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Late-Term Effects of Extracorporeal Shock Wave Lithotripsy on Renal Functions

Ekstrakorporeal Şok Dalga Litotripsinin Böbrek Fonksiyonları Üzerinde Geç Dönem Etkileri

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ABSTRACT

Background: It has been reported that ischemia-reperfusion injury due to extracorporeal shock wave lithotripsy (ESWL) may adversely affect renal function by causing renal tubular damage in the acute and chronic periods. The aim of this study was to determine the late effects of ESWL on renal function in the treatment of kidney stones.

Materials and Methods: Between June and December 2023, 96 patients with renal calculi who applied to the urology ESWL unit, met the study criteria, and did not have chronic renal disease were included in the study. Of the patients, 66 (69%) were male, 30 (31%) were female, and the mean age of the patients was 41±10 years. All patients underwent a total of 3 sessions of ESWL at 1 week intervals. Blood samples for preoperative baseline and 3 months postoperative serum blood urea nitrogen (BUN), creatinine, and C-reactive protein (CRP) levels and 24 hours urine samples for urine creatinine levels were obtained from all patients. Creatinine clearance in 24 hours urine (Ccr-24) was calculated using the standard creatinine clearance formula. The demographic characteristics of the patients as well as the total shock wave count (TSW) and total amount of energy (TAE) during the ESWL sessions were recorded.

Results: No statistically significant difference was found between serum BUN, creatinine, and CRP levels before and after ESWL application [28.2±9.0 vs. 28.6±7.4 mg/dL, 0.83 (0.40-2, 70) vs. 0.84 (0.47-1.88) mg/dL and 3.0 (0.1-79.0) vs. 3.0 (0.1-70.5) mg/L]. The postop Ccr-24 value was statistically lower than the preop value (101.3±18.4 vs. 97.6±18.8 mL/min; p=0.0058). In addition, there were no significant differences in BUN, creatinine, CRP, and Ccr-24 values between the groups of patients with TSW <8000 and ≥8000 (p>0.05).

Conclusion: We found that ESWL may affect renal function by decreasing the glomerular filtration rate calculated by Ccr-24 in the late period, independent of the session number, TSW, and TAE.

Keywords: Kidney stone, ESWL, kidney function, Ccr-24, total shock wave count

ÖZ

Amaç: Ekstrakorporeal şok dalga litotripsin (ESWL) uygulamasına bağlı iskemi-reperfüzyon hasarının akut ve kronik dönemde renal tübüler hasara neden olarak böbrek fonksiyonlarını olumsuz yönde etkileyebileceği bildirilmektedir. Bu çalışmada amaç, böbrek taşı tedavisinde uygulanan ESWL'nin böbrek fonksiyonu üzerindeki geç dönem etkilerini belirlemekti.

Gereç ve Yöntemler: Haziran-Aralık 2023 tarihleri arasında, üroloji ESWL ünitesine müracaat eden, çalışma kriterlerine uygun ve kronik renal hastalığı olmayan böbrek taşı olan toplam 96 hasta çalışmaya dahil edildi. Hastaların 66'sı (%69) erkek, 30'u (%31) kadın ve hastaların yaş ortalaması 41±10 idi. Tüm hastalara 1 haftalık aralıklarla toplam 3 seans ESWL uygulandı. Tüm hastaların operasyon öncesi bazal ve operasyon sonrası 3. aydaki serum BUN, kreatinin, C-reaktif protein (CRP) düzeyleri için kanları ve idrar kreatinin düzeyleri için 24 saatlik idrarları alındı. Standart kreatinin klirensi formülü ile 24 saatlik idrarda kreatinin klirensi (Ccr-24) hesaplandı. Hastaların demografik özellikleri yanı sıra ESWL seanslarında uygulanan toplam şok dalga sayısı (TŞD) ve toplam enerji miktarı (TEM) kayıt altına alındı.

Bulgular: ESWL uygulaması öncesi ve uygulama sonrası serum BUN, kreatinin ve CRP düzeyleri arasında istatistiksel anlamlı fark saptanmazken [sırasıyla 28,2±9,0'a karşı 28,6±7,4 mg/dL, 0,83'e (0,40-2,70) karşı 0,84 (0,47-1,88) mg/dL ve 3,0'a (0,1-79,0) karşı 3,0 (0,1-70,5) mg/L], postop Ccr-24 değeri preop değerinden istatistiksel olarak daha düşük saptandı (101,3±18,4'e karşı

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ÖZ

97,6±18,8 mL/dk; p=0,0058). Ayrıca TŞD<8000 olan ve ≥8000 olan hasta grupları arasında BUN, kreatinin, CRP ve Ccr-24 değerleri açısından fark yoktu (p>0,05).

Sonuç: ESWL uygulamasının seans sayısı, TŞD ve TEM'den bağımsız olarak geç dönemde Ccr-24 ile hesaplanan glomerüler filtrasyon hızını düşürerek böbrek fonksiyonlarını etkileyebileceği saptandı.

Anahtar Kelimeler: Böbrek taşı, ESWL, renal fonksiyon, Ccr-24, toplam şok dalga sayısı

