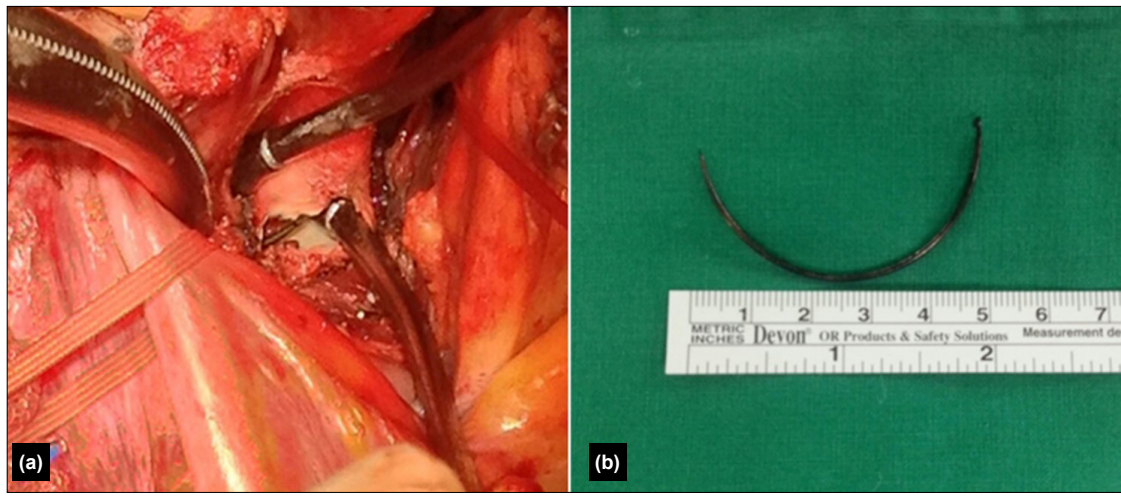

Figure 3. (a) Intraoperative image showing the tip of a large semicircular hand needle penetrating through the wall of the thoracic aorta. **(b)** The extracted semicircular hand needle measures approximately 5 cm in diameter.

blood cell count was 10,500/μL, with 88.4% neutrophils and 4.7% lymphocytes. A chest X-ray demonstrated a large semicircular metallic foreign body at the level of the carina (Fig. 1), and an axial contrast-enhanced computed tomography (CT) scan revealed gas collections and fluid accumulation within the prevertebral space, consistent with mediastinal infection or abscess formation. The inflammatory process extended superiorly to involve the aortopulmonary window and the region surrounding the aortic arch. The large, curved metallic foreign body had perforated the esophageal wall, traversed the prevertebral space, and appeared to penetrate the thoracic aorta with its tip (Fig. 2). The patient underwent emergency surgery under cardiopulmonary bypass and circulatory arrest. During surgical preparation following anesthesia induction, massive hematemesis occurred, prompting immediate establishment of cardiopulmonary bypass to maintain circulation. However, severe hemodynamic instability prior to resuscitation likely contributed to early multi-organ dysfunction. A large semicircular hand needle, approximately 5 cm in diameter, was found penetrating the thoracic aorta (Fig. 3). The foreign body was removed, and both the aortic and esophageal defects were repaired. Postoperatively, the patient remained hypotensive due to profound vasoplegia and ultimately died on postoperative day 1 as a result of progressive sepsis. Written informed consent was obtained from the patient's parent, who was the legal representative of the deceased patient.

DISCUSSION

Aortoesophageal fistula is an abnormal communication between the esophagus and the aorta. It is a rare and life-threatening condition, most commonly caused by thoracic aortic aneurysm. Other etiologies include esophageal malignancy, ingestion of foreign bodies, postoperative complications, and infection. The clinical course of AEF typically deteriorates abruptly into a life-threatening state at the onset of massive hematemesis, which is often characterized by bright red arterial bleeding.[1] Foreign body ingestion is the second most common cause of AEF. Most impacted foreign bodies are identified within 24 hours of ingestion, and with prompt recognition, nearly all can be successfully removed endoscopically without the need for surgical intervention.[2,3] However, when sharp or pointed metallic objects, fish bones, or clips are ingested—or when diagnosis is delayed—impaction or perforation can occur at sites of acute angulation or physiologic narrowing, most commonly within the esophagus, potentially progressing to AEF.[1,2] Once the diagnosis of AEF resulting from a foreign body is established, prompt surgical intervention is crucial to control hemorrhage and address both the foreign body and the fistula. Aortic repair is particularly challenging due to contamination of the surgical field by fistulous contents and the extensive inflammatory response surrounding the defect. Consequently, the mortality rate associated with the management of AEF remains significantly high.[2,4]

