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Dear Colleagues,

The Journal of Comprehensive Surgery concludes its first year, we take immense pleasure in coming together with you in the final issue of the year. This year, we sincerely wish to extend our gratitude to all the authors who contributed to the advancement and enrichment of our journal. It is through your dedicated efforts and the quality of your articles that our journal has continued to expand and flourish.

Exciting projections await us for the upcoming issues. In our quest to further diversify and expand our journal, we are engaged in exploring new concepts and subjects. Towards this end, our aim is to incorporate a more comprehensive and varied range of content by collaborating with authors from various surgical disciplines. Furthermore, we are dedicated to making our journal more accessible, tailoring our content to align with the interests of our readers based on their feedback.

In our forthcoming issues, we will continue to address topics that will captivate and pique your interest, aiming to leave a lasting impact on our readers. If there are specific subjects or areas of interest you wish to see featured in our journal, please do not hesitate to share your suggestions with us.

Together with our esteemed readers, we will persist in our efforts to enhance our journal each day. We extend our heartfelt thanks for your support and eagerly anticipate meeting you in our next edition.

Best regards..

Alparslan KOÇ MD. Assoc. Prof.

Editor

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Comparison of pathologies in patients operated for transverse colon tumor with embryogenic and anatomical insights

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ABSTRACT

Aims: Transverse colon cancers account for only about 10% of all colon cancers. It is generally known that proximal and distal colon tumours have different genetic and biological features. The transverse colon serves as the division point between proximal and distal regions. In this study, transverse colon cancer was classified both embryologically and anatomically, and a comparative analysis was conducted based on pathological results.

Methods: A retrospective study was conducted on patients who underwent surgery for transverse colon cancer at Ankara Bilkent City Hospital between 2019 and 2023. Patients were classified embryologically as proximal (Group A) and distal (Group B), and anatomically as hepatic angle (Group 1), middle (Group 2), and splenic angle (Group 3), and pathological results were compared among these groups.

Results: For embryogenic classification in terms of the final pathological staging, group A had 1 (1.47%) in Stage 1, 32 (47.05%) in Stage 2, 26 (38.23%) in Stage 3, and 9 (13.23%) in Stage 4. Group B had 2 (2.54%) in Stage 1, 29 (50%) in Stage 2, 20 (34.48%) in Stage 3, and 7 (12.06%) in Stage 4. There was no significant difference between the groups. For anatomical classification, the number of patients in Stages 1, 2, 3, and 4 for groups 1, 2, and 3 were as follows: Stage 1: 2 (3.5%), 1 (3.57%), 0 (0%); Stage 2: 29 (50.87%), 17 (60.81%), 15 (37.5%); Stage 3: 20 (35.7%), 7 (25%), 19 (47.5%); Stage 4: 7 (12.28%), 3 (10.71%), 6 (15%). There was no statistically significant difference between the groups ($p>0.05$).

Conclusion: The pathological results and stages of transverse colon cancers classified embryologically and anatomically showed no significant differences among the groups.

Keywords: Colon cancer, transverse colon, embryology, anatomy

INTRODUCTION

Colorectal carcinoma constitutes approximately 10% of all carcinomas and ranks as the third most commonly diagnosed cancer, with the fourth highest mortality rate.¹ Neoplasms located proximally and distally in the colon exhibit molecular, biological, anatomical and embryological differences.^{1,2} Transverse colon cancers, on the other hand, are situated right in the middle between proximal and distal (or right/left) colon tumors and have been reported to have a poorer prognosis compared to cancers in other regions.³ The complex embryology and anatomy of the transverse colon, which originates from the junction of the midgut and foregut and is in close proximity to foregut-derived organs such as the pancreas, omentum, and stomach, are believed to contribute to the unfavorable prognosis of transverse colon cancers.³ Furthermore, the classification of the transverse colon as either proximal or distal has been deemed problematic, as evidenced by its exclusion in the CALGB80405 study conducted by Venook.²

The surgical management of transverse colon cancers is a subject of debate; however, the generally accepted surgical treatment is Complete Mesocolic Excision (CME). CME is considered the standard treatment for colon cancers.⁴ The goal of CME is to ligate at their roots the arteries that feed the relevant part of the colon and eliminate the region with the same embryological base.⁵ Resection with embryological integrity and central vascular ligation lowers recurrence not only in the rectum but also in other colon segments.⁴⁻⁶ Transverse colon tumors are treated with different surgical procedures depending on their localization. Tumors near the hepatic angle are treated with extended right hemicolectomy, those near the splenic angle undergo extended left hemicolectomy, and medial tumors are managed with transverse colectomy. Consequently, different embryogenic tissues and arteries are included in the specimen.³ These treatments can be carried out through open, laparoscopic, or robotic approaches and have equivalent oncological outcomes.^{5,7,8}



Due to the anatomical and embryological characteristics of the transverse colon, as well as its propensity for invasion of adjacent organs and extra-mesenteric lymph node metastasis, managing transverse colon cancer poses additional challenges.⁹

The challenges in the treatment of transverse colon cancers due to their unique characteristics are well-known. However, there have been no reported differences within transverse colon tumors based on their classification and pathological results. In this study, transverse colon tumors were classified embryologically as cancers originating from the midgut and hindgut, and anatomically as tumors located in the hepatic angle, splenic angle, and medial regions. The aim was to compare pathological results within these classifications.

METHODS

A retrospective analysis was conducted on 126 patients who underwent extended right hemicolectomy, extended left hemicolectomy, and transverse colectomy due to hepatic angle, splenic angle, and transverse colon tumors at Ankara Bilkent City Hospital between May 2019 and May 2023. Approval number E1-23-3693 was received for the study from Ankara Bilkent City Hospital Ethics Committee (Date: 19.06.2023). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The patients' demographic characteristics, preoperative stages, pathological findings, morbidity, and mortality data were examined. Patients who underwent these procedures for reasons other than benign causes, hepatic angle, transverse colon, and splenic angle tumors were not included in the study.

The patients were classified anatomically as Group 1 for hepatic angle tumors, Group 2 for transverse colon tumors, and Group 3 for splenic angle tumors. They were also classified embryologically as Group A for tumors originating from the midgut and Group B for tumors originating from the hindgut. The groups that were separated anatomically and embryologically were compared with each other in terms of preoperative hematological parameters, tumor markers, clinical stages, surgical margin positivity, the number of removed lymph nodes, and pathological stages.

Inclusion and Exclusion Criteria

All patients over the age of 18 who were diagnosed with transverse colon cancer and operated on were included. Patients who underwent transverse colon resection for another reason, resection for palliation, or patients who did not undergo oncological resection were not included in the study.

Statistical Analysis

Descriptive statistics were used to summarize patient demographics, including mean age, gender distribution, and more. The chi-squared test was applied to assess whether there was a significant relationship between anatomical groups (Group 1, 2, 3) and gender distribution. An independent samples t-test was utilized to determine if there was a significant age difference between embryological groups (Group A vs. Group B). Analysis of Variance (ANOVA) was conducted to examine if anatomical groups had varying impacts on the number of lymph nodes removed.

Additionally, a Mann-Whitney U test was employed to compare tumor stage distribution between embryological groups (Group A vs. Group B). Lastly, a chi-squared test was used to investigate associations between anatomical groups and final pathological stages. The data analysis was conducted using the IBM SPSS Statistics 23 statistical package software (IBM Corp., Armonk, NY, 2016). In the study, the significance level was set at $p < 0.05$.

RESULTS

Embryological Classification

Embryologically, there were 68 patients in Group A and 58 patients in Group B, and there was no statistically significant difference between them ($p > 0.05$). The mean age of Group A was 67.2, and Group B was 66.4, with no statistical difference between the groups ($p > 0.05$). Of the total 126 patients, 44 (34.64%) were female, and 83 (65.36%) were male. Among female patients, 22 (50%) were of midgut origin, while the other 50% were of hindgut origin. Among male patients, 47 (56.62%) were of midgut origin, and 36 (43.38%) were of hindgut origin, and no statistically significant difference was found ($p > 0.05$) (Table 1).

Table 1. Demographic data and preoperative stages

	Embryologic Classification		Anatomic Classification		
	A (n:68)	B (n:58)	1 (n:57)	2 (n:29)	3 (n:40)
Age	67.2	66.4	68.1	68	64.9
Gender					
Female	22 (50%)	22 (50%)	22 (50%)	9 (20.45%)	13 (29.55%)
Male	47 (56.62%)	35 (43.38%)	35 (43.38%)	20 (29.85%)	27 (40.29%)
Preoperative stage					
1	10 (14.70%)	8 (13.79%)	8 (13.9%)	4 (14.28%)	6 (15%)
2	35 (51.47%)	29 (50%)	29 (51.25%)	16 (57.14%)	19 (47.50%)
3	16 (23.52%)	16 (27.58%)	16 (27.58%)	5 (17.85%)	1 (2.75%)
4	7 (10.29%)	5 (8.49%)	5 (8.62%)	3 (10.61%)	4 (10%)

Of the tumors originating from the midgut, 10 (14.70%) were in Stage 1, 35 (51.47%) were in Stage 2, 16 (23.52%) were in Stage 3, and 7 (10.29%) were in Stage 4. Among tumors originating from the hindgut, 8 (13.79%) were in Stage 1, 29 (50%) were in Stage 2, 16 (27.58%) were in Stage 3, and 5 (8.49%) were in Stage 4. There was no significant difference detected between the stages of Groups A and B ($p > 0.05$).

When evaluating the pathological results, it was found that in Group A, the average number of lymph nodes removed was 19, while in Group B, it was 14.2. In Group A, 20 (29.41%) had Grade 1 differentiation, 31 (45.58%) had Grade 2, 12 (17.64%) had Grade 3, and 5 (7.35%) had Grade 4. In Group B, 17 (29.31%) had Grade 1 differentiation, 29 (50%) had Grade 2, 9 (15.51%) had Grade 3, and 3 (5.17%) had Grade 4. There was no statistically significant difference in any of these data. The circumferential margin was positive in only 1 (1.47%) patient in Group B, with no positive cases in Group A. Both groups had negative proximal and distal surgical margins. Macroperforation was detected in 1 (1.47%) patient in Group A and 1 (1.72%) patient in Group B, with no significant difference between the groups ($p > 0.05$). The presence of perineural invasion, perivascular invasion, tumor deposits, and peritoneal invasion in Group A and B

was as follows: 28 (42.17%) and 21 (36.20%), 34 (50%) and 27 (46.55%), 18 (26.47%) and 17 (29.31%), 7 (10.21%) and 2 (3.44%), respectively, and there was no difference between the groups ($p>0.05$). In terms of the final pathological staging, Group A had 1 (1.47%) in Stage 1, 32 (47.05%) in Stage 2, 26 (38.23%) in Stage 3, and 9 (13.23%) in Stage 4. Group B had 2 (2.54%) in Stage 1, 29 (50%) in Stage 2, 20 (34.48%) in Stage 3, and 7 (12.06%) in Stage 4. There was no significant difference between the groups. (Table 2)

Table 2. Comparison of pathologic results between embryologic class

	Group A	Group B
NHLN	19	14.2
Differentiation		
Grade 1	20 (29.41%)	17 (29.31%)
Grade 2	31 (45.58%)	29 (50%)
Grade 3	12 (17.64%)	9 (15.51%)
Grade 4	5 (7.35%)	3 (5.17%)
Surgical margin tumor		
Proximal	0	0
Distal	0	0
Circumpharantial	0	1 (1.47%)
Perineural invasion	28 (42.17%)	21 (36.20%)
Perivascular invasion	34 (50%)	27 (46.65%)
Tumor deposit	18 (26.47%)	17 (29.31%)
Peritoneal invasion	7 (10.21%)	2 (3.44%)
Patologic stage		
1	1 (1.47%)	2 (2.54%)
2	32 (47.05%)	29 (50%)
3	26 (38.23%)	20 (34.48%)
4	9 (13.23%)	7 (12.06%)

Anatomical Classification

In the anatomical classification, the number of patients in Groups 1, 2, and 3 was 57, 29, and 40, respectively, and there was no statistically significant difference ($p>0.05$). The mean ages of these groups were 68.1, 68, and 64.9, respectively, and no statistically significant difference was found ($p>0.05$). In Group 1, there were 22 (50%) female and 35 (43.38%) male patients; in Group 2, there were 9 (20.45%) female and 20 (29.85%) male patients; and in Group 3, there were 13 (29.55%) female and 27 (40.29%) male patients. There was no significant difference in gender among the groups ($p>0.05$).

In Group 1, 8 (13.79%) patients were in Stage 1, 29 (51.25%) were in Stage 2, 16 (27.58%) were in Stage 3, and 5 (8.62%) were in Stage 4. In Group 2, 4 (14.28%) patients were in Stage 1, 16 (57.14%) were in Stage 2, 5 (17.85%) were in Stage 3, and 3 (10.71%) were in Stage 4. In Group 3, 6 (15%) patients were in Stage 1, 19 (47.5%) were in Stage 2, 1 (2.75%) was in Stage 3, and 4 (10%) were in Stage 4. When the stages of Groups 1, 2, and 3 were compared, no significant difference was found between them ($p>0.05$). (Table 3)

When comparing pathological results, it was found that Group 1 had an average of 19.6 lymph nodes removed, Group 2 had an average of 16.1, and Group 3 had an average of 13.6 lymph nodes removed. There was no statistically significant difference between the groups ($p>0.05$). In terms of grade differentiation, Group 1 had 17 (29.82%) with Grade 1 differentiation, 29 (51.25%) with Grade 2, 9 (15.78%) with Grade 3, and 3 (5.26%) with Grade 4. Group 2 had 11 (39.28%) with Grade 1 differentiation, 11 (39.28%) with Grade 2, 5 (17.85%) with Grade 3, and 1 (3.57%) with Grade 4. Group 3 had 9 (22.5%) with Grade 1 differentiation, 20 (50%) with Grade 2, 7 (17.5%) with Grade 3, and 4 (10%) with Grade 4. There was no significant difference between the groups in terms of grade differentiation ($p>0.05$). Only one patient in Group 3 (2.5%) had a positive circumferential margin. In all other groups, there were no positive circumferential, proximal, or distal surgical margins, and there was no significant difference between the groups ($p>0.05$). Macroperforation was positive in one patient in both Group 1 and Group 2 (1.72% and 3.57%, respectively), and there was no difference between the groups. The presence of perineural invasion, perivascular invasion, tumor deposits, and peritoneal invasion in Groups 1, 2, and 3 was as follows: 21 (36.2%), 8 (28.57%), 20 (50%); 27 (47.36%), 13 (46.42%), 21 (52.5%); 17 (29.82%), 7 (25%), 11 (27.5%); and 2 (3.5%), 3 (10.71%), 4 (10%), respectively. There was no statistically significant difference between the groups ($p>0.05$). When comparing pathological stages, the number of patients in Stages 1, 2, 3, and 4 for Groups 1, 2, and 3 were as follows: Stage 1: 2 (3.5%), 1 (3.57%), 0 (0%); Stage 2: 29 (50.87%), 17 (60.81%), 15 (37.5%); Stage 3: 20 (35.7%), 7 (25%), 19 (47.5%); Stage 4: 7 (12.28%), 3 (10.71%), 6 (15%). There was no statistically significant difference between the groups ($p>0.05$).

(17.85%) with Grade 3, and 1 (3.57%) with Grade 4. Group 3 had 9 (22.5%) with Grade 1 differentiation, 20 (50%) with Grade 2, 7 (17.5%) with Grade 3, and 4 (10%) with Grade 4. There was no significant difference between the groups in terms of grade differentiation ($p>0.05$). Only one patient in Group 3 (2.5%) had a positive circumferential margin. In all other groups, there were no positive circumferential, proximal, or distal surgical margins, and there was no significant difference between the groups ($p>0.05$). Macroperforation was positive in one patient in both Group 1 and Group 2 (1.72% and 3.57%, respectively), and there was no difference between the groups. The presence of perineural invasion, perivascular invasion, tumor deposits, and peritoneal invasion in Groups 1, 2, and 3 was as follows: 21 (36.2%), 8 (28.57%), 20 (50%); 27 (47.36%), 13 (46.42%), 21 (52.5%); 17 (29.82%), 7 (25%), 11 (27.5%); and 2 (3.5%), 3 (10.71%), 4 (10%), respectively. There was no statistically significant difference between the groups ($p>0.05$). When comparing pathological stages, the number of patients in Stages 1, 2, 3, and 4 for Groups 1, 2, and 3 were as follows: Stage 1: 2 (3.5%), 1 (3.57%), 0 (0%); Stage 2: 29 (50.87%), 17 (60.81%), 15 (37.5%); Stage 3: 20 (35.7%), 7 (25%), 19 (47.5%); Stage 4: 7 (12.28%), 3 (10.71%), 6 (15%). There was no statistically significant difference between the groups ($p>0.05$).

Table 3. Comparison of pathologic results between anatomic class

	Group 1 (n:57)	Group 2 (n:29)	Group 3 (n:40)
NHLN	19.6	16.1	13.6
Differentiation			
Grade 1	17 (29.82%)	11 (39.28%)	9 (22.5%)
Grade 2	29 (51.25%)	11 (39.28%)	20 (50%)
Grade 3	9 (15.78%)	5 (17.85%)	7 (17.50%)
Grade 4	3 (5.26%)	1 (3.57%)	4 (10%)
Surgical margin tumor			
Proximal	0	0	0
Distal	0	0	0
Circumpharantial	0	0	1 (2.5%)
Perineural invasion	21 (36.20%)	8 (28.57%)	20 (50%)
Perivascular invasion	27 (47.36%)	13 (46.42%)	21 (52.5%)
Tumor deposit	17 (29.82%)	7 (25%)	11 (27.50%)
Peritoneal invasion	2 (3.50%)	2 (10.71%)	4 (10%)
Patologic stage			
1	2 (3.50%)	1 (3.57%)	0
2	29 (50.87%)	17 (60.81%)	15 (37.50%)
3	20 (35.70%)	7 (25%)	19 (47.50%)
4	7 (12.28%)	3 (10.71%)	6 (15%)

DISCUSSION

When colon cancers are divided into proximal and distal or right and left colon cancers, it is known that proximal and distal colon cancers have different genetic, biological, and clinicopathological characteristics.¹⁰⁻¹³ Transverse colon cancers, which are separated at the site where this distinction is made, have been reported to have a different course compared to other segments of the colon.^{3,9} In this study, it was theoretically expected to find clinical and pathological differences between proximal and distal colon cancers, but no differences were found between the groups in both embryological and anatomical classifications.

Studies have shown that right colon cancers are generally associated with a worse prognosis than left colon cancers, regardless of the local stage of the tumor, as long as they are not metastatic.^{14,15} These studies often attribute this difference to genetic and environmental factors. However, other studies have reported no significant differences when comparing the stages of right and left colon cancers, and the worse prognosis associated with right colon cancers may be due to the fact that they are often diagnosed at a later stage than left colon cancers.^{16,17} Studies have also indicated an increasing frequency of right colon cancers in recent years, and one explanation for this is that right colon cancers are being diagnosed earlier. This may be attributed to increased awareness of colon cancer, more effective colonoscopy procedures, and the ability to remove adenomatous polyps, which are often found in the distal colon, through colonoscopic interventions.¹⁸⁻²⁰ In this study, no differences were found in the stages when transverse colon cancers were divided into proximal and distal. This may be attributed to increased awareness of colon cancer among both healthcare professionals and the public, as well as the increased use of colonoscopic, radiological, and laboratory-based screenings.