Introduction

Urinary tract stone diseases have become an important public health problem due to their increase in parallel with changes in lifestyle, nutritional content, and climatic conditions all over the world (1). Today, extracorporeal shock wave lithotripsy (ESWL), rigid and flexible ureterorenoscopy, percutaneous nephrolithotomy, robotic and laparoscopic methods, as well as open surgical methods, which are relatively rarely used, are used in the treatment of upper urinary tract stone diseases (2). Among these, ESWL is a highly effective and non-invasive treatment method and has been used since the 1980s (3). Although pregnancy, coagulopathy, and active urinary tract infection are absolute contraindications for ESWL, its use is becoming widespread worldwide due to its high success rates in renal and ureteral calculi. ESWL acts on urinary system stones by creating a series of mechanical forces, defined as pressure-induced fracture, fragmentation, cavitation, and dynamic fatigue, which causes the stones to disintegrate. Of these, cavitation is considered to play a major role in tissue damage. While mechanical forces create the desired effect on the stone, they also cause undesirable effects in the kidney and adjacent organs, such as the release of cellular inflammatory mediators and tissue infiltration of inflammatory response cells (4). These undesirable effects range from early complications, such as short-term hematuria and hematoma, to late complications affecting renal function and systemic hypertension. Studies showing histopathological changes in the kidneys after ESWL have demonstrated endothelial cell damage in the medium-sized arteries, veins, and glomerular capillaries of the kidneys (5,6). This damage is usually local and especially affects the arcuate veins located at the corticomedullary junction, resulting in hematuria and haematoma (5). Hematuria is the most common complication and resolves spontaneously within a few days. Hematoma is usually located intrarenal, subcapsular, or perirenal and is observed in less than 1% of patients (7).

Although there is no clear consensus regarding the effect of ESWL on renal function, the general consensus is that renal function decreases in the acute period and returns to its previous values within a short period. On the other hand, there is still controversy about its late effects.

In this study, we aimed to retrospectively evaluate the late-term effects of ESWL on renal function using BUN, creatinine, C-reactive protein (CRP), and creatinine clearance in 24 hours urine (Ccr-24) levels. In addition, the relationship between this late-term effect and the number of sessions, the total shock wave count (TSW) and total amount of energy (TAE) was analyzed.

Materials and Methods

Between June 2023 and December 2023, a total of 96 patients who met the study criteria among 108 patients who applied to the ESWL unit of the Urology Clinic of Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital for kidney stones were included in the study. Patients with bleeding disorder, solitary kidney, urogenital system abnormality, acute or chronic renal failure, rheumatic disease (systemic lupus erythematosus, rheumatoid arthritis, Behçet's disease, ankylosing spondylitis, etc.), and previous treatment with urolithiasis were excluded. Before starting the ESWL procedure, all patients' medical histories were obtained, and physical examinations were performed. Age, gender, imaging method, and stone location and size were recorded. Serum BUN, creatinine, CRP, and 24 hours urine creatinine levels were measured before ESWL. To estimate the glomerular filtration rate (GFR), Ccr-24 was calculated using the following formula (8):

Ccr24=[(Ucr x V)/Scr] x 1.73/A,
Ccr=(mL/min/1.73 m^2), Ucr=Urinary creatinine (µmol/L)
Scr=Serum creatinine (µmol/L), V=Urine volume (mL/min)
A=Body surface area=(4xweight+7)/(weight+90)

Urine analysis and/or urine culture were performed in all patients. Appropriate antibiotic treatment was started in patients with urine culture growth, and ESWL sessions were postponed until urine culture was negative.

The ESWL procedure was performed with a Storz Medical X-FP-S device while the patient was in the supine position. A maximum of 4000 shock waves with 60-80 kV power were applied in each session. Fluoroscopy

was used for localization of radiopaque stones and ultrasonography for radiolucent stones. At the end of the ESWL session, if the stone did not break (or did not shrink sufficiently) and no complications developed, a repeat session was planned 7 days later, and a total of 3 sessions were performed. Success was defined as a stone-free status or the presence of clinically insignificant residual fragments (≤4 mm). Patients who were not successful at the end of the third session were referred to alternative treatment approaches. Patients considered successful were called for follow-up at 3 months after ESWL. Serum BUN, creatinine, and CRP levels and 24 hours urine creatinine levels were measured in these patients. Ccr-24 values were recalculated.

Statistical Analysis

SPSS Statistic (IBM Corp, 25 Version, Chicago, USA) software was used for data analysis. The Kolmogorov-Smirnov normality test was applied to test the data distribution. The chi-square test was used to analyze categorical variables. The paired t-test was used to compare parametric data of dependent groups consisting of two groups, and the Wilcoxon matched-pairs test was used to compare non-parametric data. The unpaired t-test and Mann-Whitney U test were used to compare parametric data of independent groups consisting of two groups and non-parametric data, respectively. Pearson's correlation analysis was used for parametric data and Spearman's correlation analysis for non-parametric data to evaluate the relationship between independent variables.

Ethical Approval

Ethical approval for this study was granted by the Scientific Research Ethics Committee of Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital (approval number: E-46059653- 050.99-243909969, dated: 16.05.2024). All patients were informed about the study and provided informed consent.

Power Analysis of the Study

The minimum number of subjects required for this study was based on data from a study investigating renal function markers after percutaneous nephrolithotomy in patients with one kidney (9). Based on these data, an a priori power analysis (G*Power, Version 3.1, Düsseldorf, Germany) estimated that a study using the eGFR test to estimate GFR required at least 70 dependent experimental subjects (effect size d=0.3021, α=0.05, power=0.80). However, for a stronger prediction, the dependent group of this independent study comprised 96 subjects.

Results

The mean age of the 96 patients (Male/Female: 66/30) included in the study was 41±10 years and the mean body mass index (BMI) was 27.1±4.7 (Table 1). The right/left location of the stones was 61/38 (63%/39%). There were 52 (55%) stones localized in the renal pelvis, 19 (20%) in the upper calyx, 12 (12.5%) in the middle calyx and 13 (13.5%) in the lower calyx. Complications developed in a total of 6 patients after ESWL procedure. One patient with intrarenal hematoma was hospitalized and treated conservatively. Two patients who developed the stone-tract were treated with ureteroscopy. Two patients with severe pain and 1 patient with high fever were treated conservatively.