Accidental ingestion of foreign bodies occurs more frequently in vulnerable populations such as young children, the elderly with dental issues, and individuals with intellectual disabilities or psychiatric disorders.[1,5,6] In patients with impaired communication, diagnosis may be significantly delayed (especially when ingestion does not provoke acute discomfort) resulting in progression to AEF. The clinical progression of AEF is classically described by the Chiari triad, which includes mid-thoracic pain, a sentinel hemorrhage (a minor initial bleeding episode), and subsequent fatal exsanguination.[7] A notable feature of the Chiari triad is the presence of an asymptomatic interval between the initial pain or sentinel hemorrhage and the final catastrophic bleeding event, which can range from several hours to days or even weeks. In cases of AEF caused by foreign body ingestion, this asymptomatic window plays a particularly critical role in influencing clinical outcomes.[1] When accompanied by severe necrotizing mediastinitis due

to delayed diagnosis, the clinical course becomes even more devastating. Surgical management is often challenging due to extensive infection and tissue destruction, and outcomes are poor despite aggressive intervention.[8]

CONCLUSION

Why Should an Emergency Physician Be Aware of This?

We report an extremely rare case of AEF and mediastinitis resulting from delayed recognition of an ingested large semicircular hand needle in a nonverbal adult with autism. This case highlights the importance of clinicians recognizing the potential for an asymptomatic period following sharp metallic foreign body ingestion, which can lead to severe complications, including the formation of a fistula with adjacent structures, particularly in nonverbal adults with intellectual disabilities or pediatric patients with communication impairments. Although this condition is extremely rare, it may be easily overlooked as a typical foreign body case, as a radiopaque metallic foreign body is readily identifiable on the routine initial chest X-ray commonly performed in the emergency department. Moreover, in this patient, where melena was the primary complaint upon presentation to the Emergency Room (ER), it could have been misinterpreted as a simple esophageal injury rather than a more serious condition such as AEF. In such situations, there is a risk of prematurely performing endoscopic removal, which may not be appropriate and could potentially induce life-threatening bleeding. The prolonged asymptomatic interval following foreign body ingestion may lead to progressive complications such as luminal erosion, rupture, or even the development of AEF. Emergency physicians must maintain a high index of suspicion for AEF, especially in patients with foreign body ingestion who present with gastrointestinal bleeding accompanied by signs of severe infection. Timely use of CT imaging is critical for confirming the diagnosis and determining the need for emergency surgical intervention. This case underscores the necessity of thorough evaluation in managing potentially life-threatening foreign body ingestion.

Peer-review: Written informed consent was obtained from the patient's parent, who was the legal representative of the deceased patient.

Peer-review: Externally peer-reviewed.

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OLGU SUNUMU - *ÖZ*

Otizmli, konuşamayan bir yetişkinde yutulan büyük el iğnesinden kaynaklanan aortoesofageal fistül