It is known that right and left colon cancers have different genetic and biological foundations.^{16,21,22} In a study conducted by Lee, although there were genetic differences between right and left colon cancers, no significant differences in prognosis were observed in Stage 2 tumors, while in Stage 3 tumors, right colon tumors had a slightly worse prognosis.²² However, in this study, no significant differences were found in the grades of tumors, and genetic differences were more associated with prognostic value through metastatic lymph nodes.²² Another study by G.H. Lee highlighted these genetic differences and suggested that histologically more aggressive types (such as mucinous tumors) were more commonly associated with right colon cancers, rather than a direct relationship with tumor grade.²³ The biological behavior of tumors, as indicated by histomorphological features such as perineural invasion, perivascular invasion, and tumor deposits, is known to be associated with a worse prognosis. However, there have been no significant differences reported in tumor localization among these parameters.²³⁻²⁶ Nevertheless, in a study by Pai, it was reported that the high incidence of BRAF and MMR gene mutations in right colon tumors led to increased lymphovascular and perineural invasion.²⁷ In this study, although numerical data showed that tumor grade and histopathological findings such as perineural and perivascular invasion were more common in proximal tumors, there were no statistically significant differences, which is consistent with the literature.

Lymph node dissection is an important step in colorectal cancer surgery, and it is recommended to remove at least 12 lymph nodes for surgical adequacy.^{28,29} Webber's study even showed that patients who had more than 20 lymph nodes removed had higher five-year survival rates.³⁰ It has been reported that a greater number of adequate lymph nodes are removed after surgery in proximal colon tumors.³⁰⁻³² Yang's study suggested that in proximal colon cancers, the number of lymph nodes is more prognostic. The extent of lymph node dissection in the transverse colon is a topic of debate. Due to the proximity of the transverse colon to mesenteric lymph nodes, there can also be metastasis to extramesenteric lymph nodes.⁹ Consistent with the literature, this study also found that more lymph nodes were removed in proximal colon

cancers, although it was not statistically significant. Adequate numbers of lymph nodes were removed in all localizations and surgical procedures.

Study Limitation

The most significant limitation of the study is its retrospective nature, which may lead to potential errors and inaccuracies in the data. Additionally, the exclusion of patients due to missing information can be considered another limitation of the retrospective study. The small number of patients is also another obstacle in generalizing the findings.

CONCLUSION

When transverse colon cancers are classified embryologically and anatomically, no statistically significant differences were observed in parameters such as histological grade, lymph node count, perineural invasion, and perivascular invasion, similar to what is observed in proximal and distal colon cancers. However, hepatic corner and mid-transverse colon tumors nominally resemble proximal colon cancers.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by the Ankara Bilkent City Hospital Ethics Committee (Date:19.06.2023, Decision No: E1-23-3693).

Informed Consent: All patients signed and free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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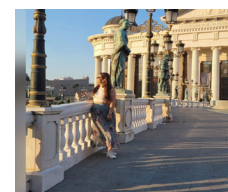
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Evaluation of the effectiveness of the short-segment thoracolumbar instrumentation: a single-center study

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ABSTRACT

Aims: This prospective study aimed to compare the long-term follow-up findings of patients with short-segment thoracolumbar instrumentation with the long-term follow-up findings results of patients with long-segment thoracolumbar instrumentation.

Methods: Patients who underwent surgery for a thoracolumbar junction spine fracture were included in this study. The patient's age, gender, and neurological impairment, "AOSpine Classification Scale", "Visual Analog Scale (VAS)", "modified Japanese Orthopedic Association (mJOA)" and "Oswestry Disability Index (ODI)" scores, pedicle and/or pars interarticularis fractures, anterior, middle, and posterior height loss of the fractured vertebral body (mm), the height loss rate of the fractured vertebra, angulation degree, sagittal and axial spinal canal diameters (mm) and presence of bone fragment extending into the spinal canal on CT images were recorded at admission to the hospital, and the end of the sixth month after surgical intervention. Duration of anesthesia and surgery time, the amount of bleeding during the surgery, the radiation level (mGy) released by fluoroscopy, performing laminectomy, length of stay in the intensive care unit, and hospital were recorded. Additionally, the stability and integrity of the instrumentation were examined with dynamic X-ray images.

Results: Preoperative fractured vertebra collapse rates ($t=4.175$, $p=0.001$) and surgery times ($t=4.175$, $p=0.001$) were different between groups. In the long-segment group, preoperative VAS scores ($Z=-2.687$, $p=0.007$), mJOA scores ($Z=-2.585$, $p=0.010$), and ODI scores ($t=53.253$, $p<0.001$) were different from postoperative long-term follow-up values. In addition, in the short segment group, preoperative VAS scores ($Z=-2.214$, $p=0.027$), mJOA scores ($Z=-2.333$, $p=0.020$), and ODI scores ($t=48.338$, $p<0.001$) were different from the postoperative long-term follow-up values. ROC-curve analysis and Logistic Regression analysis results revealed that any study parameter could not predict the decision-making for inserting screws into the fractured vertebra, the need for laminectomy, the risk of developing postoperative instability, or the worse prognosis risk of mJOA.

Conclusion: This study's results showed that short-segment instrumentation, which is performed by inserting a screw into the fractured vertebra, is as effective as long-segment instrumentation in providing both clinical and radiological improvement in patients. At the same time, it has advantages such as less operating time, less surgical bleeding, and short anesthesia time. However, it was determined that no parameter of the study could predict the placement of screws in the fractured spine, the need for laminectomy, the risk of postoperative instability, or the prognosis risk of mJOA. Therefore, it was concluded that conducting this study on a larger patient population would be appropriate.

Keywords: Thoracolumbar junction, short segment instrumentation, posterior thoracolumbar approach

INTRODUCTION

Today, anterior, posterior, and combined surgical approaches are still applied in thoracolumbar vertebra fractures to restore spinal stability, prevent deformity, and provide spinal canal decompression. For this purpose, posterior approaches are mostly preferred for short or long-segment instrumentation due to ease of application, less blood loss, and small surgical area.^{1,2}

Although some advantages such as tighter fixation and

better canal healing in long-segment instrumentation have been reported, this intervention requires exposure to larger surgical fields, which increases surgical trauma, and bleeding, and extends the surgery time.^{3,4} For these reasons, spine surgeons prefer short-segment instrumentation by screwing the fractured vertebra. It has been noticed that this method has some advantages such as protecting mobile segments, reducing the kyphosis angle, preventing the increase in

anterior vertebra collapse, providing small surgical incisions with a few muscle dissection and a low amount of bleeding, and shortening surgical time. It is also claimed that screws placed in the fractured vertebra can prevent vertebral collapse by providing a mass effect.⁵⁻⁹ However, little information is available in the literature about the advantages and disadvantages of this new method compared to long-segment instrumentation.⁹⁻¹¹ In addition, there is little information available in the literature on the type of patients to whom this method can be applied.¹²

This prospective study was aimed to compare the long-term follow-up findings of patients with short-segment thoracolumbar instrumentation, in which a fractured vertebra was screwed, with the long-term follow-up findings results of patients with long-segment thoracolumbar instrumentation, in which the fractured vertebra was skipped. In addition, this study aimed to explore the clinical and or radiological markers in predicting which patient group would be treated with short-segment instrumentation.

METHODS

Ethics

This prospective clinical research study was done after approval by the Clinical Research Ethics Committee of the university to which the authors are affiliated (Date: 11.03.2021, Decision No: 2021.02-05). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. In addition, this study was supported by the Scientific Research Projects Coordination Unit of the university to which the authors are affiliated, within the scope of “Directed Project” (Project acceptance date: 27.05.2021, Project number: 2021/065).

Patients

Patients who had a thoracolumbar junction spine (T12, L1, L2) fracture for various reasons (such as falling from a height, a traffic accident, etc.) between May 2021 and May 2023 and who underwent surgery for this fracture were included in this study. Patients with pathological fractures (such as tumors, osteoporosis, and rheumatological diseases) and pediatric patients (under 15 years old) were excluded from the study. Patients were then grouped as follows:

- Short-segment group (formed from patients who underwent instrumentation by placing screws in the fractured spine, n=6)
- Long-segment group (created from patients who underwent instrumentation by omitting the fractured vertebra, n=9)

In addition, patients were grouped according to their gender.

Materials

The patients' age, gender, and neurological deficiency levels, “AOSpine Classification Scale”, “Dennis's Classification Scale”, “Visual Analog Scale (VAS)”, “modified Japanese Orthopedic Association (mJOA)” and “Oswestry Disability Index” scores, pedicle fractures and pars interarticularis fractures, anterior, middle, and posterior height loss of the fractured vertebral body (mm), the height loss rate of the fractured vertebra, degree of angulation, the sagittal and axial spinal canal diameter (mm) and presence of bone fragment extending into the spinal canal on CT images were

recorded at the time of admission to the hospital, and the end of the sixth month after surgical intervention. The pedicle diameters of the vertebrae (mm) were also recorded. The anesthesia time applied to the patients during the surgery and the duration of the surgery, the amount of bleeding during the surgery, the radiation level (mGy) released by fluoroscopy, performing laminectomy, length of stay in the intensive care unit, and hospital were recorded. Additionally, the stability

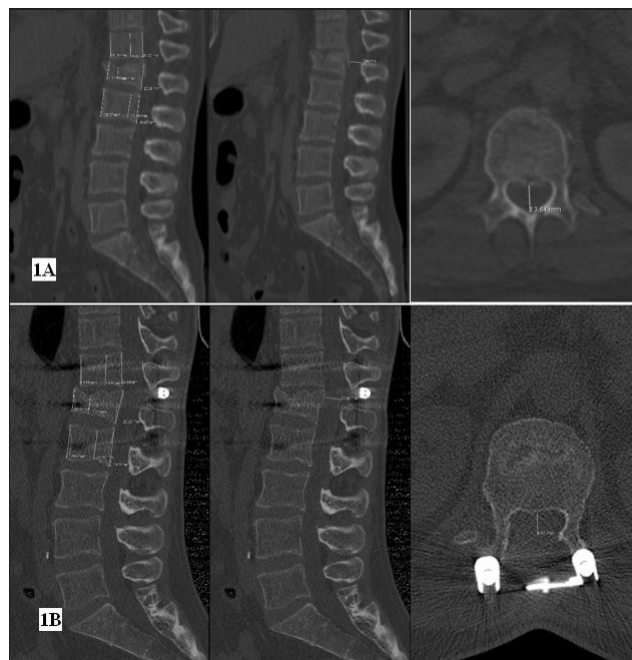


Figure 1. The pictures show the measurement techniques of the anterior, middle, and posterior height loss of the fractured vertebral body (mm), the height loss rate of the fractured vertebra, and the sagittal and axial diameter of the spinal canal (mm) on the preoperative (1A) and postoperative long-term follow-up (1B) CT images of a patient who underwent short-segment instrumentation



Figure 2. The pictures show no instability in the postoperative long-term follow-up X-ray images of a patient who underwent short-segment instrumentation, and the instrument's structural integrity is preserved

and integrity of the instrumentation were examined with dynamic X-ray images (Figure 1, Figure 2, Figure 3, Figure 4).

The ratio between the height of the vertebra above the broken vertebra and the height of the broken vertebra was calculated.

Additionally, the ratio between the height of the vertebra below the broken vertebra and the height of the broken vertebra was calculated. The collapse rate in the fractured vertebra was obtained by averaging these two values. The spinal canal diameters were measured from front to back of the narrowest part of the spinal canal at the fractured vertebra level. The angulation degree in the broken spinal segment, reflecting the kyphosis, was measured between the upper and lower end plates of the broken vertebra.

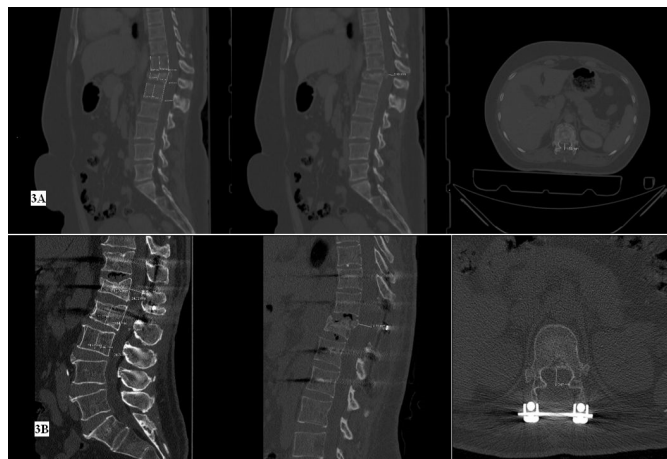


Figure 3. The pictures show the measurement techniques of the anterior, middle, and posterior height loss of the fractured vertebral body (mm), the height loss rate of the fractured vertebra, the sagittal and axial diameter of the spinal canal on the preoperative (3A) and postoperative long-term follow-up (3B) CT images in a patient who underwent long-segment instrumentation



Figure 4. The pictures show no instability on the postoperative long-term follow-up X-ray images of a patient who underwent long-segment instrumentation and the instrument's structural integrity is preserved

Surgery

Under general anesthesia, the injured spinal segment was explored through the standard posterior midline approach. Then, under fluoroscopy (Philips C-Arm Image Intensifier BV Vectra 718400, Product ID: 84343616, Serial Number: 200038), bilateral pedicle screws were inserted into the broken spine segment with (short segment) or without (long segment) screw placement into the fractured vertebra. Ligamentotaxis was also performed. Then, kyphosis was corrected and the screws were locked with distraction and cross-link was applied. If CT images revealed the spinal canal narrowing and/or a bone fragment in the spinal colon, total laminectomy and foraminotomy were performed if necessary.

Statistical Analysis

Study data were analyzed using SPSS v. 20.0 (IBM).

Independent Samples t-test was used to analyze the parametric study findings ($p < 0.05$). Mann-Whitney U test was used to compare the non-parametric study findings ($p < 0.05$). Categorical variables were analyzed using the Pearson chi-square test ($p < 0.05$). The statistical correlation between the data was analyzed by Spearman's rho correlation ($p < 0.05$). Paired Samples t-test and Wilcoxon Signed Ranks test were used to analyze repeated data ($p < 0.05$). The ROC-curve test was applied to determine the predictive variable(s) in decision-making for inserting a screw into the fractured vertebra. Binary Logistic Regression analysis was used to reveal the best predictive variable(s) ($p < 0.05$).

RESULTS

The average age of all patients included in the study was 48 years (minimum 20 years, maximum 87 years), and of these patients, 4 were female and 11 were male. When the preoperative findings of all patients were examined, it was determined that most of the patients had an L1 corpus fracture (73.3%), whereas most patients did not have a pars interarticularis fracture (80%) or pedicle fracture (73.3%) and most of the patients had no neurological impairment (73.3%). On the other hand, it was found that most patients had a bone fragment extending into the spinal canal (86.7%).

Preoperative fractured vertebra collapse rates ($t=4.175$, $p=0.001$) and surgery times ($t=4.175$, $p=0.001$) were found different between the short-segment and long-segment groups. However, no statistical difference was found between the two groups in terms of age, sex, broken vertebra level, pedicle and pars interarticularis fracture, bone fragment extending into the spinal canal, presence of the neurological impairment, AOSpine and Dennis's classification scores, preoperative VAS, mJOA and ODI scores (Table 1, Table 2).

In the long-segment group, preoperative VAS scores ($Z=-2.687$, $p=0.007$), mJOA scores ($Z=-2.585$, $p=0.010$), and ODI scores ($t=53.253$, $p < 0.001$) were different from postoperative long-term follow-up values. In addition, in the short segment group, preoperative VAS scores ($Z=-2.214$, $p=0.027$), mJOA scores ($Z=-2.333$, $p=0.020$), and ODI scores ($t=48.338$, $p < 0.001$) were different from the postoperative long-term follow-up values (Table 3).

On the other hand, no study parameter value was different between the male and female patient groups.

A positive correlation was found between the pedicle fracture and duration of anesthesia ($r=0.683$, $p=0.005$), duration of surgery ($r=0.687$, $p=0.007$), radiation dose ($r=0.725$, $p=0.027$), length of stay in intensive care unit ($r=0.649$, $p=0.009$) and length of hospital stay ($r=0.556$, $p=0.031$). A positive correlation was detected between pars fracture and the mid-height of the fractured vertebra ($r=0.656$, $p=0.008$), AOSpine score ($r=0.593$, $p=0.020$) and length of stay in the intensive care unit ($r=0.782$, $p=0.001$). A negative correlation was detected between the mid-height of the fractured vertebra and the collapse rate of the fractured vertebra ($r=-0.913$, $p < 0.001$) and the presence of intracanal fragments ($r=-0.545$, $p=0.036$). A negative correlation was found between the anterior height of the fractured vertebra and laminectomy ($r=-0.756$, $p=0.001$). There was a positive correlation between AOSpine scores and length of stay in the intensive care unit ($r=0.570$, $p=0.027$). A negative correlation

Table 1. Distribution table of patients' demographic, radiological, and clinical data by groups

		Long-segment	Short-segment		
		Mean $\pm$ SD/	Mean $\pm$ SD/		
		Median (min-max)/	Median (min-max)/		
Variable		n (%)	n (%)	t/ Z/ X2	p
Age		51.00 $\pm$ 19.01	45.50 $\pm$ 16.86	0.573*	0.576
Sex	Female	3 (20.0%)	1 (6.7%)	0.511‡	0.475
	Male	6 (40.0%)	5 (33.3%)		
Fractured vertebra	T12	2 (13.3%)	0 (0.0%)	1.553‡	0.460
	L1	6 (40.0%)	5 (33.3%)		
	L2	1 (6.7%)	1 (6.7%)		
Pedicle fracture	No	5 (33.3%)	6 (40.0%)	3.636‡	0.057
	Yes	4 (26.7%)	0 (0.0%)		
Pars interarticularis fracture	No	7 (46.7%)	5 (33.3%)	0.069‡	0.792
	Yes	2 (13.3%)	1 (6.7%)		
Bone fragment in the spinal canal	No	0 (0.0%)	2 (13.3%)	3.462‡	0.063
	Yes	9 (60.0%)	4 (26.7%)		
Neurological impairment	No	5 (33.3%)	6 (40.0%)	3.636‡	0.057
	Yes	4 (26.7%)	0 (0.0%)		
AOSpine score	A3	4 (26.7%)	3 (20.0%)	5.774‡	0.217
	A4	1 (6.7%)	1 (6.7%)		
	B1	0 (0.0%)	2 (13.3%)		
	B2	3 (20.0%)	0 (0.0%)		
	C	1 (6.7%)	0 (0.0%)		
Dennis's Classification score	2 colons	5 (33.3%)	4 (26.7%)	0.185‡	0.667
	3 colons	4 (26.7%)	2 (13.3%)		
Preoperative VAS score		9 (7-10)	8.5 (6-9)	-0.754†	0.451
Preoperative mJOA score		13 (10-18)	13 (13-13)	-0.505†	0.613
Preoperative Oswestry score		58.11 $\pm$ 2.03	56.33 $\pm$ 1.75	1.751†	0.103

(*) t value, Independent Samples t test; (†) Z value, Mann Whitney U test; (‡) X2 value, Pearson Chi-square test; p<0.05 (SD: standard deviation, min: minimum, max: maximum, N: number of patients, VAS: Visual Analog Scale, mJOA: modified Japanese Orthopaedic Association)

was found between spinal canal sagittal diameter and anesthesia duration ($r=-0.578$, $p=0.024$), number of screws ($r=-0.542$, $p=0.037$), and hospitalization duration ($r=-0.655$, $p=0.008$). A positive correlation was found between the presence of neurological deficiency and duration of anesthesia ($r=0.596$, $p=0.019$), duration of surgery ($r=0.570$, $p=0.033$), amount of bleeding ($r=0.734$, $p=0.002$), number of screws ($r=0.564$, $p=0.029$), and the duration of stay in the intensive care unit ($r=0.649$, $p=0.009$). A positive correlation was found between anesthesia duration and laminectomy ($r=0.554$, $p=0.032$) and the number of screws ($r=0.839$, $p<0.001$). A positive correlation was found between surgery time and radiation dose ($r=0.807$, $p=0.009$), laminectomy ($r=0.592$, $p=0.026$), and the number of screws ($r=0.843$, $p<0.001$). A negative correlation was found between laminectomy and mJOA prognosis scores ($r=0.608$, $p=0.016$).