When serum BUN, creatinine, and CRP levels before (preop) and after (postop) ESWL application were analyzed, there was no statistically significant difference between pre-op and post-op BUN, creatinine, and CRP levels (p>0.05) (Figures 1A, 1B, 1D, Table 2). However, there was a statistically significant difference between preop and postop Ccr-24 values (Figure 1C). The postop Ccr-24 values were statistically lower compared to preop (p=0.0058). In the correlation analysis performed to explain this decrease in postop Ccr-24 levels after ESWL, there was no statistically significant correlation between postop Ccr-24 levels and TAE, session number, and TSW values [Spearman's r (rs) <0.20 and p>0.05] (Figure 2). There was a high positive correlation between TAE values, session number, and TSW (rs=0.8913, 95% CI: 0.8393-0.9271, p<0.0001 and rs=0.8668, 95% CI: 0.8043-0.9103, p<0.0001, respectively). There was also a statistically strong positive correlation between session number and TSW (rs=0.8978, 95% CI: 0.8488-0.9316, p<0.0001).

Table 1. Demographic and clinical characteristics of patients included in the study

Demographic and clinical characteristics		n (%)
Gender, M/F		66/30 (69%/31%)
Kidney with stone, right or left		61/38 (63%/39%)
Stone location	Pelvis	52 (55%)
	Upper calyx	19 (20%)
	Middle calyx	12 (12.5%)
	Lower calyx	13 (13.5%)
Complications	Hematoma	1 (1%)
	Stone pathway	2 (2.1%)
	Severe pain	2 (2.1%)
	High fever	1 (1%)
	Total	6 (6.25%)

M/F: Male/Female

These significant correlations were expected. Because the number of sessions increased, the amount of TAE and TSW naturally applied increased.

When the ESWL-treated patients were compared according to the TSW (Table 3), no significant difference was observed between the groups with TSW <8000 and TSW ⩾8000 in terms of gender, age, BMI, stone size and stone hardness (p>0.05). Similarly, there was no statistically significant difference between preop and postop BUN, creatinine, CRP, and Ccr-24 levels in these groups (p>0.05). The TAE and session number values of the group with TSW⩾8000 were found to be statistically significantly higher than those of the group with TSW <8000 [180 (120-210) vs. 65 (40-140) and 3.0 (2.0-3.0) vs. 1.0 (1.0-2.0); p<0.0001]. These results are expected. Because the number of exposed joules and the number of sessions will also be high in those with high TSW values. As a result, there would be no difference in terms of renal function between those who were exposed to high-energy (or sessions number) and those who were not.

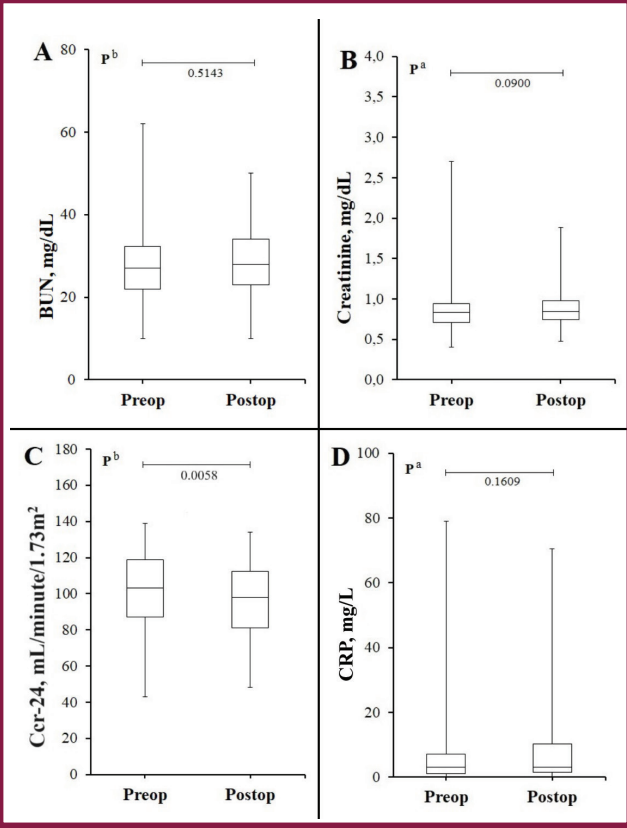

Figure 1. Bar graph representing (A) serum BUN, (B) creatinine, (C) Ccr-24, and (D) CRP levels before (preop) and after (postop) ESWL application. There was no difference between A) serum BUN, B) creatinine, and D) CRP levels before (preop) and after (postop) ESWL application. C) On the other hand, postop Ccr-24 values were observed to be statistically lower than preop values. [a]Wilcoxon matched-pairs test, [b]Paired t-test

BUN: Blood urea nitrogen, Ccr-24: Creatinine clearance in 24 hours urine, CRP: C-reactive protein, ESWL: Extracorporeal shock wave lithotripsy

Discussion

ESWL has been frequently accepted and applied as the first choice in the treatment of upper urinary tract stone diseases. The fact that it does not require hospitalization and is non-invasive are among the reasons for its preference. It is also one of the most useful methods available for the treatment of urolithiasis because

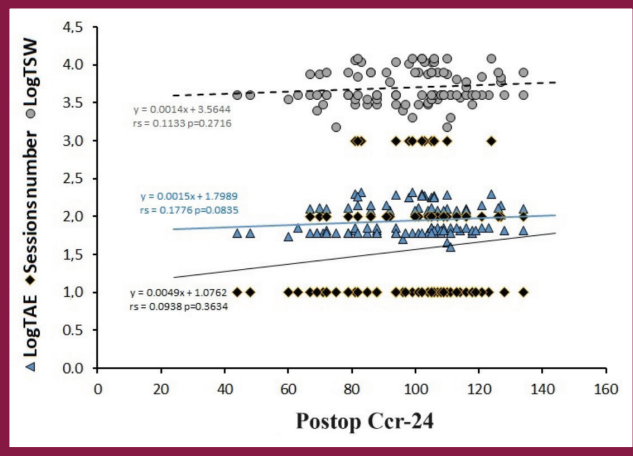

Figure 2. Corelation between Ccr-24 and TAE, session number, and TSW. TAE, sessions number and TSW values were not statistically significant correlations between the postop Ccr-24 values in the correlation analysis

rs: Spearman correlation coefficient, Ccr-24: Creatinine clearance in 24 hours urine, TSW: Total shock wave count, TAE: Total amount of energy