Aortoesofageal fistül (AEF), yabancı cisim yutulması sonucu ortaya çıkabilen, özellikle iletişim bozukluğu olan savunmasız popülasyonlarda tanı gecikmesine neden olabilen, nadir görülen ve yaşamı tehdit eden bir durumdur. Şiddetli otizm ve sınırlı ifade yeteneği olan 26 yaşındaki bir erkek hasta, iki gündür süren ateş ve melena şikayetiyle acil servise başvurdu. Hastanın acil servise gelmesinden iki saat önce, ağızdan beslenme denemesi sırasında hematemezis meydana geldi. Bakıcılar, son 10 gün içinde hastanın davranışlarında değişiklikler ve genel durumunda kötüleşme olduğunu bildirdi. Tanı amaçlı görüntüleme, özofagus duvarını delip prevertebral boşluğu geçen ve ucu torasik aortu delmiş gibi görünen büyük, kavisli metalik bir yabancı cisim ortaya çıkardı. Bu durum mediastinit ve AEF'ye yol açtı. Kardiyopulmoner baypas ile acil cerrahi müdahaleye rağmen, hasta ameliyat sonrası 24 saat içinde sepsis ve çoklu organ yetmezliği nedeniyle hayatını kaybetti. Bu vaka, özellikle iletişim bozukluğu olan hastalarda ciddi komplikasyonlara yol açabilen keskin metalik yabancı cisim yutulmasının ardından asemptomatik bir dönem olasılığını klinisyenlerin dikkate almasının önemini vurgulamaktadır. Asemptomatik dönem, lümen erozyonu, rüptür veya komşu yapılarla fistül gelişimi gibi önemli komplikasyonlara yol açabilir. Acil tıp hekimleri, özellikle yabancı cisim yutma öyküsü olan hastalarda, gastrointestinal kanamaya şiddetli enfeksiyon belirtileri eşlik ettiğinde AEF'yi şüphelenmelidir. Tanı teyit etmek ve acil cerrahi müdahale ihtiyacını belirlemek için bilgisayarlı tomografi (BT) görüntülemesinin zamanında kullanılması çok önemlidir. Bu vaka, potansiyel olarak yaşamı tehdit eden yabancı cisim yutulmasının tedavisinde kapsamlı değerlendirmenin gerekliliğini vurgulamaktadır.

Anahtar sözcükler: Aortoesofageal fistül; mediastinit; otizm; yabancı cisim yutulması.

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CASE REPORT

Cardiopulmonary resuscitation-related renal vein and multivisceral organ injuries: a rare forensic autopsy case

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ABSTRACT

Cardiopulmonary resuscitation (CPR) is a vital life-saving intervention but may result in various traumatic injuries, particularly with vigorous or prolonged efforts. Although visceral injuries are uncommon, they can be fatal. In this report, we present a rare postmortem case demonstrating multiple internal injuries-including pericardial and myocardial lacerations, liver laceration, and renal pelvis and renal vein injury-following CPR. A 70-year-old male was found unresponsive on the roadside and transported to the emergency department, where CPR was initiated due to cardiac arrest. Despite all medical interventions, resuscitation efforts were unsuccessful. Laboratory tests showed elevated cardiac and liver enzymes. A forensic autopsy was performed due to the suspicious nature of the death. External examination revealed no signs of assault; a burn over the sternum was consistent with defibrillator pad contact. CPR-related rib and sternal fractures were observed. A non-transmural myocardial laceration with pericardial injury was noted. Minor intraperitoneal hemorrhage, small hepatic and renal lacerations, and a millimetric tear in the left renal vein were identified. Histopathology revealed severe coronary atherosclerosis with ~80% luminal narrowing. Toxicology detected only therapeutic drug levels. The patient had a history of hypertension without recent cardiac follow-up. Surveillance footage showed the individual clutching his chest before collapsing. In conclusion, this case underscores that multiple internal organ injuries, although uncommon, may arise as complications of CPR. In elderly individuals, reduced tissue resilience may predispose to pericardial, myocardial, hepatic, and renal venous injuries, which should be considered in both clinical management and forensic evaluations.

Keywords: Autopsy; cardiopulmonary resuscitation; resuscitation injuries; renal injury.

INTRODUCTION

Ischemic heart disease is the leading cause of death worldwide, accounting for 13% of all fatalities.[1] Cardiopulmonary resuscitation (CPR) is a critical emergency intervention performed to re-establish oxygen-rich blood circulation to vital organs such as the brain and heart following cardiac arrest.[2] Despite its life-saving potential, CPR can result in a variety of traumatic injuries, particularly in cases involving prolonged or forceful compressions.