As a result of the ROC-curve analysis and Binary Logistic Regression analysis, it was determined that no study parameter could predict the inserting of screws into the fractured vertebra, the need for laminectomy, the risk of developing postoperative instability, or the worse prognosis risk of mJOA.

DISCUSSION

Conventional methods of stabilizing the spine involve two vertebrae above and two vertebrae below the injured vertebra

to supply enough stabilization to allow early mobilization and recovery without incurring post-traumatic kyphosis risk, instrument fracture, and late neurological impairment. However, besides these advantages, they also cause immobilization of the spine due to the immobilization of at least five vertebral segments which may lead to insufficient long-term reduction and instrumentation failure along with kyphosis.^{11,12} To prevent these unfavorable events, some authors advocate the placement of peduncular screws in fractured vertebrae to strengthen the structure.^{3,5,7,13}

This study showed no statistical difference between the long-segment and short-segment groups in the preoperative period in terms of age, gender, fractured vertebra level, pedicle fracture, pars fracture, preoperative kyphotic degree, spinal canal diameters, pedicle diameters, presence of the fractured bone fragment extending into the spinal canal, and presence of the neurological impairment. In addition, AOSpine Classification, Dennis's Classification, VAS, mJOA, and ODI scores were also similar between these two groups. On the other hand, it was found that the collapse rates of fractured vertebrae were lower in the short-segment group. With these findings, it was thought that the two groups had a similar and homogeneous structure.

In addition, it was observed that the duration of the anesthesia, amounts of bleeding, and radiation doses applied during surgery were similar between these two patient groups, but short-segment instrumentation procedures took

Table 2. Distribution table of preoperative, intraoperative, and postoperative long-term follow-up radiological and clinical data of the patients according to groups

			Long segment	Short segment		
			Mean ± SD/	Mean ± SD/		
			Median (min-max)/	Median (min-max)/		
			N (%)	N (%)	t/ Z/ X2	p
Preoperative values						
Fractured vertebra anterior height			19.16±4.15	20.19±2.01	-0.559*	0.585
Fractured vertebra middle height			12.31±3.54	14.32±5.06	-0.910*	0.380
Fractured vertebra posterior height			25.32±0.85	26.46±4.05	-0.746*	0.469
Fractured vertebra compression rate			45.46±15.15	37.20±19.17	4.175*	0.001
Angulation degree			1.03±9.93	2.55±10.11	-0.288*	0.778
Spinal canal sagittal diameter			8.43±1.99	10.03±1.76	-1.592*	0.135
Spinal canal axial diameter			9.95±2.82	12.49±1.68	-1.966*	0.071
Right pedicle diameter			6.51±1.91	6.55±1.84	-0.039*	0.969
Left pedicle diameter			6.85±1.86	6.82±1.56	0.031*	0.975
Follow-up values						
Multiaxial screws number		6	1 (6.7%)	6 (40.0%)	11.429‡	0.001
		8	8 (53.3%)	0 (0.0%)		
Laminectomy		No	4 (26.7%)	5 (33.3%)	2.269‡	0.132
		Yes	5 (33.3%)	1 (6.7%)		
Fractured vertebra anterior height			18.72±4.15	16.93±2.00	0.979*	0.346
Fractured vertebra middle height			10.76±3.64	11.66±4.17	-0.445*	0.664
Fractured vertebra posterior height			24.74±2.04	24.84±3.26	0.076*	0.941
Fractured vertebra compression rate			50.47±17.97	48.90±15.35	-0.175*	0.864
Anesthesia time (minute)			205.33±86.53	162.00±21.68	-1.188*	0.256
Surgery time (minute)			182.62±35.73	115.33±18.73	4.175*	0.001
Bleeding volume (mL)			519.44±457.66	244.17±137.13	1.416*	0.180
Radiation dosage (mGy)			15.47±5.37	9.69±3.44	1.856*	0.106
Follow-up instability		No	9 (60%)	4 (26.7%)	3.462‡	0.063
		Yes	0 (0%)	2 (13.3%)		
Postoperative VAS score (1 day)			6 (2-7)	3.50 (2-7)	-1.752†	0.080
Follow-up VAS score (6 months)			0 (0-2)	0 (0-2)	-0.455	0.649
Postoperative mJOA score (1 day)			17 (11-18)	17 (13-18)	0.000†	1.000
Follow-up mJOA score (6 months)			18 (13-18)	18 (14-18)	-0.253†	0.800
mJOA score improvement rate			100 (37.5-100)	100 (20-100)	-0.084†	0.933
Postoperative Oswestry score (1 day)			42.44±6.39	39.67±3.33	0.973*	0.348
Follow-up Oswestry score (6 months)			11.33±2.18	11.33±2.16	0.000*	1.000
Duration of stay in intensive care unit			0 (0-4)	0 (0-0)	0.232†	0.529
Duration of stay in hospital			6 (3-10)	4.5 (4-7)	-0.909†	0.363
(*) t value, Independent Samples t test; (†) Z value, Mann Whitney U test; (‡) X2 value, Pearson Chi-square test; p<0.05 (SD: standard deviation, min: minimum, max: maximum, N: number of patients, VAS: Visual Analog Scale, mJOA: modified Japanese Orthopaedic Association)						

(*) t value, Independent Samples t test; (†) Z value, Mann Whitney U test; (‡) X2 value, Pearson Chi-square test; p<0.05
(SD: standard deviation, min: minimum, max: maximum, N: number of patients, VAS: Visual Analog Scale, mJOA: modified Japanese Orthopaedic Association)

less time. With these findings, it was thought that applying short-segment instrumentation was easier and less tiring for the surgeon. However, when looking at the numerical data, although no statistically significant difference was found, it was seen that the duration of anesthesia applied during surgery, the amount of bleeding due to surgery, and the radiation doses applied were less in patients who received short segment instrumentation. Thus, it was argued that applying short-segment instrumentation could be an advantage for both surgeons and patients.

On the other hand, in patients who underwent long-segment instrumentation, there was no difference between

the preoperative and long-term follow-up findings in terms of anterior, middle, and posterior height loss of the fractured vertebra and collapse rates of the fractured vertebra. In this patient group, a meaningful decrease in VAS and ODI scores and a meaningful increase in mJOA scores were detected in the long-term follow-up. Thus, it was determined that long-segment instrumentation provided both clinical and radiological improvement in these patients. In addition, in patients who underwent short-segment instrumentation, anterior and posterior height values of the fractured vertebra in the long-term follow-up slightly decreased compared to the preoperative values, but the mid-height values of the fractured

Table 3. Comparison table of preoperative radiological and clinical data of each group with postoperative long-term follow-up data

Group	Variable	Preoperative	Follow-up	t/ Z	P
		Mean $\pm$ SD/	Mean $\pm$ SD/		
		Median (min-max)	Median (min-max)		
Long segment	Fractured vertebra anterior height	19.16 $\pm$ 4.15	18.72 $\pm$ 4.15	0.324*	0.754
	Fractured vertebra middle height	12.31 $\pm$ 3.54	10.76 $\pm$ 3.64	1.523*	0.166
	Fractured vertebra posterior height	25.32 $\pm$ 0.85	24.74 $\pm$ 2.04	1.199*	0.265
	Fractured vertebra compression rate	45.46 $\pm$ 15.15	50.47 $\pm$ 17.97	-1.112*	0.299
	VAS score	9 (7-10)	0 (0-2)	-2.687†	0.007
	mJOA score	13 (10-18)	18 (13-18)	-2.585†	0.010
	Oswestry score	58.11 $\pm$ 2.03	11.33 $\pm$ 2.18	53.253†	<0.001
Short segment	Fractured vertebra anterior height	20.19 $\pm$ 2.01	16.93 $\pm$ 2.00	3.076*	0.028
	Fractured vertebra middle height	14.32 $\pm$ 5.06	11.66 $\pm$ 4.17	1.620*	0.166
	Fractured vertebra posterior height	26.46 $\pm$ 4.05	24.84 $\pm$ 3.26	2.717*	0.042
	Fractured vertebra compression rate	37.20 $\pm$ 19.17	48.90 $\pm$ 15.35	-2.011*	0.101
	VAS score	8.5 (6-9)	0 (0-2)	-2.214†	0.027
	mJOA score	13 (13-13)	18 (14-18)	-2.333†	0.020
	Oswestry score	56.33 $\pm$ 1.75	11.33 $\pm$ 2.16	48.338†	<0.001

(*) t value, Paired Samples t test; (†) Z value, Wilcoxon Signed Ranks test; p<0.05
 (SD: standard deviation, min: minimum, max: maximum, VAS: Visual Analog Scale, mJOA: modified Japanese Orthopaedic Association)

vertebra did not change. In this patient group, a meaningful decrease in VAS and ODI scores and a meaningful increase in mJOA scores were detected in the postoperative long-term follow-up compared to preoperative values. Thus, it was determined that short-segment instrumentation provided both clinical and radiological improvement in these patients. Besides, it was seen that the preoperative collapse rates were similar in both patient groups and did not increase in the postoperative long-term follow-up and instability did not develop. There was a meaningful decrease in postoperative VAS and ODI scores and a significant increase in mJOA scores and these values were not different between the groups preoperatively and postoperatively. With these findings, it could be suggested that patients in both groups could benefit from these surgeries significantly, and short-segment instrumentation could be as effective as long-segment instrumentation in both the clinical and radiological recovery of patients.

On the other hand, ROC analysis and Binary Logistic Regression analysis showed that any study parameter could not predict the decision-making for inserting the screws into the fractured vertebra, the necessity of laminectomy, the development risk of postoperative instability, or worse prognosis risk. On the other hand, it was observed that no screw was sent to the fractured vertebra of any patient with a pedicle fracture. However, it was determined that a pedicle screw was inserted into the fractured vertebra of a patient with a pars interarticularis fracture. It was also observed that no screw was inserted into the fractured vertebra in any patient with an AOSpine classification score of B1 or above. Thus, it was thought that pedicle fracture and high AOSpine score may be a risk for performing screws to the fractured vertebra, while pars interarticularis fracture may

be a relative risk. Finally, based on this, it was thought that the experience of the surgeon, as well as the patient's clinical and neurological conditions and radiological findings, may be important in deciding which patient can receive short-segment instrumentation.

Limitations

This study had some limitations. First, the number of patients included in the study was very small, and therefore it was assumed that the results of this study could not reflect the general population. Second, since the study did not include a pediatric patient group, no idea could be obtained about the results in these patients. Third, this study did not contain the outcomes of other surgical interventions (such as anterior corpectomy and cage placement). Fourth, very long-term (two years or more) surgical outcomes of the patients were not included in the study. Finally, since this study was conducted in a single center, the experiences of other external center surgeons and their results were not included in this study. However, despite all these limitations, the study findings were quite interesting, and therefore, it was concluded that conducting this study in a multi-center with a larger patient population would be appropriate.

CONCLUSION

This study's results showed that short-segment instrumentation, which is performed by inserting a screw into the fractured vertebra, is as effective as long-segment instrumentation in providing both clinical and radiological improvement in patients. At the same time, it has some advantages such as less operating time, less surgical bleeding, and short anesthesia time. However, it was determined that

no study parameter could predict the placement of screws into the fractured vertebra, the need for laminectomy, the risk of postoperative instability, or the worse prognosis risk of mJOA. Therefore, it was concluded that conducting this study on a larger patient population would be appropriate.

Declaration of Interest

There is no “conflict of interest” among the authors. Furthermore, through any of the products used in this research, no financial engagement has been established with any company that makes and/or markets these products or with any corporation that produces and/or markets a competing product.

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I was born in Kayseri in 1976. I finished my primary, secondary, and high school education here. I completed my medical education at Karadeniz Technical University between 1993-1999. Between 2000 and 2006, I completed my assistant training in the Neurosurgery Clinic at Erciyes University Faculty of Medicine. In 2015, I worked as an assistant professor at Kırıkkale University Faculty of Medicine Neurosurgery Clinic and started my academic life. I was appointed to the position of Associate Professor in April 2020. I still continue to work at the same place.



The comparison of corneal endothelium morphology through specular microscopy in morbid obesity with healthy controls

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ABSTRACT

Aims: To evaluate the morphological changes in corneal endothelial cells with morbid obesity, and to analyze the relationship between BMI and corneal endothelial features.

Methods: The central corneal thickness (CCT), the average endothelial cell density (ECD) (cell/mm²), average cell area (CA) (µm²), coefficient of variation of cell area (CV) - (CV: Standard deviation/CA) values were recorded via specular microscopy in morbidly obese patients and controls. The whole parameters were compared.

Results: The morbid obese patients had significantly thicker corneas (p=0.013), and significant loss of hexagonality (p=0.012) compared with controls, while there was no significant difference in ECD (p=0.311), CA (p=0.292), and CA (p=0.161). In linear regression analysis, there was no significant correlation between CCT, abdominal circumference, and the endothelium parameters.

Conclusion: Although BMI has the effect of changing corneal morphology, this change is not correlated with an increase in BMI.

Keywords: Morbid obesity, specular microscopy, corneal endothelium

INTRODUCTION

Obesity has been recently a public health issue with an increased trend worldwide. Morbid obesity may affect the several layers of the eye, both isolated and due to systemic diseases.¹ According to the World Health Organisation (WHO), the definition of obesity is the accumulation of abnormal or excessive fat in adipose tissue.² A body mass index (BMI) (weight in kilograms (or pounds) divided by the square of height in meters – kg/m²) over 25 is considered overweight, and over 30 is obese.³

The adipose tissue has an active metabolism in obesity, and also releases systemic inflammatory cytokines actively.¹ The effect of obesity on ocular structures has been previously reported⁴⁻⁶, and one of these tissue is cornea which includes the most of refractive power of total eye, and also provides optical clearance for vision. The maintenance of corneal clarity is related to the healthy function and normal morphology of hexagonal corneal endothelium cells.⁷ The morphology of corneal endothelium can be displayed through specular microscopy while the function can be indirectly stated by central corneal thickness (CCT). Specular microscopy is a method that can quantitatively evaluate the endothelial cell layer, which is the most important layer in

ensuring corneal transparency, in vivo. It has high reliability in repeated measurements.⁹ With this method, an idea can be obtained about both the number of corneal cells and their morphology (polymegathism, polymorphism).¹⁰

According to our hypothesis, the morbid obesity which is known as increased inflammatory cytokine status may affect corneal endothelium and may cause damage in endothelium cell morphology that leads to increased CCT. In the light of these information, the aim of the study is to define morphological changes in corneal endothelial cells with obesity and to evaluate the relationship between BMI and corneal endothelial features. In our knowledge, this is the first report that reveals the relationship between corneal endothelium and obesity.

METHODS

This cross-sectional study followed the tenets of the Declaration of Helsinki, and it was approved by the Balıkesir University Faculty of Medicine Clinical Researches Ethics Committee (Date: 09.10.2019, Decision No: 2019/136).



Informed consent was obtained from all cases. The participants were selected from the morbidly obese patients who were admitted to the department of general surgery for bariatric surgery between December 2022 – October 2023. The morbid obesity was defined as the patients who have BMI >40 or ≥ 35 kg/m² when associated with comorbidities such as arterial hypertension, dyslipidemia, sleep apnea, or diabetes. The patients were directed to the department of ophthalmology after the demographical features, detailed anamnesis, routine hemogram, biochemical, and hormone tests were recorded and BMI and abdominal circumference (AC) were measured. The AC was measured is measured at the midpoint of the line between the rib or costal margin and the iliac crest in the midaxillary line. The age and sex-matched healthy participants who were admitted to the hospital for routine control with BMI within the normal limits were held as controls. The exclusion criteria were the blood test that was outside the normal limits (other than 3.4-9.6 103/ μ L for leukocytosis, 13.2-16.6 d/dL for hemoglobine, 74-100 mg/dL for blood sugar, >5.7 HbA1C, >200 mg/dL for total cholesterol, >150 mg/dL for trigliserit, >5 mg/L C-reactive protein, abnormal liver and kidnet function tests according to the laboratory reference limits), refractive error of more than ± 3 D, the history of corneal or intraocular surgery, corneal opacity or dystrophy, any type of glaucoma, the presence of systemic rheumatological disease, diabetes mellitus, hypertension, cardiovascular or kidney disease, active or previous uveitis, contact lens usage, genetical or systemic inflammatory disease. After detailed ophthalmological examination including spherical equivalent (SE), best-corrected visual acuity (BCVA), and intraocular pressure (IOP) through Goldmann applanation tonometry; the corneal endothelial evaluation through specular microscopy was completed. The whole measurements have been achieved only from the right eyes of participants.

Specular microscopy:

The analysis of corneal endothelium has been completed through specular microscopy CEM-530 (Nidek Co, Ltd, Japan). The patients were asked to place his or her chin and head firmly on the device and look directly ahead during measurements. The device automatically focuses on the endothelial layer of the cornea and the image is automatically recorded when the clearest image was detected. All measurements were repeated three times by the same technician between 09:00 and 10:00. The average of the values was accepted as valid.

The CCT, the average endothelial cell density (ECD) (cell/mm²), average cell area (CA) (μ m²), and coefficient of variation of cell area (CV)-(CV: Standard deviation/CA) values were recorded via specular microscopy. The CV is considered as an indicator of changes in CA and is defined as polymegathism. The percentage of cells with a hexagonal structure is defined by the hexagonality (HEX) parameter, and changes in these cell shapes are defined as polymorphism (Figure).