Table 2. Comparison of kidney function tests and Ccr-24 values preop and postop ESWL application

	ESWL		p-value
	Preop	Postop	
n	96	96	
BUN, mg/dL	28.2±9.0	28.6±7.4	[b]0.5143
Kreatinin, mg/dL	0.83 (0.40-2.70)	0.84 (0.47-1.88)	[a]0.0900
Ccr-24, mL/min/1.73 m²	101.3±18,4	97.6±18.8	[b]0.0058
CRP, mg/L	3.0 (0.1-79.0)	3.0 (0.1-70.5)	[a]0.1609

[a]Wilcoxon matched pairs test; [b]Paired t-test. The statistical significance level is p<0.05. Parametric data were presented as mean ± standard deviation, and non-parametric data were presented as median (minimum-maximum), ESWL: Extracorporeal shock wave lithotripsy, BUN: Blood urea nitrogen, Ccr-24: Creatinine clearance in 24 hours urine, CRP: C-reactive protein

there is no alternative to this method, and this method is currently being developed. After its widespread use, various studies have been conducted to investigate the early and late adverse effects of ESWL on renal function, and reversible histological changes have been observed in the renal parenchyma in the acute period (10,11). Ischemia-reperfusion-mediated oxidative stress during the procedure was attributed to the physiopathology of the event. This condition has been suggested to cause parenchymal or tubular damage in the kidney. Renal parenchymal damage may affect renal function and GFR, leading to decreased urea/creatinine excretion (or serum retention). These changes led to the observation of ESWL-induced renal injury (11). Among these, serum creatinine is still the gold standard for renal injury despite its many interferences and renal excretion problems. In recent years, biomarkers such as kidney injury molecule-1 (KIM-1), neutrophil gelatinase-associated lipocalin (NGAL), and cystatin C have been proposed for the detection of renal injury (12). However, for most such devices, the problem of standardization or harmonization for routine use has still not been solved. Studies showing the effects of ESWL on renal function have shown that GFR decreases after ESWL, but this change returns to normal within the first 24 hours (13,14). Until recently, several markers that may reveal renal damage before and after ESWL treatment have been evaluated. However, because their results are not conclusive, more detailed studies with larger samples should be performed (11). In this study, urea, creatinine, Ccr-24, and CRP (an important indicator of tissue damage/inflammation), which are routine laboratory tests, were used to monitor the presence of ESWL-induced damage in our patients.

Although various mechanisms have been proposed to explain the mechanism of tissue damage, cavitation is more prominent. In addition to the direct mechanical effects caused by cavitation, free radicals play an important role in cell destruction (15). There are also various studies showing that it causes morphological changes in renal tissues, such as focal parenchymal damage and subcapsular haematoma (16). In our study, renal hematoma developed in 1 patient. In animal experiments, ESWL has been shown to cause damage to blood vessels, renal tubules, Bowman's capsule, renal corpuscles, and mesangial cells (17). Studies on urinary enzymes indicating renal damage have also shown that urinary enzyme levels are transiently elevated and return to normal within a few days (18).

To date, there are no studies showing the long-term effects of ESWL on the kidneys. Animal studies in rabbits and dogs have shown that renal fibrosis develops in a dose-dependent manner (17,19). Willis et al. (20) showed that renal damage after ESWL is directly proportional to the number

Table 3. Comparison of renal function and CRP levels according to the total number of shock waves received by patients with ESWL

	Total shock number		p-value
	<8000	≥8000	
n	69	27	-
Sex, M (%)	48 (70%)	18 (67%)	[c]0.810
Age	41 (21-63)	44 (15-65)	[d]0.2556
BMI, kg/m^2	27 (18-38)	26 (17-38)	[d]0.6956
Stone size (mm)	10 (5-16)	9 (5-12)	[d]0.1389
Stone hardness, HU,	890 (312-1615)	1040 (508-1456)	[d]0.1749
Number of sessions, n	1.0 (1.0-2.0)	3.0 (2.0-3.0)	[d]<0.0001
TAE, joule	65 (40-140)	180 (120-210)	[d]<0.0001
Preop BUN level, (mg/dL)	29 (10-62)	25 (18-44)	[d]0.3944
Postop BUN, (mg/dL)	30 (10-50)	25 (17-38)	[d]0.0841
Preop kreatinin level, (mg/dL)	0.82 (0.40-2.70)	0.84 (0.49-1.14)	[d]0.9902
Postop kreatinin (mg/dL)	0.88 (0.47-1.88)	0.83 (0.50-1.22)	[d]0.3202
Preop Ccr-24, mL/min/1.73m^2	105 (43-139)	103 (62-140)	[d]0.6249
Postop Ccr-24, mL/min/1.73m^2	102 (44-134)	102 (72-134)	[d]0.8930
Preop CRP level, (mg/L)	3.0 (0.1-79.0)	4.6 (0.6-69.0)	[d]0.3472
Postop CRP level, (mg/L)	3.0 (0.1-70.5)	3.0 (0.1-30.0)	[d]0.9297

[c]Chi-square test, [d]Mann-Whitney U test, [e] Unpaired t-test, the statistical significance level is p<0.05. Parametric data were presented as mean ± standard deviation, and non-parametric data were presented as median (minimum-maximum), CRP: C-reactive protein, ESWL: Extracorporeal shock wave lithotripsy, M: Male, BMI: Body mass index, HU: Hounsfield unit, TAE: Total amount of energy, BUN: Blood urea nitrogen, Ccr-24: Creatinine clearance in 24 hours urine

of shock waves and the amount of energy (20). In studies conducted to investigate the effects of ESWL on GFR, Sheir and Gad (21) reported a significant increase in GFR after ESWL, Saxby (22) reported a significant decrease in GFR, and Cass (23) reported a decrease in GFR in some patients and an increase in others. When these reports are compared with the results obtained in our study, it can be understood that some of the results do not completely overlap with other results. The finding of a significant decrease in Ccr-24, which is still the most important indicator of GFR, overlapped with our study. In addition, the lack of significant changes in BUN, creatinine, and CRP among the parameters evaluated in our study was similar to previous studies (24,25).