Sixty percent of patients sustained CPR-related injury among all CPR cases.[3] The most frequently encountered complications are rib and sternal fractures; however, injuries to internal organs such as the heart, pericardium, liver, spleen, and great vessels have also been reported.[4,5] Although these complications are well documented, visceral organ injuries are relatively rare but may have fatal consequences.[4] While isolated injuries to the myocardium or liver have been sporadically described, the simultaneous occurrence of traumatic damage involving the pericardium, myocardium, liver, and renal vein following CPR is extremely uncommon.[5,6]

Recognition of such rare presentations is critical for both clinical assessment and forensic evaluation. In this report, we present a rare postmortem case featuring multiple internal in-

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juries, including pericardial and myocardial injury, liver laceration, renal pelvis, and renal vein injury, following CPR.

Ethical approval for this study was obtained from the Artvin Çoruh University Scientific Research and Publication Ethics Committee (Decision Number: E-18457941-050.99-175400, dated 28.03.2025). The study was conducted in accordance with the principles of the Declaration of Helsinki.

CASE REPORT

A 70-year-old male was found unresponsive in a prone position on the roadside and was immediately transported by emergency medical services to the district state hospital emergency department. Cardiopulmonary resuscitation was initiated due to cardiac arrest; however, no response was obtained, and the patient was declared dead. Initial biochemical analyses revealed elevated levels of alanine aminotransferase (ALT: 135 U/L, ref: 0-41), aspartate aminotransferase (AST: 114 U/L, ref: 0-40), creatine kinase-myocardial band (CK-MB: 60.3 U/L, ref: 0-25), and troponin I (0.015 ng/mL, ref: 0.003-0.014). As the death was classified as sudden and suspicious, a forensic autopsy was performed.

External examination showed no signs of external trauma or assault. A 4×2 cm area of skin burn was observed over the sternum, suggestive of defibrillator pad contact during CPR (Fig. 1).

During the autopsy, bilateral pneumothorax tests were negative. Multiple rib fractures were identified: on the left side at the parasternal line (2nd-4th ribs), and on the right side at the midclavicular line (2nd rib) and anterior axillary line (5th and 6th ribs). These were determined to be resuscitation-related. The sternum showed a transverse fracture at the level of the 3rd rib and a vertically oriented fracture extending from the same level down to the xiphoid process (Fig. 1). These fractures were associated with a laceration of the anterior pericardium.

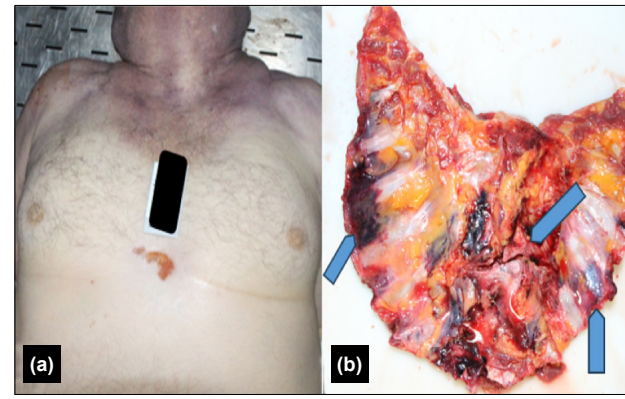

Figure 1. Skin burn and rib and sternum fractures caused by resuscitation. **(a)** Skin burn on the sternum **(b)**Displaced fractures of the sternum and ribs with surrounding ecchymosis.

Examination of the heart revealed a non-transmural myocardial laceration (3.5×1 cm) corresponding to the area of pericardial injury, which did not extend into the cardiac chambers or major vessels (Fig. 2). Upon opening the abdominal cavity, approximately 150–200 cc of intraperitoneal hemorrhage was observed. A 1.5 cm laceration was detected on the anterior surface of the liver (Fig. 3). The left kidney was surrounded by capsular and perirenal hemorrhage, and a 1.5 cm laceration was observed on the posterior surface of the right kidney. Upon further evaluation using a blunt-tipped instrument, all renal vessels appeared macroscopically intact. However, when fluid was injected into the lumen of the left renal vein using a syringe, minor leakage was observed in the mid-portion of the vein, indicating a millimetric injury to the vessel wall (Fig. 4).