Statistical Analysis

The statistical analysis were completed by using SPSS 23.0 program. The suitability of the data for normal distribution was evaluated with the Kolmogorov-Smirnov test. The results were expressed as mean $\pm$ standard deviation. Chi-square test was used for categorical variables such as gender. Independent samples t-test was used for comparisons on numerical variables between groups. Linear regression analyses were used to detect variability between

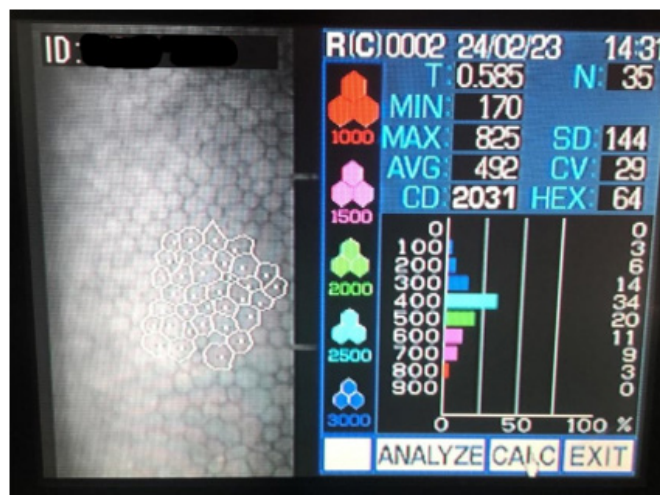


Figure. Specular microscopy screen output

parameters. A p value of less than 0.05 was considered statistically significant.

RESULTS

In the current study, 72 patients who had the diagnosis of morbid obesity were prospectively evaluated. Twelve of 72 patients had abnormal blood tests (7 of them had higher HbA1c, 5 of them had hypercholesterolemia) 8 of them had corneal opacity, and 2 of them had degenerative myopia. These patients were excluded according to the strict exclusion criteria. As a consequence, the study included 50 eyes of 50 patients with a mean age of 27.6 ± 7.1 years in morbid obese group (Group 1) and 52 eyes of 52 patients with a mean age of 31.3 ± 6.4 years in the control group (Group 2) ($p=0.167$). There was no significant difference between the groups in terms of gender (F/M: 18/32 and 15/37 in Groups 1 and 2, respectively; $p=0.514$). Among anthropometric measurements, BMI and AC were 45.9 ± 2.7 and 137.2 ± 4.5 kg/m² in Group 1, and 20.2 ± 1.2 and 78.3 ± 6.1 cm in Group 2 ($p<0.001$ for BMI and WC) respectively. In Group 1 and 2, the BCVA was 0.99 ± 0.02 and 0.99 ± 0.02 ($p=0.806$), IOP was 14.2 ± 2.6 and 14.9 ± 2.9 mmHg ($p=0.557$) and SE was 0.19 ± 0.63 and 0.33 ± 0.58 D ($p=0.545$) respectively the parameters in specular microscopy among groups were summarized in Table.

Table. The comparison of corneal endothelial parameters between morbidly obese patients and controls

	Group 1 (n:50)	Group 2 (n:52)	p-value
CCT	541.7 ± 34.6	514.5 ± 7.6	0.013*
ECD (cell/mm ²)	2273.6 ± 307.5	2385.8 ± 256.8	0.311
CA (μ m ²)	450.3 ± 76.3	423.7 ± 45.6	0.292
CV	37.1 ± 13.7	31.0 ± 5.1	0.161
HEX	42.9 ± 22.7	62.2 ± 21.0	0.012*

CCT: Central corneal thickness, ECD: Endothelial cell density, CA: Cell area, CV: Coefficient of variation of cell area, HEX: Hexagonality
p-value: statistically significant ratio

In linear regression analysis, there was no significant correlation between CCT, AC, and CCT, EHD, CA, CV, and HEX. (BMI and CCT $p=0.085$, EHD $p=0.274$, CA $p=0.334$, CV $p=0.931$, HEX $p=0.061$) (AC and CCT $p=0.080$, EHD $p=0.148$, CA $p=0.281$, CV $p=0.980$, HEX $p=0.069$).

DISCUSSION

In this study, the central corneal thickness of morbidly obese patients was found to be significantly thicker compared to the controls. This difference was not related to the change in endothelial cell number. While a non-significant increase in endothelial cell area was detected in morbid obese patients, this did not lead to polymegatism. Although there was no compensatory increase in cell size, a significant loss of hexagonality was detected in the cell structures. Similarly, Bu et al.⁸ detected a decrease in endothelial cell density and loss of hexagonality in rats that developed obesity as a result of feeding a hyperlipidemic diet. The authors attributed this situation to the loss of tight connections between corneal epithelial cells and increased oxidative stress in obesity. In our study, the increased CCT can be explained by the loss of epithelial tight junctions and the secondary relative corneal edema seen in the anterior layers of the cornea.

Corneal endothelial cells are most commonly affected by intraocular surgeries. It can lead to corneal decompensation with a significant decrease, especially after complicated cataract surgeries.¹¹ Even if there is no history of intraocular surgery, endothelial cell loss is observed at a rate of 0.6% annually with age.^{12,13} In our study, a significant increase in corneal thickness, which is an indirect indicator of corneal endothelial cell function, was detected in obese patients. This situation is independent of the number of endothelial cells. Despite the deterioration of the hexagonal structure of the cells, the compensatory polymegatism has not yet developed to predict the order in which the damage will develop.

Morbid obesity is a state of low-grade systemic inflammation caused by the release of inflammatory cytokines, adipokines, and reactive oxygen species.¹⁴ We think that the loss of hexagonality and increase in corneal thickness observed in morbidly obese patients in our study may be related to this. Although patients with abnormal sedimentation and C-reactive protein values were excluded from the study, correlation analyses of these parameters with endothelial cell properties could not be performed. On the other hand, in regression analyses, no significant difference was detected between the level of obesity and endothelial cell parameters.

In our study, no significant difference has been found in IOP between the two groups. However, in morbidly obese patients, an increase in episcleral venous pressure and decreased posttrabecular drainage of the aqueous humor may be observed secondary to increased venous pressure.¹⁵ Although no significant difference was detected between the two groups, fluctuations due to diurnal rhythm and/or lying position were not analyzed. Thus, the mechanical pressure on the endothelial cells due to IOP fluctuations and morphological changes in the endothelial cells may have started. Although it seems unlikely that obesity alone will cause endothelial cell damage and result in corneal decompensation, it has been shown that possible IOP elevations and optic nerve damage may be associated with obesity, especially in patients of advanced age and with glaucomatous pathology.¹⁶

Since correlation analyses of endothelial cell parameters and systemic inflammatory markers were not performed in our study, it cannot be commented on whether there is a direct relationship. Although any parameter in the blood tests that were outside normal limits was considered an exclusion

criterion, the correlation analyses could not be performed. Another limitation is that diurnal measurements were not taken, especially to detect fluctuations in IOP. To overcome this limitation, all participants were measured at early and fixed times of the day, but the variations during the day were not detected.

CONCLUSION

As a result, although BMI has the effect of changing corneal morphology, this change is not correlated with an increase in BMI. For more certain results, studies on larger patient groups are needed.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of the Balıkesir University Faculty of Medicine Clinical Researches Ethics Committee (Date: 09.10.2019, Decision No: 2019/136).

Informed Consent: The written informed consents were obtained. All patients signed and free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

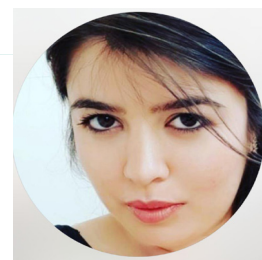
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Closed globe injuries in children

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ABSTRACT

Aims: Our study aims to investigate the etiology of pediatric closed-globe injuries (CGI) according to gender differences.

Methods: This retrospective study includes patients with closed-globe injuries. Demographic data of the patients, type of injury, location of the injury, object causing injury, initial visual acuity, and anterior and posterior segment findings were recorded. Findings were compared according to gender.

Results: Out of 114 pediatric ocular trauma patients, 28 (24.5%) had open-globe injuries, and 86 (75.6%) had CGI. The most common cause was home in 26 (30.2%). Trauma was caused by striking a thrown object in 22 (25.5%) patients. 68 (79%) of the CGIs were contusions and 18 (21%) were lamellar lacerations. The injury zone was zone 1 in 54 (62.7%) patients, zone 2 in 28 (32.5%) patients, and zone 3 in 4 (4.6%) patients.

Conclusion: CGU can cause severe and permanent vision damage. Injuries that may occur can be prevented by taking the necessary protective measures.

Keywords: Pediatric, ocular trauma, injury

INTRODUCTION

Eye trauma is the most crucial cause of monocular vision loss in developed countries.¹ Loss of workforce and rehabilitation costs caused by people with vision loss due to these injuries are high.²⁻⁴ It is possible to minimize these injuries with various simple precautions. Therefore, understanding the types and causes of injury is crucial for developing the measures.

Ocular trauma in children is a condition that needs to be managed promptly and adequately because of the damage caused by the injury and the predisposition of this age group to amblyopia. 8%-14% of traumas in children are eye trauma.⁵ Although some studies indicate that open globe injuries (OGI) are more common in children, many studies claim the opposite. Many studies have addressed pediatric OGI and evaluated their prognosis.¹⁰⁻¹² Children are more prone to eye traumas by nature, and closed traumas are also high in these injuries.

Our study aims to investigate the etiology of pediatric closed globe injuries (CGI) according to gender differences.

METHODS

This retrospective study includes patients who applied to Balıkesir University Faculty of Medicine Ophthalmology Department with eye trauma between January 2020 and December 2022. The study was started after the approval of the Balıkesir University Non-invasive Clinical Researches Ethics Committee (Date: 04.01.2023, Decision No: 2023/11)

and was carried out in accordance with the Declaration of Helsinki.

Closed globe injury was defined as a contusion or lamellar laceration by ocular trauma classification.¹³ Demographic data of the patients, type of injury, location of the injury, object causing injury, initial visual acuity, and anterior and posterior segment findings were recorded. Findings were compared according to gender.

Categorical data were expressed as numbers and percentages, and continuous variables as mean and standard deviation. Categorical data were evaluated with the chi-square test, and intergroup variables were evaluated with the one-way ANOVA (post hoc Tukey) test. Statistical analysis was performed using the Statistical Package for Social Science (SPSS 21.0, SPSS, Chicago, IL). A p-value of <0.05 was considered statistically significant.

RESULTS

Of 114 pediatric ocular trauma patients, 28 (24.5%) had OGI and 86 (75.6%) had CGI. 37 (43%) of the female CGI patients had a mean age of 8.37 ± 4.17 ; 49 (57%) years, males were 8.55 ± 3.78 years. 38 (44.1%) of the patients had the right eye, 31 (36%) had the left eye, and 17 (19.9%) had bilateral trauma.

When the trauma place was examined, the most common cause was home in 26 (30.2%) patients and school in 25 (25%)

patients. Other causes were playgrounds in 18 (21%) patients and streets in 17 (19.8). Trauma location by gender is shown in Table 1. Trauma was caused by striking a thrown object in 22 (25.5%) patients. It was sports injury in 20 (23.2%) patients, self/friend injury and animal/pet in 18 (20.9%) patients, and airgun toy in 4 (4.6%) patients. In Table 2, the causes of Trauma are classified according to gender. The most common object causing trauma was body parts in 18 (20.9%) patients, toys in 16 (18.6) patients, and stationery items such as pencils and erasers in 12 (13.%) patients. Other objects were animal rakes, wood, glass, and fiery fireworks, sparklers.

Table 1. Injury locations by gender

	Female	Male
Home	16 (43.2%)	10 (20.4%)
School	10 (27%)	15 (30.6)
Park /playground	7 (18.9)	11 (22.4%)
Street	4 (10.8%)	13 (26.5%)
p=0.090		

Table 2. Mechanism of injury by gender

	Female	Male
Self-injury, injury by friend	11 (29.7%)	7 (14.3%)
Object thrown	12 (32.4%)	14 (28.6%)
Sport-related	7 (18.9%)	13 (26.5%)
Animal/pet	7 (18.9%)	11 (22.4%)
Airgun/toy	0 (0%)	4 (8.2%)
p=0.186		

According to the OTCS, 68 (79%) of the CGI were contusions, and 18 (21%) were lamellar lacerations. The injury zone was zone 1 in 54 (62.7%) patients, zone 2 in 28 (32.5%) patients, and zone 3 in 4 (4.6%) patients. Zone 1 injuries were in the form of corneal abrasion and subconjunctival hemorrhage. Zone 2 injuries were traumatic hyphema, traumatic cataract, and traumatic iridocyclitis; zone 3 injuries were vitreous hemorrhage, retinal tear, and commotio retina.

DISCUSSION

Closed eye injuries constitute a vital group among pediatric eye traumas. In our study, CGI most commonly occurred at home due to the thrown object. It was usually in the form of contusion and zone 1 localization.

Male predominance was also present in our study, similar to the literature.^{7,14-16} The fact that boys prefer more aggressive games and their reflexes are not sufficiently developed are the most critical factors in this situation. In terms of gender, injury locations and forms may also differ. The injury location in females tended to be more outdoors. Falls due to sports and injuries with febrile substances were also more common in boys. Generally speaking, most eye injuries occur due to accidentally striking or poking an object during casual play. These injuries can generally be prevented by more frequent supervision of children or by removing objects that may cause an accident.

In the literature, initial visual acuity, injury zone and concomitant pathologies are associated with prognosis in open globe injuries.¹⁰⁻¹² There are few studies on prognostic markers in closed-globe traumas.^{14,15} Few studies indicate that initial visual acuity is also associated with prognosis in CGI. CGI inherently have a better prognosis than OGI.

The most common type of injury in CGI is contusion. In our study, subconjunctival hemorrhage was observed most frequently. In one study, the most common injury site was stated as the conjunctiva.¹⁵ The most common cause of subconjunctival hemorrhage in adults is nontraumatic; in children, it is due to trauma.^{17,18} One of the most severe conditions resulting from contusion is hyphema. Several studies have reported that hyphema is most common in CGI patients.⁷⁻⁹ Correct management of the hyphema is essential regarding damage to the corneal endothelium and irreversible optic nerve damage that may occur due to its severity. This difference between studies can be attributed to the population differences in which the studies were conducted and the ease of access to the hospital. In cases such as a retinal tear, vitreous hemorrhage and commotio retina, vision can be severely affected, and permanent damage may occur. Zone 3 injuries are generally seen as sports injuries. This risk can be minimized with appropriate clothing and protective equipment that will ensure the safety of the children.

The most important limitation of our study was its retrospective design. In addition, many patients' follow-up and long-term visual results were unavailable. However, since our study aimed at CGI's etiology, our study design is independent of the long-term results.

CONCLUSION

Closed-eye traumas can cause severe and permanent vision damage. Significantly younger children can harm themselves or their playmates. Sports injuries can progress with zone 3 damage. Injuries that may occur can be prevented by taking the necessary protective measures.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of the Balikesir University Non-invasive Clinical Researches Ethics Committee (Date: 04.01.2023 Decision No: 2023/11).

Informed Consent: Since the study was designed retrospectively, no written informed consent forms were obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Comparison of the decompressive craniectomy results in patients with ischemic stroke and acute subdural hematoma and determination of prognostic markers

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ABSTRACT

Aims: This study aimed to investigate the therapeutic effectiveness of decompressive craniectomy in patients with traumatic acute subdural hematoma and stroke patients and to determine the parameters that could predict the risk of mortality in these patients.

Methods: Patients diagnosed and operated on with acute subdural hematoma (ASH) or stroke between January 2022 and September 2023 were grouped into the ASH group and the CVO group. The patients were also divided into DEAD and SURVIVED groups according to mortality. Age, gender, anisocoria, the area of the craniectomy field, length of stay in the intensive care unit (ICU), length of stay in the hospital, and Glasgow Outcome Scale scores were recorded. In addition, Glasgow Coma Scale (GCS) scores, the amount of midline shift, and the blood biochemistry results were recorded pre-and postoperatively.

Results: This study consisted of 11 (5 male and 6 female) patients. Sex, preoperative GCS score, anisocoria, postoperative sedation anesthesia time, postoperative GCS score, duration of stay in the ICU, preoperative serum blood urine nitrogen, preoperative serum C-reactive protein (CRP), postoperative neutrophil-to-lymphocyte ratio, and postoperative CRP values were different between the ASH and CVO groups ($p < 0.05$). Furthermore, the preoperative GCS score, postoperative GCS score, postoperative sedation anesthesia duration, postoperative serum aspartate aminotransferase (AST), and postoperative serum CRP level values were different between the DEAD and SURVIVED groups ($p < 0.05$). The correlation analysis results revealed a positive correlation between mortality and preoperative GCS score and a negative correlation between mortality and anisocoria ($p < 0.05$). The ROC-curve analysis revealed that preoperative GCS and postoperative GCS score, postoperative serum AST level value, and postoperative serum CRP level value could predict mortality risk ($p < 0.05$). However, Logistic Regression analysis showed that any study parameter could be used as the best marker for prediction of the postoperative mortality risk ($p > 0.05$).

Conclusion: This study showed that decompressive craniectomy may offer more satisfactory results in severe head trauma patients. It was also argued that preoperative and postoperative GCS scores, postoperative midline shift values, and postoperative serum AST and CRP level values could be used to predict mortality risk.

Keywords: Decompressive craniectomy, acute subdural hematoma, stroke, mortality risk

INTRODUCTION

Decompressive craniectomy is currently applied to reduce increased intracranial pressure in cases of traumatic acute subdural hemorrhage and severe cerebral ischemia (stroke). Studies have shown that the mortality occurring in these patients may be related to age, the type and severity of the injury, the time the patient was taken to surgery, the planned surgical intervention, and the duration of postoperative intensive care stay.¹ Considering all these factors, the necessity

of determining predictive factors of patient prognosis to improve the neurological condition and reduce mortality rates in these patients has begun to be discussed in the literature.²⁻⁵ Many studies in the literature regarding this discussion have examined many factors and parameters for the prediction of prognosis, but many different results have been reported.⁶

This study aimed to investigate the therapeutic effectiveness of decompressive craniectomy in patients with



traumatic acute subdural hematoma and stroke patients and to determine the parameters that could predict the mortality risk in the hospital in these patients.

METHODS

Ethics

This prospective clinical research study was done after approval by the Kırıkkale University Clinical Researches Ethics Committee (Date: 02.09.2021, Decision number: 12/01). We obtained an informed consent form from all patients for the procedure. All procedures were carried out according to the ethical rules and the principles of the Declaration of Helsinki.

In addition, this study was supported by the Kırıkkale University Scientific Research Projects Coordination Unit within the scope of "Directed Project" (Project acceptance date: 08.11.2021, Project number: 2021/105).

Patients

Data of patients diagnosed with acute subdural hematoma (ASH) or stroke on brain computed tomography (CT) between January 2022 and September 2023 were recorded.