It was an interesting finding that there was no difference in blood creatinine levels before and 3 months after ESWL, but there was a difference in Ccr-24 levels calculated from the creatinine levels. The possible reason for this was the fact that blood creatinine levels were not a sensitive indicator of kidney damage. However, Ccr-24, which was performed using both urine and blood creatinine levels and was found to have a high correlation with GFR, is a more sensitive measure of kidney function than serum creatinine (26,27). Creatinine is the breakdown product of creatine phosphate found in dietary meat and skeletal muscle. Its production in the body depends on muscle mass. Because the glomerulus freely filters creatinine, the Ccr-24 ratio is close to the GFR calculation. When blood creatinine levels are very high, Ccr-24 may overestimate GFR by approximately 10% because creatinine excretion by peritubular capillary increases. However, this error is relatively minor in people without renal problems and those with creatinine conversion within the physiological limits. In addition, despite problems such as incomplete urine collection in non-cooperative patients, Ccr-24 measurement is a standardized method widely used in GFR measurement due to its high accuracy (26,28). In this study, we investigated whether ESWL application has a constructive effect on renal damage in the postoperative chronic period. We actually found a significant decrease in Ccr-24 levels, while we did not detect a significant change in blood creatinine and BUN levels to coincide with the above information. The possible physiopathological explanation for this finding is that loss of renal function or damage in the chronic period should be detected using more sensitive biomarkers. In conclusion, a well-organized Ccr-24 test is a good indicator of renal function loss during the chronic period of ESWL. In this context, ESWL is not a completely noninvasive approach. It should be kept in mind that it may have chronic effects as well as acute effects.

Study Limitations

Because this study is a retrospective analytical study, the cause-effect relationship is weaker than that in prospective studies. Whether the change in Ccr-24 values in the late period is related to the number of sessions, TSW, and TAE needs to be tested with a larger sample. In addition, the study should be confirmed with a study including other markers of renal damage, such as NGAL and KIM-1, since incomplete collection of 24 hours urine in some patients may affect the results.

Conclusion

It was found that ESWL may affect renal function by decreasing the GFR calculated using Ccr-24 in the late period. However, no significant relationship was found between this late effect and the number of sessions, TSW, and TAE.

Ethics

Ethics Committee Approval: Ethical approval for this study was granted by the Scientific Research Ethics Committee of Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital (approval number: E-46059653-050.99-243909969, dated: 16.05.2024).

Informed Consent: All patients were informed about the study and provided informed consent.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: E.E, Concept: E.E, Design: E.E, Data Collection or Processing: E.E, Analysis or Interpretation: E.E, M.Ş., Literature Search: E.E, M.Ş., Writing: E.E, M.Ş.

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REFERENCES

1. Scales CD Jr, Smith AC, Hanley JM, Saigal CS. Urologic Diseases in America Project. Prevalence of kidney stones in the United States. Eur Urol. 2012;62:160-165. [Crossref]
2. Geraghty RM, Jones P, Somani BK. Worldwide trends of urinary stone disease treatment over the last two decades: a systematic review. J Endourol. 2017;31:547-556. [Crossref]
3. Chaussy C, Schüller J, Schmiedt E, Brandl H, Jocham D, Liedl B. Extracorporeal shock-wave lithotripsy (ESWL) for treatment of urolithiasis. Urology. 1984;23:59-66. [Crossref]