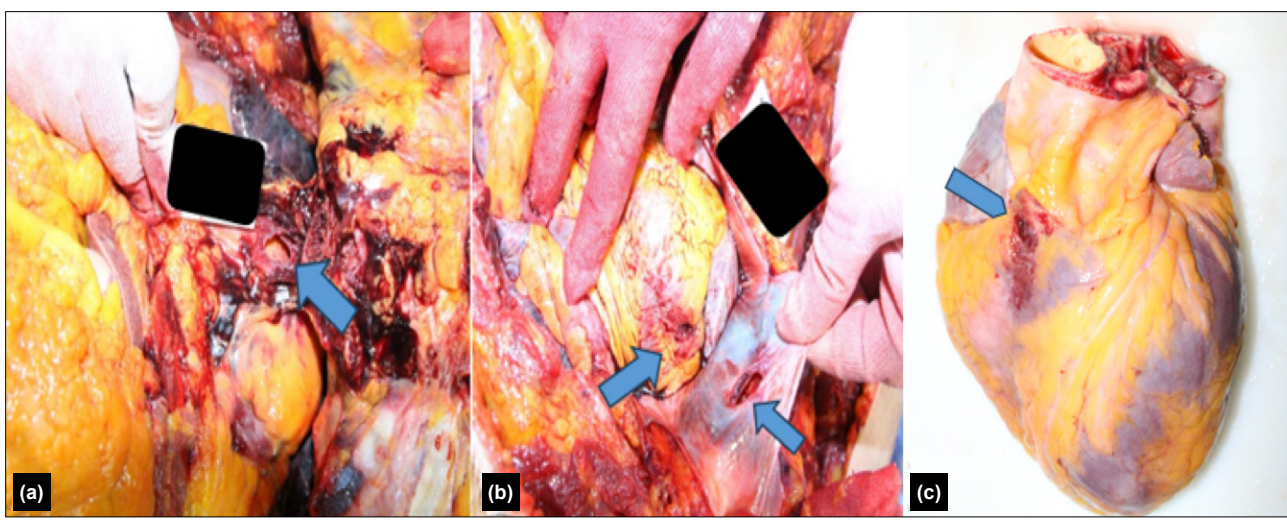

Figure 2. Pericardial and myocardial injuries caused by resuscitation. **(a)** Pericardial laceration **(b)** Combined pericardial and myocardial laceration **(c)** Non-transmural myocardial laceration.

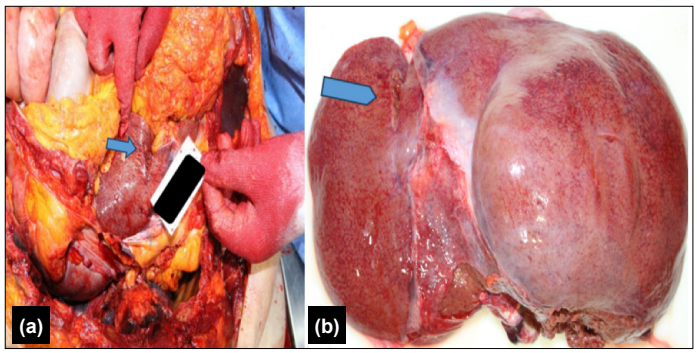

Figure 3. Liver injury caused by resuscitation. **(a)** Liver laceration observed after abdominal dissection **(b)** Anterior surface appearance of the liver laceration on the dissection table.

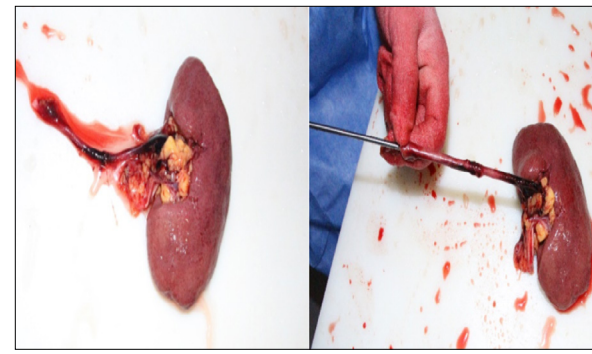

Figure 4. Smearing-type hemorrhage in the left kidney and appearance of the renal vein with blood clots.