The patients were then grouped as follows:

- ASH group (consisting of patients with ASH, n=6).
- CVO group (consisting of patients with stroke, n=5)

The patients were divided into two groups according to mortality:

- DEAD group (consisted of patients who died in the hospital after surgical treatment, n=5)
- SURVIVED group (consisted of patients who survived after surgical treatment and were discharged from the hospital, n=6)

The patients were also divided into the male group (n=5) and female group (n=6) according to gender.

Medical treatment consisted of sedation and analgesia or barbiturate coma, bed elevation, and hyperosmolar therapy. Prophylactic anticoagulation was started 48-72 hours after surgical treatment, provided that intracranial hemorrhagic lesions were stable.

Those patients who died in the emergency department after a diagnosis of stroke or ASH, who had a combination of head and general body trauma or a life-threatening major organ injury, who had another intracranial hemorrhage secondary to trauma (e.g. epidural hematoma, subarachnoid hemorrhage, spontaneous intracerebral hemorrhage, etc.), secondary to trauma patients with non-existent subdural hematoma, subacute/chronic subdural hematoma, missing data, or patients in the pediatric age group (<16 years) were not included in the study.

Materials

For each patient, age, gender, Glasgow Coma Scale (GCS) scores at admission, pupil dilation/reactivity findings (i.e., anisocoria), length of stay in the intensive care unit, length of hospital stay, GCS scores at hospital discharge after surgery, and Glasgow Outcome Scale (GOS) scores were recorded. Higher scores on these scales indicated a better neurological status.^{7,8} In addition, the brain CT images obtained during admission to the hospital and after the surgical intervention were examined and the amount of preoperative and postoperative midline shift, and area of the craniectomy field were recorded (Figure 1, Figure 2, Figure 3).⁹ Finally, the first blood biochemistry results at the time of admission to the hospital and the last biochemistry analysis results obtained before discharge from the hospital or death were also recorded.

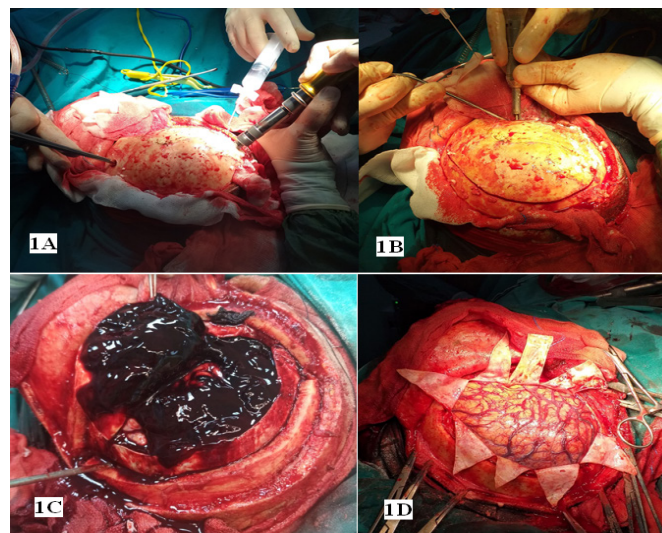


Figure 1. After the multiple burr-hole openings (1A), a wide craniectomy flap was removed (1B), and the dura mater was opened appropriately in the traumatic acute subdural hematoma side (1C) or stroke side (1D)

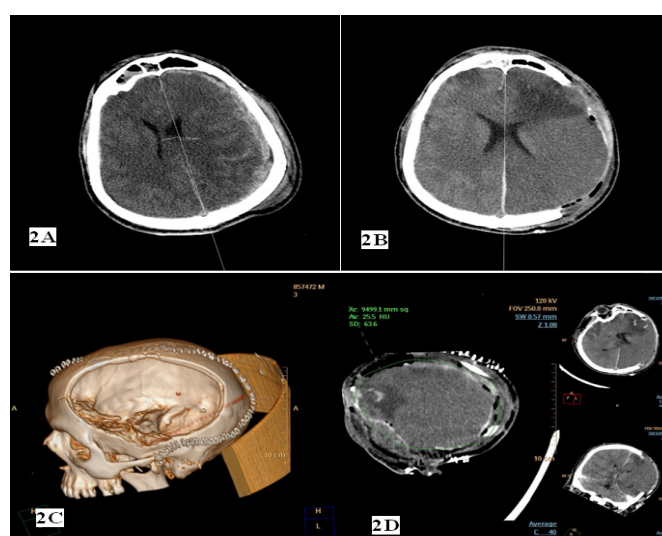


Figure 2. Photographs show the preoperative (2A) and postoperative (2B, 2C) cranial CT images of a patient with traumatic acute subdural hematoma. Photographs also show the measurement technique of the craniectomy area in sagittal, coronal, and axial CT images of this patient (2D)

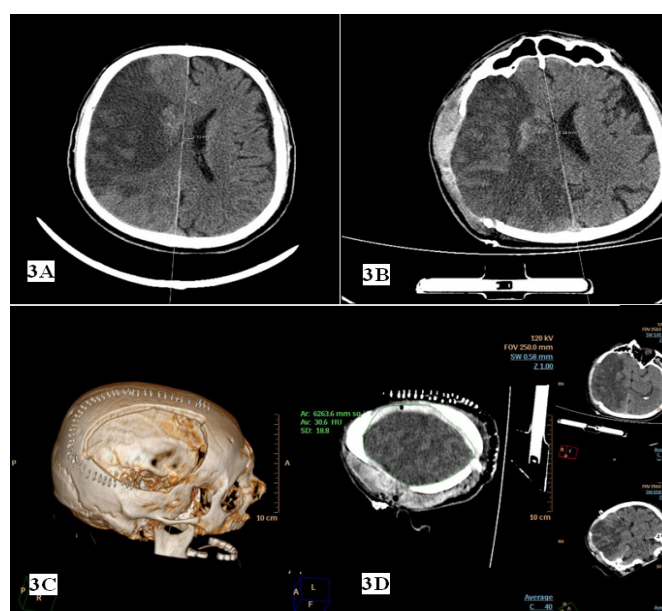


Figure 3. Photographs show the preoperative (3A) and postoperative (3B, 3C) cranial CT images of a patient with stroke. Photographs also show the measurement technique of the craniectomy area in sagittal, coronal, and axial CT images of this patient (4D)

Surgery

After general anesthesia was administered to all patients, wide fronto-temporo-parietal craniectomy was performed by the surgeon (M.O., U.Y., and B.B.) using a high-speed craniotome (AESCULAP®, ELAN 4 Electro Craniotome & Attachments, Braun, Germany) on the ASH or stroke side. In the CVO group, after the craniectomy flap was lifted, the dura mater was opened in a “star” shape and duraplasty was performed using a large graft taken from the cranial periosteum. In the ASH group, after the craniectomy flap was lifted, the dura was opened in a “C” shape, the hematoma was evacuated, and then duraplasty was performed after hemostasis using a large graft taken from the cranial periosteum (Figure 1). No patient underwent lobectomy. Surgical folds were closed anatomically. In patients whose brains were severely swollen during the surgery, the craniectomy bone flap was left on the abdominal fascia or tensor fascia lata, and the surgical area on that side was anatomically closed and the surgery was terminated. Then, intubated patients were observed under sedation anesthesia in the intensive care unit for at least 48 hours.

Biochemical Analysis

In venous blood samples taken from patients, hemoglobin level values (reference range: 10-18 g/dl) and leukocyte (reference range: 4400-11300 u/L), neutrophil (reference range: 110-9600 u/L), lymphocyte (reference range: 500-6000 u/L), monocyte (reference range: 100-1400 u/L), eosinophil (reference range: 0-1000 u/L), basophil (reference range: 0-300 u/L) and platelet (reference range: 150.000-500.000 u/L) counts were obtained using an automatic analyzer device (Mindray BC-6800, Shenzhen, China). In addition, preoperative and postoperative neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and monocyte-to-lymphocyte ratio values were also recorded. Furthermore, in the same blood samples, serum glucose (reference range: 74-109 mg/dl), BUN (reference range: 17-43 mg/dl), creatinine (reference range: 0.84-1.24 mg/dl), ALT (reference range: 5-41 u/L), AST (reference range: 5-40 u/L), CRP (reference range: 0.15-5 mg/dl), sodium (reference range: 136-146 mmol/L) and potassium (reference range: 3.5-5.1 mmol/L) level values were obtained using an automatic device with their original kits (COBAS c501, Roche).

Statistical Analysis

SPSS v.20.0 software was used for statistical analysis. The Kolmogorov-Smirnov test was used to test the normal distribution of the study data.

Independent Samples t-test was used for parametric study findings ($p < 0.05$). Mann-Whitney U test was used for statistical analysis of non-parametric study findings ($p < 0.05$). Spearman's rho correlation test was used to determine the existence of a correlation between the parameters of the patients ($p < 0.05$). The ROC-Curve test was applied to determine the predictive properties of the study parameters for prognosis and mortality level. Additionally, a Logistic Regression test was used to determine which of these parameters could be the “best parameter” ($p < 0.05$).

RESULTS

This study consisted of 11 (5 male and 6 female) patients. Before the surgery, it was determined that 4 (36.4%) of the

patients had anisocoria and 2 (18.2%) of the patients had fixed dilated pupils. Additionally, 5 (45.5%) patients were found to be unconscious. Before surgery, the GCS score in the ASH group was approximately 14 (3-15) and the midline shift was 8.66 ± 6.99 mm. In the CVO group, the GCS score was approximately 3 (3-3) and the midline shift was 13.07 ± 3.98 mm. Postoperatively, the GCS score in the ASH group was approximately 15 (3-15) and the midline shift was 3.01 ± 2.78 mm. In the CVO group, the GCS score was found to be approximately 3 (3-3) and the midline shift was 4.90 ± 3.79 mm. It was observed that 2 patients in the ASH group died after the surgery due to the very low GCS score. Furthermore, 4 patients in the CVO group died after the surgery due to congestive heart failure (1 patient) or pneumonia (3 patients). The average duration of hospital stay after surgery was found to be 8.00 ± 5.76 days in the ASH patient group and 13.60 ± 8.99 days in the CVO group.

Sex ($X^2 = 4.412$, $p = 0.036$), preoperative GCS score ($Z = -2.128$, $p = 0.033$), anisocoria sign ($X^2 = 7.773$, $p = 0.021$), postoperative sedation anesthesia application time ($t = -2.304$, $p = 0.047$), postoperative GCS score ($Z = -2.128$, $p = 0.029$) and duration of stay in the ICU ($Z = -2.401$, $p = 0.016$) were found to be different between the ASH and CVO groups. Additionally, between the two groups, preoperative BUN ($t = -3.124$, $p = 0.012$), preoperative CRP ($Z = -2.309$, $p = 0.021$), postoperative NLR ($t = -3.486$, $p = 0.008$), and postoperative CRP ($t = -3.960$, $p = 0.003$) values were also found to be different (Table 1, Table 2, Figure 4).

When the preoperative and postoperative data of the ASH patient group were compared, hemoglobin levels ($t = 3.383$, $p = 0.020$) and ALT values ($t = -4.008$, $p = 0.010$) were found to be different. When the preoperative data of the CVO group were compared with the postoperative data, it was seen that the hemoglobin levels ($t = 7.214$, $p = 0.002$) and serum sodium level values ($t = -2.935$, $p = 0.043$) were found to be different (Table 3).

When the patients were divided into SURVIVED and DEAD groups, the preoperative GCS score ($Z = -2.553$, $p = 0.011$), postoperative GCS score ($Z = -2.619$, $p = 0.009$), postoperative sedation anesthesia duration ($t = 2.927$, $p = 0.017$), postoperative serum AST ($Z = -2.191$, $p = 0.028$), and postoperative CRP ($t = 2.515$, $p = 0.033$) level values were found to be different between groups (Table 4, Table 5, Figure 5).

When the preoperative data and postoperative data of the DEAD group were compared, the midline shift values ($t = 3.380$, $p = 0.020$), hemoglobin levels ($t = 7.243$, $p = 0.001$), neutrophil counts ($Z = -2.023$, $p = 0.043$), AST ($Z = -2.023$, $p = 0.043$) and CRP ($Z = -2.023$, $p = 0.043$) levels were found statistically different. On the other hand, when the preoperative data and postoperative data of the SURVIVED group were compared, serum potassium ($t = -3.058$, $p = 0.038$) and BUN ($t = 3.334$, $p = 0.029$) values were found to be different (Table 6).

When the patients included in the study were divided into male and female groups according to gender, no statistical difference was detected between the two groups in terms of any study parameter.

The correlation analysis results revealed a positive correlation between mortality and preoperative GCS score ($r = 0.807$, $p = 0.003$). Additionally, a negative correlation was found between mortality and anisocoria ($r = -0.654$, $p = 0.029$). However, no statistical relationship was found between other study parameters and mortality risk.

Table 1. The descriptive table shows the demographic, clinical, and radiological findings of the ASH and CVO groups

		ASH	CVO	t/Z/X ²	p
Preoperative variables		Mean± SD/ Median (min-max) n (%)	Mean± SD/ Median (min-max)/ n (%)		
Age (year)		47.50 (25-75)	66 (60-76)	-1.281†	0.200
Gender	Male	5 (45.5%)	1 (9.1%)	4.412‡	0.036
	Female	1 (9.1%)	4 (36.4%)		
Glasgow Coma Scale score		14 (3-15)	3 (3-3)	-2.128†	0.033
Midline shift level (mm)		8.66±6.99	13.07±3.98	-1.246*	0.244
Pupillary dilatation	No	4 (36.4%)	1 (9.1%)	7.773‡	0.021
	Yes	0 (0.0%)	4 (36.4%)		
	Fixed	2 (18.2%)	0 (0.0%)		
Consciousness	Worse	2 (18.2%)	3 (27.3%)	0.782‡	0.376
	Well	4 (36.4%)	2 (18.2%)		
Hematoma thickness (mm)		12.09±6.33	0.00±0.00	-	-
Postoperative variables					
Decision time for DC		6 (4-24)	24 (5-72)	-1.784†	0.074
DC site	Left	3 (27.3%)	2 (18.2%)	0.110‡	0.740
	Right	3 (27.3%)	3 (27.3%)		
DC area (cm ²)		69.94±32,31	86.66±13.69	-1.072*	0.311
Sedation anesthesia time (day)		1.66±1.86	4.40±2.07	-2.304*	0.047
Midline shift level (mm)		3.01±2.78	4.90±3.79	-0.953*	0.365
Glasgow Coma Scale score		15 (3-15)	3 (3-3)	-2.182†	0.029
Duration of stay in ICU (day)		1.50 (0-5)	12 (2-26)	-2.401†	0.016
Duration of stay in hospital (day)		8.00±5.76	13.60±8.99	-1.254*	0.241
Glasgow Outcome Scale score		1.50 (1-5)	5 (4-5)	-1.812†	0.070
Mortality rate	Survived	4 (36.4%)	1 (9.1%)	2.396‡	0.122
	Exitus	2 (18.2%)	4 (36.4%)		

(*) t value, Independent Samples t-test; (†) Z value, Mann Whitney U test; (‡) X2 value Pearson's chi-square test, p<0.05

(SD: standard deviation, min: minimum, max: maximum, N: number of patients, DC: decompressive craniotomy, ICU: intensive care unit)

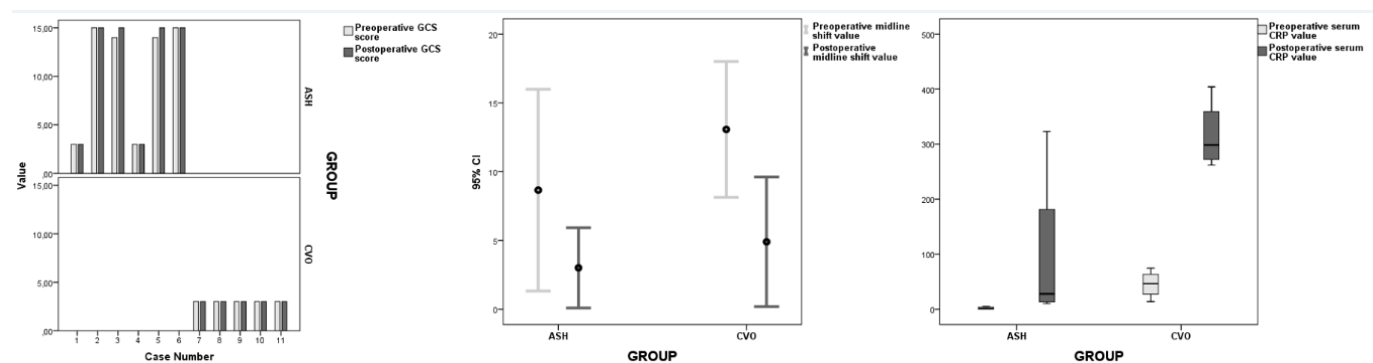


Figure 4. Graphics show the preoperative and postoperative Glasgow Coma Scale (GCS) scores, midline shift values, and serum C-reactive protein (CRP) level values of the ASH and CVO groups' patients.

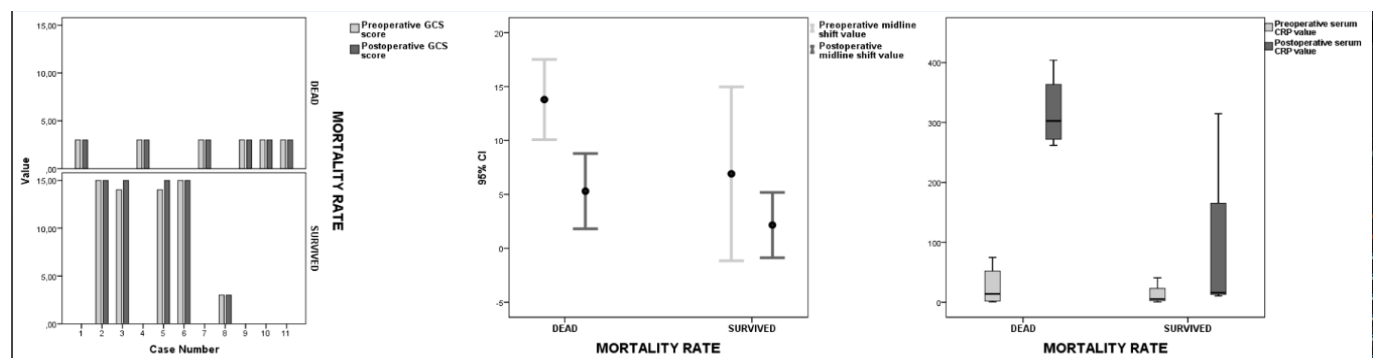


Figure 5. Graphics show the preoperative and postoperative Glasgow Coma Scale (GCS) scores, midline shift values, and serum C-reactive protein (CRP) level values of the DEAD and SURVIVED groups' patients.