4. Gnessin, E, Lingeman JE. Bioeffects of Shock Wave Lithotripsy. In: Talati J, Tiselius HG, Albala D, YE Z (eds). Urolithiasis. Springer, London. [Crossref]
5. Karlsen SJ, Smevik B, Hovig T. Acute morphological changes in canine kidneys after exposure to extracorporeal shock waves. A light and electron microscopic study. Urol Res. 1991;19:105-115. [Crossref]
6. Recker F, Hofmann W, Bex A, Tscholl R. Quantitative determination of urinary marker proteins: a model to detect intrarenal bioeffects after extracorporeal lithotripsy. J Urol. 1992;148:1000-1006. [Crossref]
7. Dhar NB, Thornton J, Karafa MT, Streem SB. A multivariate analysis of risk factors associated with subcapsular hematoma formation following electromagnetic shock wave lithotripsy. J Urol. 2004;172:2271-2274. [Crossref]
8. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976;16:31-41. [Crossref]
9. Ghadian A, Einollahi B, Ebrahimi M, Javanbakht M, Asadi M, Kazemi R. Renal function markers in single-kidney patients after percutaneous nephrolithotomy: A pilot study. J Res Med Sci. 2022;27:17. [Crossref]
10. Gunasekaran S, Donovan JM, Chvapil M, Drach GW. Effects of extracorporeal shock wave lithotripsy on the structure and function of rabbit kidney. J Urol. 1989;141:1250-1254. [Crossref]
11. Dzięgała M, Krajewski W, Kołodziej A, Dembowski J, Zdrojowy R. Evaluation and physiopathology of minor transient shock wave lithotripsy-induced renal injury based on urinary biomarkers levels. Cent European J Urol. 2018;71:214-220. [Crossref]
12. Medić B, Rovcanin B, Vujovic KS, Obradovic D, Duric D, Prostran M. Evaluation of novel biomarkers of acute kidney injury: The Possibilities and Limitations. Curr Med Chem. 2016;23:1981-1997. [Crossref]
13. Connors BA, Evan AP, Willis LR, Blomgren PM, Lingeman JE, Fineberg NS. The effect of discharge voltage on renal injury and impairment caused by lithotripsy in the pig. J Am Soc Nephrol. 2000;11:310-318. [Crossref]
14. Rutz-Danielczak A, Pupek-Musialik D, Raszeja-Wanic B. Effects of extracorporeal shock wave lithotripsy on renal function in patients with kidney stone disease. Nephron. 1998;79:162-166. [Crossref]
15. Cohen TD, Durrani AF, Brown SA, Ferraro R, Preminger GM. Lipid peroxidation induced by shockwave lithotripsy. J Endourol. 1998;12:229–232. [Crossref]
16. Evan AP, Connors BA, Pennington DJ, Blomgren PM, Lingeman JE, Fineberg NS, et al. Renal disease potentiates the injury caused by SWL. J Endourol. 1999;13:619-628. [Crossref]
17. Newman R, Hackett R, Senior D, Brock K, Feldman J, Sosnowski J, et al. Pathologic effects of ESWL on canine renal tissue. Urology. 1987;29:194-200. [Crossref]
18. Assimos DG, Boyce WH, Furr EG, Espeland MA, Holmes RP, Harrison LH, et al. Selective elevation of urinary enzyme levels after extracorporeal shock wave lithotripsy. J Urol. 1989;142:687-690. [Crossref]
19. Morris JS, Husmann DA, Wilson WT, Preminger GM. Temporal effects of shock wave lithotripsy. J Urol. 1991;145:881-883. [Crossref]
20. Willis LR, Evan AP, Connors BA, Shao Y, Blomgren PM, Pratt JH, et al. Shockwave lithotripsy: dose-related effects on renal structure, hemodynamics, and tubular function. J Endourol. 2005;19:90-101. [Crossref]
21. Sheir KZ, Gad HM. Prospective study of the effects of shock wave lithotripsy on renal function: role of post-shock wave lithotripsy obstruction. Urology. 2003;61:1102-1106. [Crossref]
22. Saxby MF. Effects of percutaneous nephrolithotomy and extracorporeal shock wave lithotripsy on renal function and prostaglandin excretion. Scand J Urol Nephrol. 1997;31:141-144. [Crossref]
23. Cass AS. Renal function after bilateral extracorporeal shockwave lithotripsy. J Endourol. 1994;8:395-399. [Crossref]
24. Villányi KK, Székely JG, Farkas LM, Jávor E, Pusztai C. Short-term changes in renal function after extracorporeal shock wave lithotripsy in children. J Urol. 2001;166:222-224. [Crossref]
25. Hughes SF, Jones N, Thomas-Wright SJ, Banwell J, Moyes AJ, Shergill I. Shock wave lithotripsy, for the treatment of kidney stones, results in changes to routine blood tests and novel biomarkers: a prospective clinical pilot-study. Eur J Med Res. 2020;25:18. [Crossref]
26. Hafeez AR, Idrees MK, Akhtar SF. Accuracy of GFR estimation formula in determination of glomerular filtration rate in kidney donors: Comparison with 24 h urine creatinine clearance. Saudi J Kidney Dis Transpl. 2016;27:320-325. [Crossref]
27. Serdar MA, Kurt I, Ozcelik F, Urhan M, Ilgan S, Yenicesu M, et al. A practical approach to glomerular filtration rate measurements: creatinine clearance estimation using cimetidine. Ann Clin Lab Sci. 2001;31:265-273. [Crossref]
28. Shahbaz H, Rout P, Gupta M. Creatinine Clearance. 2024 Jul 27. [Crossref]

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Program Evaluation of the Problem-Based Learning Module of Hamidiye Medical Faculty First Year Students

Hamidiye Tıp Fakültesi Dönem 1 Öğrencilerinin Probleme Dayalı Öğrenme Modülünün Program Değerlendirmesi

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ABSTRACT

Background: Problem-based learning (PBL) is a small group education in which students direct their own learning processes. Our aim in our study is to evaluate the program of the PBL module that we conducted with first-year students.

Materials and Methods: A total of 176 first-year students and 16 instructors attended the training. The PBL module was completed in 3 days. A pre-test with 16 questions and a post-test consisting of the same pre-test questions were administered to the students at the end of the training. Data analysis was performed using SPSS 25. Compliance of the data with normal distribution was determined using the Shapiro-Wilk test. The changes between pre- and post-training scores were examined using the Wilcoxon test. In this study, the type I error rate was 0.05. Approximately 4 weeks after the training, a focus group was held, and the interview was recorded. The qualitative data were evaluated by two researchers. The transcribed text was divided into themes and subthemes. The Kirkpatrick and logic model for program evaluation were used as the program evaluation model.

Results: According to Kirkpatrick level 1 evaluation, satisfaction with the training was high in both surveys and focus group studies. According to Kirkpatrick level 2, a significant increase in success was detected between the pretest and posttest of the students (pre-test average: 7, post-test average: 12, $p<0.05$). In addition, the average success rate of students was 35 out of 39 points. With the logic model evaluation, the inputs (resources), activities, results, short, medium and long-term goals of education were revealed, and it was determined that the short- and medium-term goals were achieved.

Conclusion: As a result of the program evaluation, it was determined that the satisfaction of first-year students and instructors with the PBL education was high, and the PBL success of the students was at the desired level.

Keywords: Problem based learning, PBL, program evaluation, qualitative research

ÖZ

Amaç: Probleme dayalı öğrenim (PBL), tıp fakültesi öğrencilerinin kendi öğrenmelerine kendilerinin yön verdiği, öğrenci merkezli çok önemli bir küçük grup eğitim yöntemidir. Çalışmamızdaki amacımız dönem 1 öğrencilerimizle gerçekleştirdiğimiz PBL modülünün program değerlendirmesini yapmaktır.