Histopathological examination of the coronary arteries revealed advanced atherosclerosis, with approximately 80% luminal narrowing due to calcified atheromatous plaques. Toxicological analysis detected only therapeutic levels of medications.

Review of the patient's medical history through the national health record system revealed a known history of hypertension and long-term antihypertensive use, but no cardiology outpatient visits within the past decade (2015-2025).

Surveillance footage from the scene showed the individual clutching his chest before collapsing. Based on the minimal nature of the renal vein injury and the limited volume of intra-abdominal hemorrhage, this finding was not considered to be the direct cause of death. In light of the elevated cardiac enzymes (CK-MB, troponin I), liver transaminases (AST, ALT), and the presence of severe coronary artery disease on histological analysis, the cause of death was determined to be "atherosclerotic and ischemic heart disease."

DISCUSSION

Cardiopulmonary resuscitation, while a life-saving intervention in cases of sudden cardiac arrest, may lead to serious traumatic complications, particularly when chest compressions are forceful or prolonged. Although rib and sternal fractures are the most frequently reported complications,[4,5] as demonstrated in this case, CPR can also result in injuries to internal organs such as the heart, pericardium, liver, and kidneys.[3,6-8] To the best of our knowledge, this is the first report to document that chest compression provoked renal pelvis and vein injury, let alone caused mortality.

Pericardial and myocardial injuries may occur due to direct mechanical stress exerted on the heart during chest compressions. In elderly individuals, decreased tissue elasticity and the presence of pre-existing cardiovascular disease are significant predisposing factors for such complications.[9] In our case, the presence of both transverse and vertical sternal fractures suggests a mechanism for the pericardial laceration. The non-transmural myocardial laceration observed is likely attributable to repetitive, abrupt chest compressions during CPR.

Although rare, intra-abdominal organ injuries may also occur during CPR. Among these, hepatic and splenic lacerations, gastric dilatation, and gastric perforation are the most commonly reported. Hepatic injury is the most frequently encountered intra-abdominal complication, with an incidence ranging between 0.6% and 3%.[3,7,8] These injuries are typically associated with compressions applied just below the lower sternum. Lacerations observed on the anterior surface of the right hepatic lobe may result from compression of the liver between the diaphragm and thoracic cage during resuscitation efforts.[10] Although several case reports have described CPR-related hepatic lacerations,[4,7,8,10] these injuries are often accompanied by massive internal hemorrhage. In contrast, our case presented with limited intraperitoneal bleeding despite the presence of liver trauma.

Renal and renal vascular injuries are extremely rare following blunt trauma.[11] However, pressure transmitted to the posterior abdominal wall adjacent to the lumbar spine may result in damage to the perirenal tissues. In our case, although the renal vein appeared macroscopically intact, a fine leak detected via fluid injection into the left renal vein suggested a minor laceration of the vessel wall. This finding indicates that abrupt pressure changes within the abdominal cavity during CPR may cause subtle vascular injuries. According to the patient's clinical findings, the most probable cause of the urinary tract injury in this case was chest compression-related trauma, which needs to be taken into consideration.

To date, only one CPR-related renal injury has been reported: a 72-year-old man who sustained bilateral urinary tract damage following CPR. Hematuria and incomplete rupture of the renal pelvis and ureter were the findings of renal damage in that case. He was discharged from the hospital following treatment.[12] However, in our case, a severe renal complication of CPR was noted, which included renal vein perforation and a kidney laceration measuring 1.5 cm in length.

On the other hand, aging is an independent factor that may increase the risk of damage resulting from CPR.[9] Given the age of our case, it could be said that this finding aligns with previously reported data.[12]

Such multi-organ injuries are most often detected during autopsy and hold significant relevance in forensic investigations. Accurate identification of internal organ injuries related to CPR may provide insight into the appropriateness and effectiveness of resuscitative efforts. Furthermore, proper interpretation of these findings is critical for distinguishing CPR-related complications from trauma-induced fatalities in forensic medicine.