Table 2. Table shows the preoperative and postoperative blood biochemistry results of the patients with acute subdural hematoma or stroke

	Variable	ASH	CVO	t / Z	p
		Mean $\pm$ SD/ Median (min-max)	Mean $\pm$ SD/ Median (min-max)		
PREOPERATIVE	Hemoglobin level (g/dl)	14.27 $\pm$ 2.03	15.40 $\pm$ 2.06	-0.916*	0.384
	Leukocyte count (uL)	9812 $\pm$ 3435.25	13000 $\pm$ 7064.88	-0.982*	0.352
	Neutrophil count (uL)	5868 $\pm$ 2337.11	11050 $\pm$ 7085.38	-1.700*	0.123
	Lymphocyte count (uL)	2715 $\pm$ 2369.35	1260 $\pm$ 1105.35	1.256*	0.241
	Monocyte count (uL)	373 $\pm$ 239.39	434 $\pm$ 500.58	-0.265*	0.797
	Eosinophil count (uL)	50 (0-330)	10 (0-60)	-1.488†	0.137
	Basophil count (uL)	22 $\pm$ 19.41	24 $\pm$ 18.17	-0.204*	0.843
	Platelet count (uL)	205333 $\pm$ 73888.20	220400 $\pm$ 54187.64	-0.378*	0.714
	Neutrophil to lymphocyte ratio	1.75 (1-15)	18.53 (1.77-20.80)	-1.826†	0.068
	Platelet to lymphocyte ratio	130.11 $\pm$ 98.43	234.53 $\pm$ 96.51	-1.767*	0.111
	Monocyte-to-lymphocyte ratio	0.18 (0.01-0.93)	0.41 (0.02-1.39)	-0.730†	0.465
	Glucose (mg/dLl)	127.50 $\pm$ 22.60	201.80 $\pm$ 90.61	-1.957*	0.082
	Sodium (mmol/L)	140.50 $\pm$ 2.34	142.60 $\pm$ 7.13	-0.685*	0.511
	Potassium (mmol/L)	3.78 $\pm$ 0.33	4.40 $\pm$ 0.86	-1.628*	0.138
	Blood urea nitrogen (mg/dl)	12.77 $\pm$ 3.63	28.32 $\pm$ 11.65	-3.124*	0.012
	Creatinin (mg/dl)	0.77 $\pm$ 0.17	1.01 $\pm$ 0.21	-2.149*	0.060
	Aspartate aminotransferase (u/L)	24.33 $\pm$ 5.96	23.50 $\pm$ 9.98	0.167*	0.871
	Alanine aminotransferase (u/L)	16.00 $\pm$ 3.35	17.25 $\pm$ 8.77	-0.323*	0.755
	C-reactive protein (mg/dl)	1.22 (0.38-5.40)	46.50 (13.90-74.80)	-2.309†	0.021
POSTOPERATIVE	Hemoglobin level (g/dl)	11.98 $\pm$ 1.79	10.14 $\pm$ 3.29	1.186*	0.266
	Leukocyte count (uL)	8969.45 $\pm$ 5658.03	15368.00 $\pm$ 8076.45	-1.545*	0.157
	Neutrophil count (uL)	6440 (5840-13880)	16700 (5490-21790)	-1.461†	0.144
	Lymphocyte count (uL)	1277 $\pm$ 636.32	665 $\pm$ 304.90	-1.279*	0.201
	Monocyte count (uL)	580.00 $\pm$ 253.54	452.50 $\pm$ 509.08	0.533*	0.609
	Eosinophil count (uL)	5 (0-180)	60 (0-290)	-0.866†	0.386
	Basophil count (uL)	12 $\pm$ 11.69	32 $\pm$ 28.64	-1.600*	0.144
	Platelet count (uL)	186333 $\pm$ 74004.50	116800 $\pm$ 104834.15	1.290*	0.229
	Neutrophil to lymphocyte ratio	7.31 $\pm$ 3.53	19.83 $\pm$ 7.86	-3.486*	0.008
	Platelet to lymphocyte ratio	153.48 $\pm$ 41.38	198.77 $\pm$ 86.05	-1.131*	0.291
	Monocyte-to-lymphocyte ratio	0.48 $\pm$ 0.18	0.54 $\pm$ 0.52	-0.280*	0.787
	Glucose (mg/dl)	116.17 $\pm$ 25.90	145.60 $\pm$ 58.17	-1.122*	0.291
	Sodium (mmol/L)	140.67 $\pm$ 10.88	153.00 $\pm$ 6.63	-2.206*	0.055
	Potassium (mmol/L)	4.10 $\pm$ 0.47	4.35 $\pm$ 1.31	-0.438*	0.672
	Blood urea nitrogen (mg/dl)	20.24 $\pm$ 10.63	38.14 $\pm$ 17.95	-2.059*	0.070
	Creatinin (mg/dl)	0.70 (0.41-3)	1 (0.50-2.23)	-1.100†	0.271
	Aspartate aminotransferase (u/L)	21.50 (13-233)	41 (21-77)	-1.095†	0.273
	Alanine aminotransferase (u/L)	30.17 $\pm$ 10.17	38.60 $\pm$ 38.71	-0.518*	0.617
	C-reactive protein (mg/dl)	66.45 $\pm$ 126.37	309.46 $\pm$ 56.10	-3.960*	0.003

(*) t value, Independent Samples t-test; (†) Z value, Mann Whitney U test; p<0.05
(SD: standard deviation, min: minimum, max: maximum)

The ROC-curve analysis results revealed that the preoperative GCS score (area=0.100, p=0.028, cut-off value <8, 100% sensitivity, 80% specificity), postoperative GCS score (area=0.100, p=0.028, cut-off value <9, 100% sensitivity, 80% specificity), postoperative serum AST level value (area=0.900, p=0.028, cut-off value >31 u/L, 83% sensitivity, 80% specificity), and postoperative serum CRP level value (area=0.867, p=0.045, cut-off value >151 mg/dl, 80% sensitivity, 80% specificity) could predict mortality risk (Table 7, Figure 6). However, Logistic Regression analysis showed that any study parameter could be used as the best marker for prediction of the postoperative mortality risk.

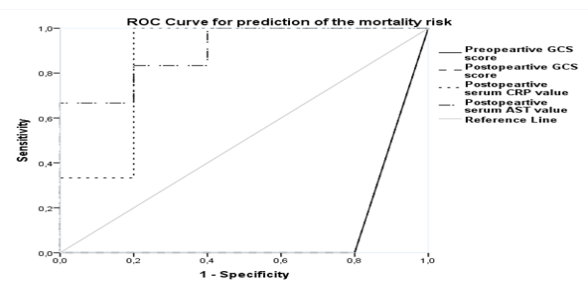


Figure 6. The ROC-Curve analysis revealed that preoperative and postoperative Glasgow Coma Scale (GCS) scores, postoperative serum alanine aminotransferase (AST), and C-reactive protein (CRP) level values could predict mortality risk in both groups.

Table 3. Table shows the comparison results of the preoperative and postoperative clinical and blood biochemistry findings of each group

		PREOPERATIVE	POSTOPERATIVE		
Variable		Mean ± SD/ Median (min-max)	Mean ± SD/ Median (min-max)	t / Z	P
ASV	Glasgow Coma Scale score	14 (3-15)	15 (3-15)	-1.414†	0.157
	Midline shift level (mm)	8.66±6.99	3.01±2.78	2.876*	0.035
	Hemoglobin level (g/dl)	14.27±2.03	11.98±1.79	3.383*	0.020
	Leukocyte count (uL)	9812±3435.25	8969.45±5658.03	0.591*	0.580
	Neutrophil count (uL)	5868±2337.11	6440 (5840-13880)	-1.483†	0.138
	Lymphocyte count (uL)	2715±2369.35	1277±636.32	1.491*	0.196
	Monocyte count (uL)	373±239.39	580.00±253.54	-1.510*	0.192
	Eosinophil count (uL)	50 (0-330)	5 (0-180)	-1.214†	0.225
	Basophil count (uL)	22±19.41	12±11.69	1.118*	0.314
	Platelet count (uL)	205333±73888.20	186333±74004.50	1.208*	0.281
	Neutrophil to lymphocyte ratio	1.75 (1-15)	7.31±3.53	-0.944†	0.345
	Platelet to lymphocyte ratio	130.11±98.43	153.48±41.38	-0.493*	0.643
	Monocyte-to-lymphocyte ratio	0.18 (0.01-0.93)	0.48±0.18	-0.944*	0.345
	Glucose (mg/dl)	127.50±22.60	116.17±25.90	0.918*	0.401
	Sodium (mmol/L)	140.50±2.34	140.67±10.88	-0.040*	0.970
	Potassium (mmol/L)	3.78±0.33	4.10±0.47	-1.652*	0.160
	Blood urea nitrogen (mg/dl)	12.77±3.63	20.24±10.63	-1.705†	0.149
	Creatinin (mg/dl)	0.77±0.17	0.70 (0.41-3)	-0.674†	0.500
	Aspartate aminotransferase (u/L)	24.33±5.96	21.50 (13-233)	-0.736†	0.462
	Alanine aminotransferase (u/L)	16.00±3.35	30.17±10.17	-4.008*	0.010
	C-reactive protein (mg/dl)	1.22 (0.38-5.40)	66.45±126.37	-1.254†	0.299
CVO	Glasgow Coma Scale score	3 (3-3)	3 (3-3)	0.000†	1.000
	Midline shift level (mm)	13.07±3.98	4.90±3.79	2.667*	0.056
	Hemoglobin level (g/dl)	15.40±2.06	10.14±3.29	7.214*	0.002
	Leukocyte count (uL)	13000±7064.88	15368.00±8076.45	-0.564*	0.603
	Neutrophil count (uL)	11050±7085.38	16700 (5490-21790)	-0.674†	0.500
	Lymphocyte count (uL)	1260±1105.35	665±304.90	1.303*	0.283
	Monocyte count (uL)	434±500.58	452.50±509.08	0.041*	0.970
	Eosinophil count (uL)	10 (0-60)	60 (0-290)	-1.461†	0.144
	Basophil count (uL)	24±18.17	32±28.64	-0.749*	0.495
	Platelet count (uL)	220400±54187.64	116800±104834.15	1.884*	0.133
	Neutrophil to lymphocyte ratio	18.53 (1.77-20.80)	19.83±7.86	-1.826†	0.068
	Platelet to lymphocyte ratio	234.53±96.51	198.77±86.05	0.400*	0.716
	Monocyte-to-lymphocyte ratio	0.41 (0.02-1.39)	0.54±0.52	-0.365†	0.715
	Glucose (mg/dl)	201.80±90.61	145.60±58.17	2.284*	0.084
	Sodium (mmol/L)	142.60±7.13	153.00±6.63	-2.935*	0.043
	Potassium (mmol/L)	4.40±0.86	4.35±1.31	0.092*	0.931
	Blood urea nitrogen (mg/dl)	28.32±11.65	38.14±17.95	-1.066*	0.346
	Creatinin (mg/dl)	1.01±0.21	1 (0.50-2.23)	-0.730†	0.465
	Aspartate aminotransferase (u/L)	23.50±9.98	41 (21-77)	-1.826†	0.068
	Alanine aminotransferase (u/L)	17.25±8.77	38.60±38.71	-1.291*	0.287
	C-reactive protein (mg/dl)	46.50 (13.90-74.80)	309.46±56.10	-1.681†	0.191

(*) t value, Paired Samples t-test; (†) Z value, Wilcoxon Signed Ranks test; p<0.05 (SD: standard deviation, min: minimum, max: maximum)

DISCUSSION

The aim of decompressive craniectomy, which is currently used in the treatment of various neurological emergencies, is to provide extra space for the edematous brain tissue due to the injury and/ or ischemia to expand.^{10,11} Therefore, the logic of decompressive craniectomy is to prevent life-threatening cerebral/cerebellar herniation and improve cerebral perfusion

by reducing intracranial pressure.^{12,13} There is good evidence that surgical decompression in ischemic stroke can control intracranial hypertension, which is strongly associated with mortality.^{5,13} However, in one study, no difference was found in terms of in-hospital mortality and length of hospital stay between patients who underwent surgery between 4 and 24

Table 4. The descriptive table shows the demographic, clinical, and radiological findings of the DEAD and SURVIVED groups

		DEAD	SURVIVED		
Preoperative variables		Mean± SD/ Median (min-max) n (%)	Mean± SD/ Median (min-max)/ n (%)	t/Z/X ²	P
Age(year)		63 (43-76)	66 (25-75)	-0.091†	0.927
Gender	Male	3 (27.3%)	3 (27.3%)	0.110‡	0.740
	Female	3 (27.3%)	2 (18.2%)		
Glasgow Coma Scale score		3 (3-3)	14 (3-15)	-2.553†	0.011
Midline shift level (mm)		13.79±3.54	6.91±6.50	2.240*	0.052
Pupillary dilatation	No	1 (9.1%)	4 (36.4%)	4.748‡	0.093
	Yes	3 (27.3%)	1 (9.1%)		
	Fixed	2 (18.2%)	0 (0.0%)		
Consciousness	Worse	4 (36.4%)	1 (9.1%)	2.396‡	0.122
	Well	2 (18.2%)	4 (36.4%)		
Hematoma thickness (mm)		4.70±7.34	8.87±8.40	-0.881*	0.401
Postoperative variables					
Decision time for DC (hour)		24 (4-72)	6 (4-24)	-0.939†	0.348
DC site	Left	3 (27.3%)	2 (18.2%)	0.110‡	0.740
	Right	3 (27.3%)	3 (27.3%)		
DC area (cm2)		86.41±16.66	66.90±32.81	1.281*	0.232
Sedation anesthesia time (day)		4.33±1.86	1.20±1.64	2.927*	0.017
Midline shift level (mm)		5.30±3.32	2.16±2.44	1.753*	0.113
Glasgow Coma Scale score		3 (3-3)	15 (3-15)	-2.619†	0.009
Duration of stay in ICU (day)		7.50 (0-26)	2 (0-18)	-1.016†	0.310
Duration of stay in hospital (day)		9.17±9.43	12.20±5.12	-0.641*	0.537
Glasgow Outcome Scale score		5 (5-5)	1 (1-4)	-3.019†	0.003

(*) t value, Independent Samples t-test; (†) Z value, Mann Whitney U test; (‡) X2 value Pearson's chi-square test, p<0.05
(SD: standard deviation, min: minimum, max: maximum, N: number of patients, DC: decompressive craniotomy, ICU: intensive care unit)

hours after admission and patients who underwent surgery within 4 hours.² Depending on the size of the bone to be removed, the literature indicates that the larger the defect, the better results are achieved with a minimum bone flap diameter of 11 to 12 cm.¹⁴ Interestingly, in recent studies, it is recommended to replace the bone flap loosely after decompression in both acute subdural hematoma and stroke patients.^{1,15} In addition, no difference in disability and quality of life outcomes has been reported between patients with traumatic acute subdural hematoma who underwent craniotomy or decompressive craniectomy.¹⁶

In this study, it was observed that the ASH group consisted mostly of male patients and the CVO group consisted mostly of female patients. It was determined that the preoperative and postoperative GCS scores of the patients in the ASH group were higher than those in the CVO group. On the other hand, it was found that anisocoria was detected more in patients in the CVO group, these patients received postoperative sedation and anesthesia for a longer time, and these patients stayed in the intensive care unit for a longer time. There was no difference in preoperative and postoperative midline shift values, GOS scores, and mortality rates between the two groups. With these results, it was argued that both patient groups were decompressed adequately. Although there was no difference between the two groups in terms of the time taken to decide on surgical treatment for the patients, when the numerical data were examined, it was seen that surgical treatment was performed earlier in the ASH group. It was thought that this was due to the transfer of CVO patients by the Neurology department.

On the other hand, preoperative and postoperative CRP values were found to be higher in the CVO group. Although there was no statistical difference between the two groups in terms of leukocyte, neutrophil, and lymphocyte values, it was observed that leukocyte and neutrophil count values in the CVO group were above normal laboratory values and lymphocyte values were lower than the ASH group values. With these findings, it was thought that the preoperative CRP elevation in the CVO group occurred more as an inflammatory response. However, when postoperative CRP values were examined, it was seen that CRP values were much higher than normal laboratory values in both groups. Although there was no statistical difference between the leukocyte, neutrophil, and lymphocyte count values of the groups, numerically, the leukocyte and neutrophil count values of the patients in the CVO group were seen to be much higher than normal laboratory values and the lymphocyte values were very low. With these findings, it was argued that the high serum CRP level values and high neutrophil count values measured in the CVO group occurred as an inflammatory response to pneumonia, while in the ASH group, the CRP elevation increased mostly as a response to trauma and/or surgical intervention.

When the preoperative data of the ASH group was compared with their postoperative findings, it was determined that there was a significant decrease in the hemoglobin levels of these patients and a significant increase in AST values after the surgery. Similarly, in the CVO group, there was a significant decrease in hemoglobin

Table 5. The table shows the preoperative and postoperative blood biochemistry results of the patients who survived or died

	Variable	DEAD	SURVIVED	t / Z	p
		Mean ± SD/ Median (min-max)	Mean ± SD/ Median (min-max)		
PREOPERATIVE	Hemoglobin level (g/dl)	15.10±2.08	14.40±2.13	0.550*	0.596
	Leukocyte count (uL)	2048±2283.86	2060±1778.31	0.019*	0.985
	Neutrophil count (uL)	8098±5086.47	8374±6553.22	-0.079*	0.939
	Lymphocyte count (uL)	2048±2283.86	2060±1778.31	-0.009*	0.993
	Monocyte count (uL)	302±248.15	520±463.95	-1.001*	0.343
	Eosinophil count (uL)	5 (0-27)	20 (10-330)	-1.302†	0.193
	Basophil count (uL)	25±22.58	20±12.25	0.441*	0.669
	Platelet count (uL)	183167±65076.62	247000±42936.00	-1.872*	0.094
	Neutrophil to lymphocyte ratio	5.90 (1-20.18)	1.78 (1.35-20.80)	-0.183†	0.855
	Platelet to lymphocyte ratio	169.25±112.18	187.56±113.56	-0.268*	0.795
	Monocyte-to-lymphocyte ratio	0.21 (0.02-0.60)	0.23 (0.01-1.39)	-0.548†	0.584
	Glucose (mg/dl)	188.00±86.49	129.20±30.07	1.438*	0.184
	Sodium (mmol/L)	142.50±6.38	140.20±2.49	0.754*	0.470
	Potassium (mmol/L)	4.33±0.82	3.74±0.23	1.550*	0.156
	Blood urea nitrogen (mg/dl)	0.93±0.24	0.82±0.20	0.771*	0.460
	Creatinin (mg/dl)	24.21±12.82	14.59±6.95	1.497*	0.169
	Aspartate aminotransferase (u/L)	25.80±9.55	22.20±4.49	0.763*	0.468
	Alanine aminotransferase (u/L)	18.40±7.09	14.60±3.65	1.065*	0.318
	C-reactive protein (mg/dl)	13.90 (0.38-74.80)	5.40 (0.43-40.90)	-0.447†	0.655
POSTOPERATIVE	Hemoglobin level (g/dl)	10.50±2.99	11.92±2.13	-0.886*	0.399
	Leukocyte count (uL)	14775±7400.21	8401±6083.46	1.537*	0.159
	Neutrophil count (uL)	13655 (5490-21790)	6640 (5480-13880)	-1.095†	0.273
	Lymphocyte count (uL)	774±133.53	1290±784.92	-1.449*	0.185
	Monocyte count (uL)	528±408.74	530±342.64	-0.008*	0.994
	Eosinophil count (uL)	30 (0-290)	10 (0-180)	-0.289†	0.773
	Basophil count (uL)	27±28.75	14±11.40	0.920*	0.382
	Platelet count (uL)	128167±86066.06	186600±97700.05	-1.056*	0.319
	Neutrophil to lymphocyte ratio	14.95±6.47	9.68±4.40	0.999*	0.347
	Platelet to lymphocyte ratio	195.07±72.85	148.12±47.33	1.208*	0.261
	Monocyte-to-lymphocyte ratio	0.64±0.42	0.37±0.15	1.319*	0.224
	Glucose (mg/dl)	144.50±52.06	111.60±26.22	1.277*	0.234
	Sodium (mmol/L)	150.67±7.66	141.00±12.59	1.573*	0.150
	Potassium (mmol/L)	4.16±1.24	4.27±0.32	-0.192*	0.852
	Blood urea nitrogen (mg/dl)	32.47±15.86	23.47±17.67	0.891*	0.396
	Creatinin (mg/dl)	1.25 (0.50-3.00)	0.70 (0.41-1.00)	-1.742†	0.081
	Aspartate aminotransferase (u/L)	51.50 (21-233)	17 (13-41)	-2.191†	0.028
	Alanine aminotransferase (u/L)	26.00±15.97	43.60±33.86	-1.139*	0.284
	C-reactive protein (mg/dl)	265.93±121.64	70.08±136.83	2.515*	0.033

(*) t value, Independent Samples t-test; (†) Z value, Mann Whitney U test, p<0.05
(SD: standard deviation, min: minimum, max: maximum)

levels after surgery. It was thought that these changes might be related to the surgery and or the anesthesia applied.