Gereç ve Yöntemler: Eğitime 176 dönem 1 öğrencisi ve 16 PBL eğitmeni katılmıştır. Eğitim modülü, her gün 2 eğitim saati olmak üzere 3 ayrı günde tamamlanmıştır. Öğrencilere 16 soruluk bir ön test ve eğitim sonunda yine ön test sorularının aynısından oluşan bir son test uygulanmıştır. Verilerin analizi SPSS 25 programı ile gerçekleştirilmiştir. Verilerin normal dağılıma uygunlukları Shapiro-Wilk testi ile eğitim öncesi ve sonrası puanlar arasındaki değişim Wilcoxon testi ile incelenmiştir. Araştırmada tip I hata oranı 0,05 olarak alınmıştır. Eğitimden yaklaşık 4 hafta sonra iki tıp eğitimcisi ve 10 öğrenciden oluşan bir odak grup çalışması yapılmış ve görüşme kayda alınmıştır. Nitel verilerin değerlendirilmesi iki araştırmacı tarafından yapılmıştır. Yazıya dökülen metin tema ve alt temalara ayrılmıştır. Program Değerlendirme için Kirkpatrick ve Logic Model program değerlendirme modeli olarak kullanılmıştır.

Bulgular: Kirkpatrick 1. düzey değerlendirmeye göre hem anketler hem de odak grup çalışmasında eğitimden duyulan memnuniyet yüksek olarak bulunmuştur. Kirkpatrick 2. düzeye göre öğrencilerin ön test ve son testleri arasında anlamlı bir başarı artışı saptanmıştır (ön test ortalama: 7, son test ortalama: 12, $p<0,05$) Ayrıca öğrencilerin ortalama başarısı 39 puan üzerinden 35 olarak bulunmuştur. Logic model değerlendirmesi ile eğitimin girdileri (kaynakları), aktiviteleri, sonuçları, kısa, orta ve uzun vadeli hedefleri ortaya konulmuş ve kısa ve orta vadeli hedeflere ulaşıldığı saptanmıştır.

Sonuç: Program değerlendirmesi sonucunda dönem 1 öğrencileri ve eğitmenlerin PBL eğitiminden duydukları memnuniyetin yüksek olduğu ayrıca öğrencilerin PBL başarılarının da istenilen düzeyde olduğu saptanmıştır.

Anahtar Kelimeler: Probleme dayalı öğrenme, PDÖ, program değerlendirme, niteliksel araştırma

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Introduction

Program evaluation is the process of systematically collecting information about the structure and quality of an educational program. Program evaluation measures whether educational programs can achieve learning objectives. It is decided whether the training program will continue or not through program evaluation strategies (1). The most frequently used program evaluation models in medical education are the Kirkpatrick program evaluation model, Context, Input, Process, Product model, and logic model.

Problem-based learning (PBL) is a student-centered and structured learning method. This method was created to reduce the intensive information load in classical medical education and ensure that theoretical knowledge becomes more permanent. The most important feature of this method is that it allows vertical integration between basic and clinical medical sciences (2).

A clinical problem defined in PBL is transformed into a scenario. This scenario was discussed with a group of 7-8 students and a training facilitator. Students try to solve this clinical problem and diagnose the patient using their knowledge. They used brainstorming to discuss possible hypotheses. When their current knowledge could not explain the hypothesis, they reached their knowledge limit and set new learning goals.

They shared the new learning objectives that they had researched with the group in the next session (3,4). PBL originates from constructivist theory and has been associated with multiple intelligence theory (5,6).

Although research has shown that PBL is appreciated by students, no studies have examined the benefits of PBL using systematic program evaluation methods (1,3,5,6,7).

In this research, our aim is to evaluate the PBL training received by Hamidiye Medical Faculty first term students. For this purpose, we aim to make a more systematic evaluation using program evaluation models. Although program evaluation models are diverse, their use in educational research is not very common. Although some researchers have evaluated their PBL training, these evaluations were not based on a program evaluation method (1,7,8,9,10). In our study, we aimed to carry out the program evaluation of PBL education by using the

Kirkpatrick program evaluation model and the Logic evaluation model together. In this context, we believe that our study will contribute to the literature.

Material and Methods

Our PBL training, which we evaluated, was conducted by 176 first-term students at the Hamidiye Medical Faculty of Medicine and 16 faculty members. Before the training, 2 meetings were held with 16 trainers regarding the implementation of problem-based training. The students were divided into groups of 11 people. PBL groups consisting of an instructor and 11 students were created. Before the PBL scenario training, students were given a pretest designed to cover all scenario learning objectives (16 questions). After the students completed the PBL training, which consisted of approximately 2 hours and 3 separate sessions, they were given a posttest with the same questions as the pretest. In addition, at the end of the training, both the instructors and students were asked to evaluate by conducting a survey.

We used Kirkpatrick's 4-stage model and the logic model together in the program evaluation of our study. We evaluated whether students and instructors were satisfied with the training at the first level of Kirkpatrick through surveys and a focus group qualitative study we conducted with the students at the end of the training.We evaluated educational success at the Kirkpatrick 2nd level using the difference between the pre- and post-tests and the model form in which the instructors evaluated the students. Using the logical model, we evaluated the inputs/resources of education, the activities carried out during education, the outputs of education and the short, medium and long-term outcomes of these outputs.

The focus group method was used for the qualitative part of the study. Ten first-year students and 2 qualitative researchers participated in the focus group study. Verbal permission was obtained from the students for the focus group meeting, and brief information was provided about the focus group study. The answers given to the semi-structured questions prepared by the trainers with the support of the literature were recorded. The interviews lasted about 45-50 minutes. At the end of the focus group discussion, the recordings were transcribed on the same day. The themes and subthemes related to the content were determined by two medical evaluators. Ethics Committee approval was obtained from the University of Health Sciences Türkiye, Hamidiye Scientific Research Ethics Committee (approval number: 24/29, date: 19.01.2024).