Although CPR is an essential life-saving intervention, it can occasionally result in rare but serious internal injuries, including those involving the heart, liver, and kidneys. These complications may not be immediately apparent in clinical settings and are often detected during postmortem examinations. Increased awareness of such injuries is crucial for physicians and emergency healthcare providers, as it may influence the evaluation of CPR outcomes and guide the management of post-resuscitation care. Recognizing the potential for visceral trauma can support more comprehensive assessments, reduce the risk of misinterpretation, and promote safer resuscitation practices.

CONCLUSION

In conclusion, this case underscores that multiple internal organ injuries, although uncommon, may arise as complications of cardiopulmonary resuscitation. Pericardial, myocardial, hepatic, and renal venous injuries-particularly in elderly individuals with decreased tissue resilience-should be taken into account during both clinical assessments and forensic investigations. The intensity and duration of chest compressions appear to be critical factors contributing to such injuries and should be carefully evaluated in post-resuscitative analyses.

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Ethics Committee Approval: This study was approved by the Artvin Çoruh University Scientific Research and Publication Ethics Committee (Date: 28.03.2025, Decision No: E-18457941-050.99-175400).

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Conflict of Interest: None declared.

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OLGU SUNUMU - *ÖZ*

Kardiyopulmoner resüsitasyona bağlı renal ven ve çoklu iç organ yaralanmaları: Nadir bir adli otopsi olgusu

Kardiyopulmoner resüsitasyon (KPR) hayat kurtarıcı bir girişim olmakla birlikte, özellikle uzun süren veya şiddetli uygulamalarda çeşitli travmatik yaralanmalara neden olabilmektedir. Viseral organ yaralanmaları nadir görülse de ölümcül sonuçlar doğurabilmektedir. Bu olgu sunumunda, KPR sonrasında gelişen perikart ve miyokart laserasyonlarının yanı sıra karaciğer laserasyonu ile renal pelvis ve renal ven yaralanmalarını içeren nadir ve çoklu iç organ yaralanmalarını içeren bir postmortem olgu sunulmaktadır. Yolda bilinci kapalı halde bulunan 70 yaşındaki erkek hasta, acil servise getirilmiş ve kardiyak arrest nedeniyle KPR uygulanmıştır. Tüm tıbbi müdahalelere rağmen yaşama döndürülememiştir. Laboratuvar testlerinde kardiyak ve karaciğer enzimlerinde yükselme saptanmıştır. Ölümün şüpheli bulunması üzerine adli otopsi yapılmıştır. Dış muayenede darp-cebir izine rastlanmamış, sternum üzerindeki yanık defibrilatör pedine bağlı olarak değerlendirilmiştir. KPR'ye bağlı sternum ve çok sayıda kosta kırığı, perikardiyal yaralanma ile birlikte miyokardda transmural olmayan laserasyon, hafif intraperitoneal hemoraji, karaciğer ve böbrekte laserasyonlar ile sol renal vende milimetrik yaralanma tespit edilmiştir. Histopatolojik incelemede koroner arterlerde ileri düzey ateroskleroz (yaklaşık %80 lümen daralması) izlenmiştir. Toksikolojik analizde yalnızca tedavi edici düzeyde ilaç saptanmıştır. Hastanın hipertansiyon öyküsü bulunmakta olup, yakın dönemde kardiyolojik takip yapılmadığı öğrenilmiştir. Güvenlik kamerası kayıtlarında kişinin göğsünü tutarak yere yığıldığı görülmüştür. Sonuç olarak, bu olgu KPR sonrası nadir görülen çoklu iç organ yaralanmalarına dikkat çekmektedir. Özellikle yaşlı bireylerde doku dayanıklılığının azalması nedeniyle perikardiyal, miyokardiyal, hepatik ve renal ven yaralanmaların hem klinik hem de adli değerlendirmelerde göz önünde bulundurulması önemlidir.
Anahtar sözcükler: Kardiyopulmoner resüsitasyon; resüsitasyon yaralanmaları; renal yaralanma; otopsi.

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