In the study group, it was observed that the midline shifts of the deceased patients decreased significantly after the surgery. However, when the data of these patients were examined, it was seen that the preoperative GCS values of two patients who died in the ASH group were 3 and these values did not change at all in the postoperative period. On the other hand, it was seen that the preoperative GCS values of all patients who died in the CVO group were 3 and that these values did not change at all in the postoperative period. These patients were followed under sedation anesthesia for

a longer time and therefore it was thought that they did not benefit from decompression. In addition, it was observed that serum CRP and neutrophil count values in the CVO group increased significantly after surgery, and three of the four patients who developed pneumonia in the postoperative period died due to sepsis despite medical treatment. However, it was determined that there was no significant difference between living patients and deceased patients in terms of biochemical data.

When the data of the SURVIVED group were examined, it was argued that GOS values were on average 1 except for one patient and they were able to show enough neurological

Table 6. Table shows the comparison results of the preoperative and postoperative clinical and blood biochemistry findings of each group

		PREOPERATIVE	POSTOPERATIVE		
Variable		Mean $\pm$ SD/ Median (min-max)	Mean $\pm$ SD/ Median (min-max)	t / Z	P
DEAD	Glasgow Coma Scale score	3 (3-3)	3 (3-3)	0.000†	1.000
	Midline shift level (mm)	13.79 $\pm$ 3.54	5.30 $\pm$ 3.32	3.380*	0.020
	Hemoglobin level (g/dl)	15.10 $\pm$ 2.08	10.50 $\pm$ 2.99	7.243*	0.001
	Leukocyte count (uL)	2048 $\pm$ 2283.86	14775 $\pm$ 7400.21	-1.700*	0.150
	Neutrophil count (uL)	8098 $\pm$ 5086.47	13655 (5490-21790)	-2.023†	0.043
	Lymphocyte count (uL)	2048 $\pm$ 2283.86	774 $\pm$ 133.53	1.432*	0.226
	Monocyte count (uL)	302 $\pm$ 248.15	528 $\pm$ 408.74	-1.541*	0.198
	Eosinophil count (uL)	5 (0-27)	30 (0-290)	-0.365†	0.715
	Basophil count (uL)	25 $\pm$ 22.58	27 $\pm$ 28.75	-0.143*	0.892
	Platelet count (uL)	183167 $\pm$ 65076.62	128167 $\pm$ 86066.06	1.567*	0.178
	Neutrophil to lymphocyte ratio	5.90 (1-20.18)	14.95 $\pm$ 6.47	-1.826†	0.068
	Platelet to lymphocyte ratio	169.25 $\pm$ 112.18	195.07 $\pm$ 72.85	-1.745*	0.156
	Monocyte-to-lymphocyte ratio	0.21 (0.02-0.60)	0.64 $\pm$ 0.42	-1.826†	0.068
	Glucose (mg/dl)	188.00 $\pm$ 86.49	144.50 $\pm$ 52.06	1.877*	0.119
	Sodium (mmol/L)	142.50 $\pm$ 6.38	150.67 $\pm$ 7.66	-2.381*	0.063
	Potassium (mmol/L)	4.33 $\pm$ 0.82	4.16 $\pm$ 1.24	0.401*	0.705
	Blood urea nitrogen (mg/dl)	0.93 $\pm$ 0.24	32.47 $\pm$ 15.86	-1.410*	0.218
	Creatinin (mg/dl)	24.21 $\pm$ 12.82	1.25 (0.50-3.00)	-1.219†	0.223
	Aspartate aminotransferase (u/L)	25.80 $\pm$ 9.55	51.50 (21-233)	-2.023†	0.043
	Alanine aminotransferase (u/L)	18.40 $\pm$ 7.09	26.00 $\pm$ 15.97	-1.880*	0.133
	C-reactive protein (mg/dl)	13.90 (0.38-74.80)	265.93 $\pm$ 121.64	-2.023†	0.043
SURVIVED	Glasgow Coma Scale score	14 (3-15)	15 (3-15)	-1.414†	0.157
	Midline shift level (mm)	6.91 $\pm$ 6.50	2.16 $\pm$ 2.44	2.203*	0.092
	Hemoglobin level (g/dl)	14.40 $\pm$ 2.13	11.92 $\pm$ 2.13	2.259*	0.087
	Leukocyte count (uL)	2060 $\pm$ 1778.31	8401 $\pm$ 6083.46	0.877*	0.430
	Neutrophil count (uL)	8374 $\pm$ 6553.22	6640 (5480-13880)	-0.135†	0.893
	Lymphocyte count (uL)	2060 $\pm$ 1778.31	1290 $\pm$ 784.92	1.202*	0.296
	Monocyte count (uL)	520 $\pm$ 463.95	530 $\pm$ 342.64	-0.029*	0.978
	Eosinophil count (uL)	20 (10-330)	10 (0-180)	-0.948†	0.343
	Basophil count (uL)	20 $\pm$ 12.25	14 $\pm$ 11.40	0.739*	0.501
	Platelet count (uL)	247000 $\pm$ 42936.00	186600 $\pm$ 97700.05	1.203*	0.295
	Neutrophil to lymphocyte ratio	1.78 (1.35-20.80)	9.68 $\pm$ 4.40	-0.674†	0.500
	Platelet to lymphocyte ratio	187.56 $\pm$ 113.56	148.12 $\pm$ 47.33	0.613*	0.573
	Monocyte-to-lymphocyte ratio	0.23 (0.01-1.39)	0.37 $\pm$ 0.15	-0.405†	0.686
	Glucose (mg/dl)	129.20 $\pm$ 30.07	111.60 $\pm$ 26.22	1.211*	0.293
	Sodium (mmol/L)	140.20 $\pm$ 2.49	141.00 $\pm$ 12.59	-0.150*	0.888
	Potassium (mmol/L)	3.74 $\pm$ 0.23	4.27 $\pm$ 0.32	-3.058*	0.038
	Blood urea nitrogen (mg/dl)	0.82 $\pm$ 0.20	23.47 $\pm$ 17.67	3.334*	0.029
	Creatinin (mg/dl)	14.59 $\pm$ 6.95	0.70 (0.41-1.00)	-1.826†	0.068
	Aspartate aminotransferase (u/L)	22.20 $\pm$ 4.49	17 (13-41)	-0.135†	0.892
	Alanine aminotransferase (u/L)	14.60 $\pm$ 3.65	43.60 $\pm$ 33.86	-1.875*	0.134
	C-reactive protein (mg/dl)	5.40 (0.43-40.90)	70.08 $\pm$ 136.83	-1.604†	0.109

(*) t value, Paired Samples t-test; (†) Z value, Wilcoxon Signed Ranks test; p<0.05
(SD: standard deviation, min: minimum, max: maximum)

recovery to sustain their daily lives and these patients could benefit from decompression. However, when looked at in general terms, it was seen that the mortality rate in all patients was 54.6% (5 patients) and most of these deceased patients (4 patients) were in the CVO group. On the other hand, correlation analysis revealed no relationship between the area of the craniectomy bone flap and neurological impairment and/ or mortality rate. Therefore, it was thought

that decompressive craniectomy could offer more satisfactory results in traumatic acute subdural hematoma patients rather than ischemic stroke patients.

On the other hand, the correlation analysis applied to the findings of all patients revealed that the GCS scores obtained during the patient's admission to the hospital may be significantly related to the risk of mortality, and the risk of mortality may increase in patients with low GCS scores.

Table 7. The table shows the parameters that can predict the mortality risk in patients with traumatic acute subdural hematoma or stroke

ROC-Curve test for mortality risk						
Group	Variable	Area	p	Cut-off value	Sensitivity	Specificity
All patients	Preoperative GCS	0.100	0.028	<8	100%	80%
	Postoperative GCS	0.100	0.028	<9	100%	80%
	Postoperative AST	0.900	0.028	>31 u/ L	83%	80%
	Postoperative CRP	0.867	0.045	>151 mg/ dL	80%	80%

ROC-Curve test, p<0.05.

(GCS: Glasgow Coma Scale, AST: aspartate aminotransferase, CRP: C-reactive protein)

In addition, it was thought that the risk of mortality might be high if anisocoria was detected in the preoperative period. However, no statistical relationship was found between midline shift and/or neurological impairment and mortality risk. Additionally, no relationship was found between the mortality risk and the blood biochemistry examination results obtained during hospital admission. As a result of the ROC analysis, it was found that the preoperative GCS score could predict the mortality risk. Furthermore, postoperative GCS score and serum AST and CRP level values could predict the mortality risk. With these results, it could be said that preoperative and/or postoperative GCS values and serum AST and CRP level values could be used as predictive markers for the mortality risk of these patients. However, the regression analysis results suggested that none of the study parameters could be used as good markers in predicting the risk of mortality in patients.

Study Limitations

This study had some limitations. First, since this study was a single-center study, the study population was quite small. Secondly, the long-term follow-up results of the patients were not included in the study as per the hypothesis of the study. Thirdly, due to technical and financial limitations, the preoperative and postoperative intracranial pressure measurement values of the patients were not included in the study. Fourthly, because the number of patients included in this study was small, the results of patients who underwent craniotomy could not be compared with the results of patients who underwent craniectomy. Finally, due to technical inadequacies, radiological imaging examination results that could show the patients' brain metabolism in the preoperative and postoperative periods were not available in this study. Therefore, it was thought that it would be appropriate to conduct this study in a larger population and use more advanced imaging methods (such as ICP monitoring, SPECT, etc.).

CONCLUSION

At the end of this study, it was thought that decompressive craniectomy may offer more satisfactory results in traumatic acute subdural hematoma patients. It was also argued that preoperative and postoperative GCS scores, and postoperative serum AST and CRP level values could be used to predict mortality risk.

ETHICAL DECLARATIONS

Ethics Committee Approval: This prospective clinical research study was done after approval by the Kırıkkale University Clinical Researches Ethics Committee (Date:02.09.2021, Decision No: 12/01).

Informed Consent: All patients signed and free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: There is no "conflict of interest" among the authors. Furthermore, through any of the products used in this research, no financial engagement has been established with any company that makes and/or markets these products or with any corporation that produces and/or markets a competing product.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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A rare cause of tumor ileus, mixed non-neuroendocrine neuroendocrine neoplasm (MINEN)

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ABSTRACT

This study aims to present two cases of a rare pathology. The findings of two patients diagnosed with ileus, whose pathology results indicated mixed neuroendocrine non-neuroendocrine neoplasm (MINEN), were evaluated and organized as case reports. Although uncommon, clinicians should consider this pathology in patients displaying symptoms of tumor ileus. MINEN, a type of neuroendocrine tumor, is an uncommon malignancy in the colon that can cause mechanical bowel obstruction similar to other tumors causing ileus. Mixed neuroendocrine-neuroendocrine neoplasms (MiNEN) are rare tumors with an unclear pathophysiology. To make this diagnosis, the tumor must contain at least 30% of both neuroendocrine cells and adenocarcinoma components. In this case report, two cases of patients who underwent surgery for tumor ileus and had postoperative pathology results compatible with MiNEN are presented.

Keywords: Ileus, neuroendocrine tumor, MINEN

INTRODUCTION

Approximately 2/3 of neuroendocrine neoplasms (NENs) are localized in the gastrointestinal tract (GI tract). These tumors, all of which have malignant potential, range from tumors with no clinical symptoms to tumors with poor prognosis. In the current World Health Organization (WHO) classification, tumors with neuroendocrine (NE) features are grouped under the main heading of NEN and classified into three main groups: well-differentiated neuroendocrine tumor (NET), poorly differentiated neuroendocrine carcinoma (NEC) and mixed neuroendocrine non-neuroendocrine neoplasm (MINEN), which includes both NE and non-NE tumor components. Mixed neuroendocrine-neuroendocrine neoplasms (MiNEN) are among rare neoplasms with unknown pathophysiology. For this diagnosis to be made, neuroendocrine cell and adenocarcinoma components must be present in at least 30% each.¹

Colorectal MiNEN is one of the most common types of MINEN. In one study, 1.1% and 2.4% of 988 resected colorectal neoplasms had pure NET and pure MINEN, respectively.² Rectal MINEN accounts for only 1-3% of rectal NEN, while colonic MINEN accounts for 14-20% of colonic NEN.³ MINEN originating from the right colon is much less common than colorectal NEN.³

In approximately 25-40% of colonic NEN cases, the neuroendocrine component is poorly differentiated neuroendocrine carcinoma (PDNEC). The second component

other than the neuroendocrine tumor component is usually adenocarcinoma, but can also be adenoma or squamous cell carcinoma.

Colorectal MiNEN has a worse prognosis than pure adenocarcinoma and is closer to PDNEC, especially in the metastatic stage. Metastatic risk has been found to be associated with the degree of neuroendocrine component.⁴

In this study, we aimed to present 2 cases of this rare pathology. The report was created by compiling preoperative imaging and postoperative pathology results of two patients who presented to the emergency department with tumor ileus and whose pathology results were reported as MINEN. The aim of the report is to provide a clear and concise documentation of these cases for academic and medical purposes.

CASE 1

A 75-year-old man with no known comorbidities other than hypertension and no previous abdominal surgery was admitted to the emergency department with abdominal pain and absence of gas and stool discharge for 3 days. On physical examination, general condition was moderate, oriented, coherent, and vital signs were stable. Abdominal distension was present. Defense and rebound were positive. Rectal touch was empty. Wbc was 12.3 and there was no

significant pathology in biochemistry. The patient had no signs of carcinoid syndrome. There were levels in the standing direct abdominal radiography (Figure 1). Contrast-enhanced tomography performed under emergency conditions showed an irregular, tumoral wall thickening and lymph nodes in the adjacent adipose tissue, which almost completely obliterated the lumen in a segment of approximately 10 cm at the level of the sigmoid colon, reaching approximately 1.5 cm on one wall, showing contrast enhancement. The diameter of the descending colon was measured as 9 cm. When the patient's previous examinations were examined, it was seen that he had never had a colonoscopy. A nasogastric catheter and a urinary catheter were inserted, 100 cc of fecaloid came into the nasogastric catheter, intravenous fluid resuscitation was started and the patient was operated urgently with a prediagnosis of tumor ileus. Perioperatively, an approximately 5 cm mass originating from the rectosigmoid junction and completely obstructing the lumen was found (Figure 2). There were no findings compatible with metastasis in other intra-abdominal organs, and since there was dilatation in the proximal colonic anus, total mesocolic excision and end ostomy were decided to be performed. In the postoperative follow-up of the patient, his ostomy worked, nasogastric and urinary catheter were withdrawn and his regimen was gradually increased and he tolerated the regimen. She was discharged uneventfully on postoperative day 4. The pathology result was Mixed Neuroendocrine Non Neuroendocrine Neoplasm (MINEN). The neuroendocrine component was 40-50% and the morphology was grade 3 poorly differentiated neuroendocrine carcinoma. Ki67

index was 80% and mitotic activity was >20-10/bba. Synaptophysin was positive. The adenocarcinoma component was moderately differentiated. No metastasis was detected in 17 removed lymph nodes and it was reported as T3N0. Postoperative surgical margins were reported as clear and the patient was referred to the oncology clinic. The patient is being followed up at the 6th postoperative month without any problems.

CASE 2

An 81-year-old male patient with no known comorbidities, drug use or previous operations was admitted to the emergency department with abdominal pain for 10 days and absence of gas and stool discharge for 2 days. General condition was moderate, consciousness was clear, oriented and coherent. Abdominal examination revealed severe distension. Defense and rebound were negative but tenderness was present in all quadrants. Rectal touch was empty. Blood biochemistry, white blood cell, hemoglobin and platelet counts were normal on admission. Adbg showed multiple air fluid levels in the abdomen. In the whole abdomen tomography taken on admission to the emergency department, there was a mass lesion in the cecum, asymmetric increase in thickness in the wall with a length of approximately 6-7 cm in the ascending colon, slightly extending to the terminal ileum, lymphadenopathies in the periocecal fat plans, the short axis of the largest of which measured 5 mm, and the appearance of contamination and infiltration in the mesenteric fat plans, and this appearance was primarily evaluated in favor of cecal carcinoma. In the proximal part of the mass, dilatation reaching approximately 5 cm in diameter and fecal sign were observed in the terminal ileum and the appearance was found to be significant in terms of subileus (Figure 3). In the colonoscopy performed 10 days ago in an external center, a mass was found in the ascending colon that did not allow the colonoscope to pass proximally, biopsies were taken and the patient was told to present with the biopsy result. The patient was admitted to the emergency surgery service with a prediagnosis of tumor ileus. Resuscitation was started rapidly. Nasogastric catheter (ng) and urinary catheter were inserted. When 200 cc of fecaloid came into ng, it was urgently operated.

Peroperatively, a mass originating from the proximal cecum and ascending colon completely obstructed the lumen. There was no metastasis in intra-abdominal organs. The patient underwent right hemicolectomy and

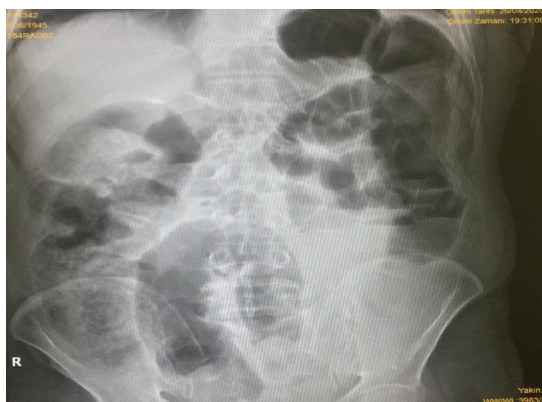


Figure 1. Air -fluid levels in standing direct abdominal radiography

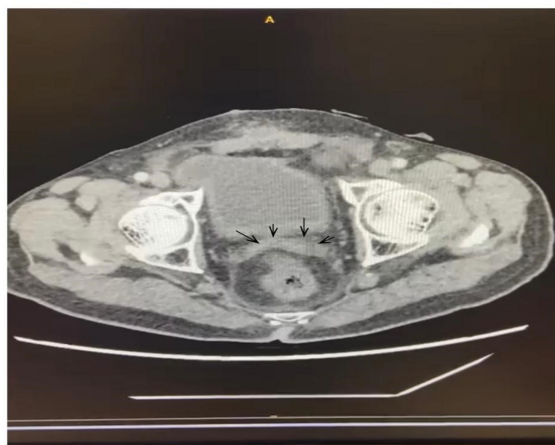


Figure 2. Mass obstruction of rectosigmoid junction ,tomographic view

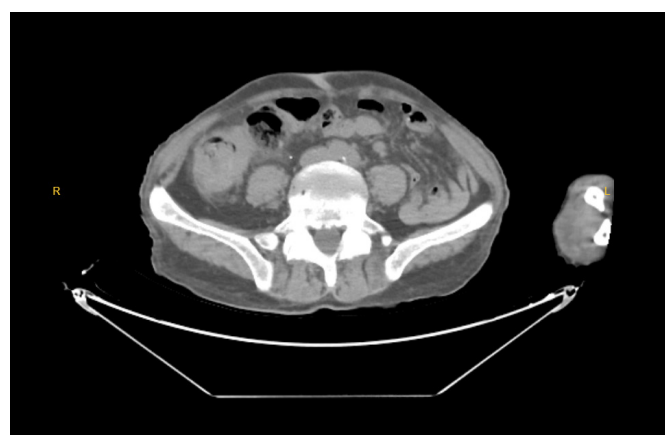


Figure 3. Dilatation of proksimal part of the mass and fecal sign

ileotransversostomy (Figure 4 and 5). Drain was placed. The patient was extubated in the intensive care unit. Oral was started on postop day 3, and the regimen was gradually increased when the patient tolerated oral. Gas and stool discharge occurred on postop day 4. Drains were removed. The wound site was clean and the patient was discharged after appropriate drug treatment was arranged at the end of surgical follow-up. Pathology report was concluded as Mixed Neuroendocrine Non Neuroendocrine Tumor. Neuroendocrine component was 40% and grade 3. Ki 67 was 80%, mitosis rate was greater than 20 in 10 magnification fields. Synaptophysin was positive. Adenocarcinoma component was 40-50% and poorly differentiated. Distal and proximal surgical margins were clear. No metastasis was detected in 14 removed lymph nodes and it was reported as T3N0. The patient was referred to the oncology clinic.



Figure 4. Peroperative view of right hemicolectomy



Figure 5. Right hemicolectomy specimen

DISCUSSION

Some of the patients admitted to the emergency room due to acute abdomen have mechanical intestinal obstruction. This condition, which prevents the distal passage of gastrointestinal content, is classified in 3 ways: causes originating from the lumen or wall of the intestine and causes that compress the intestine from the outside. The causes of obstruction are often bridges, intussusception, neoplasms, volvulus, internal/external herniations, strictures due to inflammatory bowel diseases and foreign bodies. Adenocarcinomas are the most common neoplasms.

Although they are thought to be rare tumors with an incidence of approximately 5% among all neoplasms, neuroendocrine tumors are among the tumors with increasing incidence in recent years. Two thirds of neuroendocrine tumors occur in the gastrointestinal tract, one fourth in the lungs and the rest in other endocrine tissues. The most commonly affected sites in the gastrointestinal tract are the small intestine, rectum, stomach and appendix. MINENs constitute a very small proportion of NETs. MINENs have a worse prognosis than other NETs. A study by La Rosa et al.^{4,5} proposed a grading of this malignancy. According to this study, MINENs are divided into 3 grades as high, intermediate and low grade.

High-grade MiNEN usually involves a non-neuroendocrine carcinoma (usually adenocarcinoma or acinar cell carcinoma, squamous cell carcinoma) or an adenoma (villous or tubulovillous) and a neuroendocrine component and usually has a more aggressive prognosis. The prognosis of intermediate-grade MiNEN usually includes a grade 1 (G1) or grade 2 (G2) NET component and a non-neuroendocrine component, and the prognosis depends on the non-neuroendocrine component. Low-grade MINEN includes a G1 or G2 NET and a less aggressive non-neuroendocrine component, namely adenoma.

The curative treatment for non-metastatic MINENs is surgical resection. Low-grade MINENs can be followed up without adjuvant treatment, whereas adjuvant chemotherapy is used in intermediate and high-grade MINENs.⁴

CONCLUSION

MINEN, a subtype of neuroendocrine tumors, which is a very rare colonic malignancy, may present with mechanical obstruction clinic like other tumor ileus. Pathologically, it contains adenocarcinoma and neuroendocrine tumor components. Despite the fact that the presence of neuroendocrine tumors is rare in the colon compared to other regions, it should be kept in mind that this type of tumors may be encountered in addition to adenocarcinoma.

ETHICAL DECLARATIONS

Informed Consent: All patients signed and free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

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A rare case of giant adrenal ganglioneuroma

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ABSTRACT

Ganglioneuromas (GNs) are rare benign tumors that typically occur in the posterior mediastinum or retroperitoneal region but can also be found in adrenal glands. Up to 50% of patients are asymptomatic, but symptoms can arise from the mass effect or excessive secretion of catecholamines. Careful evaluation is necessary to differentiate GNs from other adrenal tumors. A 19-year-old female patient with no previous comorbidities was diagnosed with a right adrenal incidentaloma. Physical examination and routine laboratory tests were normal. Imaging revealed a solid lesion in the right adrenal gland, and excisional adrenalectomy was performed to remove the mass, which was endocrinologically nonfunctional. Pathological examination confirmed the diagnosis of a right adrenal GN. The patient had an uneventful recovery and showed no recurrence during the follow-up period. After surgical removal of a benign neurogenic tumor, our patient had no tumor recurrence after five months, indicating a positive prognosis. However, long-term follow-up is still recommended because of reported cases of metastases and recurrence in some patients.

Keywords: Adrenal, ganglioneuroma, surgery, adrenalectomy

INTRODUCTION

Ganglioneuromas (GNs) are an uncommon benign tumor that develops from neural crest cells of the sympathetic nervous system.¹ GNs are most commonly found in the posterior mediastinum (38%), followed by the retroperitoneal region.² GNs are rarely found in adrenal glands (Figure 1).³ Up to 50% of patients show no symptoms; most are incidentally detected. If patients develop symptoms, they are most commonly caused by the mass effect of the tumor. Infrequently, patients experience hypertension due to high levels of excessive secretion of catecholamines and their metabolism by the tumor.⁴ According to previous reports, catecholamines or their metabolites are secreted by only 20–39% of GNs.^{3,4} Additionally, because adrenal GNs can vary in size, imaging, and diagnostic characteristics, some of them might be mistaken for other adrenal tumors, such as adrenocortical carcinoma (ACC) and pheochromocytoma (PC).^{5,9} Therefore, careful evaluation using endocrine examinations and multiple imaging procedures is required to rule out other types of tumors.¹⁰

In this report, we present a case of 19 years old female patient with a giant adrenal tumor incidentally diagnosed as adrenal GNs.

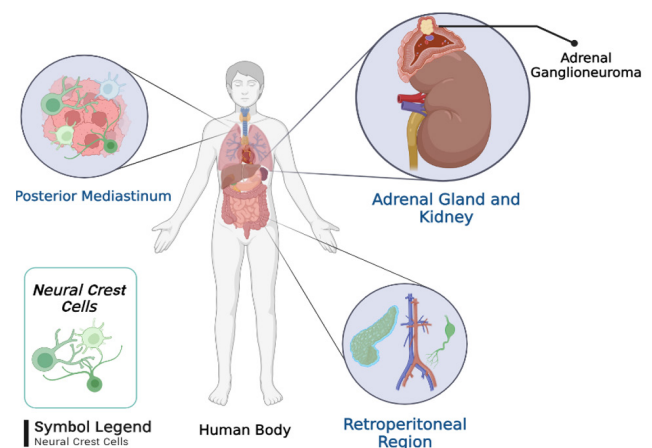


Figure 1. Ganglioneuroma (GN) is a rare benign tumor that originates from neural crest cells of the sympathetic nervous system. It is most commonly found in the posterior mediastinum (38%) and retroperitoneal location, while rarely found in adrenal glands

CASE

A 19-year-old female patient with no previous comorbidities was referred to our hospital after the discovery of a right adrenal incidentaloma during a workup for vague abdominal pain. On admission, she complained of vague

abdominal pain, with no other complaints. In her past medical history, the patient denied comorbidities as well as signs and symptoms of hypercortisolism and virilization, high blood pressure levels, or paroxysms of headache, palpitations, or sweating. There was no history of smoking, drinking, recent travel, or relevant family history. There were no previous hospital admissions or surgeries in her medical history.

Physical examination revealed no signs, and the results of routine laboratory tests were all within normal ranges. Radiography and computed tomography (CT) of the thorax, as well as electrocardiography, were standard. The results of routine laboratory and urine tests and levels of malignant tumor markers, such as carcinoembryonic antigen (CEA) and CA19-9, were all within the normal ranges. Endocrine examination values included the following: standard adrenal plasma aldosterone/plasma renin activity ratio, normal androgen hormones, normal 24-hour urinary native catecholamines and metanephrines, normal adrenal corticotrophin and cortisol rhythms, and normal 24-hour urinary free cortisol. Adrenal corticotrophin stimulation test revealed a normal plane.

Abdominal CT showed a solid lesion in the right adrenal gland, approximately 9x6.5x14 cm in size, hypodense heterogeneous density with minimal contrast, and enlargement of the liver parenchyma. Magnetic resonance imaging (MRI) findings were unfavorable for the diagnosis of cortical adenomas (Figure 2). The patient underwent excisional adrenalectomy.

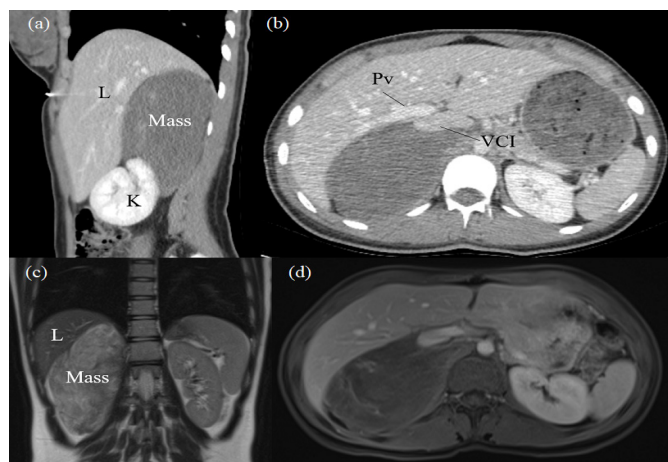


Figure 2. (a) and (b). The multislice CT shows a hypodense heterogeneous solid lesion with hypodense heterogeneous density and minimal contrast enhancement approximately 9x6.5x14 cm in size at the level of the right upper pole of the liver parenchyma, which is not easily distinguished from the right adrenal gland. On MRI images of the lesion, hyperintensities on T1-weighted images (c) and heterogeneous hyperintensities on T2 weighted images (d) are evident, causing contrast enhancement in the septations after intravenous contrast injection, and significantly compressing the right kidney and liver. L; liver, K; kidney, Pv; portal vein, VCI; vena cava inferior

The surgical specimen was an elastic hard tumor with a slightly lobular edge, measuring 15x11,7x6 cm (Figure 3). The cut surface of the tumor was light brown and covered with a thin capsule without any evidence of hemorrhage or necrosis. There was no evidence of malignancy. On pathological examination, the tumor was diagnosed as a right adrenal GNs (Figure 4). The patient was discharged without incident on postoperative day five. No recurrence was observed during the 5-month follow-up period.



Figure 3. A. Macroscopic view of the specimen at the anatomical position. The right adrenal gland in the specimen weighed 570 g and measured 15x12.3x6 cm. It was a solid, homogeneous tumor with a grayish-white surface, occasionally covered by a thin transparent capsule, and sometimes with attached adipose and membranous tissue. B. Surgical field after specimen removal. A black arrow indicates the right renal artery, while a white arrowhead indicates the right renal vein

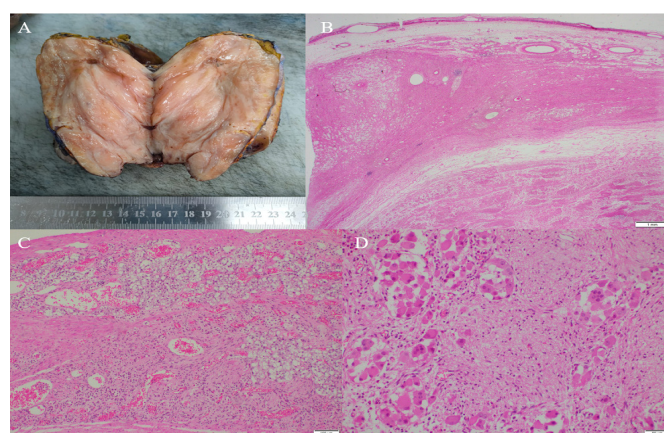


Figure 4. A. Mass of the adrenal gland, 15 cm in diameter, well-circumscribed, multilobulated, homogeneous off-white in color. On the inferolateral edge of the mass, the residual adrenal cortex is visible. B. Ganglioneuroma consisting of mature Schwann cells forming fascicles separated from the surrounding tissue by smooth borders (H&E, x12.5). C. Adrenal parenchyma (top) and ganglioneuroma (bottom) (H&E, x100). D. Mature spindle Schwann cells with large eosinophilic cytoplasm, eccentric nuclei, and prominent nucleoli, along with some multinuclear dysmorphic ganglion cells (H&E, x200)

DISCUSSION

In this report, we present the case of a 19-year-old female patient with giant adrenal GNs who was differentially diagnosed with ACC and PC.

The neural crest tissue of the sympathetic nervous system leads to a rare, benign, and slow-growing tumor known as GNs, which is histologically composed of mature Schwann cells and ganglion cells with fibrous stroma.¹ Additionally, because adrenal GNs vary in size, imaging, and diagnostic characteristics, some might be mistaken for other adrenal tumors, such as ACC and PC.^{5,9} However, there are a large number of diagnostic differentials of an adrenal mass comprising a long list, including adenoma, myelolipoma, cyst, lipoma, pheochromocytoma, adrenal cancer, metastatic cancer, hyperplasia, and tuberculosis.^{6,7,11-13} We retrospectively reviewed the hormonal status and CT and MRI features and compared this information with the histopathological findings to prevent misdiagnosis.

Adrenal incidentalomas are rare in patients under the age of 30 years but increase in frequency with age.¹³ It affects both sexes equally, and the fourth and fifth decades are the most common.¹⁴ Moreover, the pathophysiology of GNs is

influenced by genetic factors, including mutations in the tyrosine kinase receptor ERBB3.¹⁴ In the present case, the patient's age (19 years) was not within the range mentioned in previous reports, and there was no family history of Adrenal GNs.

The posterior mediastinum, retroperitoneum, and adrenal gland are the primary locations of GNs. The adrenal medulla is where 20% of GNs are found.^{2,3} As a result, GNs is rarely considered in the diagnosis of adrenal tumors. However, as seen in the present case, imaging techniques such as ultrasonography (US) and CT has recently expanded, leading to an increase in the number of adrenal GNs found incidentally. It is estimated that an adrenal tumor is incidentally found in 1-10% of cases of abdominal CT, and 1-6% of these are GNs.^{6,8,15,16} Adrenal GNs have been characterized as well-circumscribed tumors with an oval or lobular form, minimal attenuation, and homogenous or moderately heterogeneous masses in terms of imaging properties on CT.⁹ On MRI, adrenal GNs shows homogeneously low or intermediate signal intensity on T1-weighted images and heterogeneous slightly high signal intensity on T2-weighted images.¹⁷ The CT and MRI imaging characteristics were consistent with those of our case.

Hormonally silent adrenal GNs are typically found incidentally. The most frequently reported secondary symptom, as in our case, is back and abdominal pain caused by the mass effect of the tumor.^{1,3} The patient in this report had an incidentaloma, which is the most common manifestation of adrenal GNs. The patient may develop particular symptoms, including hypertension, diarrhea, weakness, and virilization when there is an excessive release of catecholamines or steroid hormones (indicative of a hormonally active disease).⁴ However, these symptoms were not observed in our patient. Therefore, surgical excision is required to confirm this diagnosis.

Surgery is the initial treatment option for adrenal GNs, particularly for large tumors. According to the National Institutes of Health State-of-the-Science Statement, non-secretory adrenal incidentalomas with dimensions >6 cm or suspicious features of malignancy should undergo adrenalectomy because of the high prevalence of malignancy in non-secretory adrenal incidentalomas.¹⁸ In the present case, the tumor size was >12 cm; therefore, we performed excisional tumor resection. As laparoscopy is less invasive than standard open surgery, it may be a superior surrogate. However, because the tumor was large and the potential of adrenal cortical carcinoma could not be ruled out in our case, we decided to perform an open tumor excision. The likelihood of a malignant tumor is higher among lesions larger than 4.5 cm, even though histological analysis may not confirm it. While our patient's tumor measured >12 cm in diameter, the pathology report indicated that it was benign. Typically, adrenal GNs consist of encapsulated masses with a solid, grayish-white cut surface, are homogenous in structure, as seen in the present case, and often have a firm consistency.¹⁰

CONCLUSION

Our patient showed no signs of tumor recurrence five months after surgery. Although there have been a few reported cases of metastases and recurrence, an excellent prognosis exists for patients who have undergone surgical removal of a benign neurogenic tumor without any further

treatment requirements. Therefore, a long-term follow-up is recommended after surgery.

ETHICAL DECLARATIONS

Informed Consent: The patient signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: A conflict of interest has not been declared by the author.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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I am a fifth-year medical student at Kahramanmaraş Sütçü İmam University. Ever since I was young, I always loved human science. I just enjoyed everything about it. How the body functions interests me, both in health and illness, how to find out what was wrong and how to address it. It has always been my dream to be a doctor. I appreciate Gazi University and Prof. Dr. Mehmet Akif Türkoğlu for this opportunity of scientific research and I'm looking forward to contribute in other studies also.