Statistical Analysis

Data analysis was performed using IBM SPSS 25. The suitability of the data for normal distribution was examined using the Shapiro-Wilk test. For quantitative variables, median, minimum, and maximum values are presented. The changes in test scores before and after training were examined using the Wilcoxon test. In this study, the type I error rate was 0.05 ($p<0.05$). Exploratory factor analysis was assessed using Kaiser Meyer Olkin (KMO) and Bartlett's test, confirmatory factor analysis using Root Mean Square Error

of Approximation (RMSEA), and reliability using Cronbach's alpha.

Thematic analysis was used to analyze qualitative data. The interview records transcribed after the focus group meeting were arranged and tabulated by removing themes and subthemes.

G Power (3.1.9.7) indicated that the power to detect small effects for the most complicated analyses (using effect size w=0.3, and desired power=0.95, alpha=0.05, two tailed; χ^2 tests -Goodness-of-fit tests: Contingency tables) would total n=172.

Results

According to student and instructor surveys in the Kirkpatrick level 1 evaluation, satisfaction with PBL was found to be at the desired level. The results of the 5-point Likert-type student PBL evaluation survey are presented in Table 1. The survey was completed by 119 of the 176 students who participated in the training. Fourty-seven of the students participating in the survey were female, and 72 were male. The average age of the students is 18.6±1.10 (15-24; median:18). The satisfaction survey of the PBL instructors is presented in Table 2. Eeleven out of the 16 instructors completed the survey. The verbal comments of the students and instructors are included at the end of both tables.

The answers received as a result of the focus group interview were shaped around 2 main themes. These are the positive aspects of the applied PBL and the aspects that require improvement. The main themes and subthemes are presented in Table 3. In the focus group interview, sentence

Table 1. Results of student PBL evaluation survey

I was informed about the structure of the PBL module, training content, and resources to be used
Strongly agree: 43.7, Agree: 43.7, Not sure: 8.4, Dissagree: 1.7, Strongly disagree: 2.5
The PBL module was well organized
Strongly agree: 73.1, Agree: 22.7, Not sure: 0, Dissagree: 3.4, Strongly disagree: 0.8
A positive studying atmosphere was created during the sessions
Strongly agree: 55.5, Agree: 39.5, No sure: 1.6, Dissagree: 0, Strongly disagree: 3.4
I understood the module learning objectives
Strongly agree: 42, Agree: 42.9, No sure: 9.2, Dissagree: 3.4, Strongly disagree: 2.5
Iwas able to actively participate in the discussions
Strongly agree: 52.9, Agree: 34.5, No sure: 6.7, Dissagree: 2.5, Strongly disagree: 3.4
I am encouraged to ask questions
Strongly agree: 42.9, Agree: 42, No sure: 9.2, Dissagree: 3.4, Strongly disagree: 2.5
The scenario met the learning objectives and guided me well
Strongly agree: 43.7, Agree: 44.5, No sure: 5.9, Dissagree: 2.5, Strongly disagree: 3.4
Easy access to educational resources
Strongly agree: 29.4, Agree: 41.2, No sure: 20.2, Dissagree: 5.8, Strongly disagree: 3.4
Most of the information requested in the scenario was related to my curriculum topics
Strongly agree: 42, Agree: 44.5, No sure: 5.9, Dissagree: 4.2, Strongly disagree: 3.4
The PBL module positively affected my personal development and motivation
Strongly agree: 50.4, Agree: 38.7, No sure: 6.7, Dissagree: 0.8, Strongly disagree: 3.4
How many points would you give to the module you applied (10 being the highest and 1 being the lowest)
Average score: 8.24
Please write down what you would like us to add
It was an excellent education The PBL should be increased It should have been included in the images along with the patient information There should have been a simpler disease in the scenario The educational environment could have been better organized I liked PBL more than the lecture material

*All numbers are percentages (%). PBL: Problem-based learning

Table 2. Results of instructor PBL evaluation survey
The PBL sessions were well organized
Strongly agree: 27, Agree: 36, Not sure: 18, Dissagree: 18, Strongly disagree: 0
The time management of the PBL sessions was successful
Strongly agree: 45, Agree: 36, Not sure: 9, Dissagree: 9, Strongly disagree: 0
Goals and learning objectives were achieved
Strongly agree: 73, Agree: 27, No sure: 0, Dissagree: 0, Strongly disagree: 0
All the students participated in discussions during the sessions
Strongly agree: 36, Agree: 55, No sure: 0, Dissagree: 9, Strongly disagree: 0
Students benefited from the resources and attended the sessions prepared
Strongly agree: 18, Agree: 27, No sure: 45, Dissagree: 0, Strongly disagree: 9
Students generally completed PBL successfully
Strongly agree: 73, Agree: 27, No sure: 0, Dissagree: 0, Strongly disagree: 0
Please write down what you would like us to add
The sessions were very fun and successful, but some students were unprepared An efficient educational strategy for students to develop positive behaviors and learn well Useful for communication, self-directed learning and permanent learning There were some problems with the physical environment. like sound insulation It is a very important goal for students to have close contact with faculty members Overall, very efficient I am satisfied with the student interest and participation
*All numbers are percentages (%). PBL: Problem-based learning

Table 3. Focus group interview results

Positive aspects of PBL	Aspects of PBL that require improvement
Positive effects on learning I experience low attention and motivation in lecture hall lessons. I did not experience these situations in the PBL. I felt like a doctor for the first time (P1) The script was very good. I was able to empathize with the patient in this scenario. Therefore, I think my knowledge is more permanent (P2) I believe we achieved more efficient education with faculty members thanks to small group work (P4) **Increasing the motivation to learn** PBL awakened a sense of curiosity in me. The lecture hall class was very monotonous; I had the chance to meet friends I had never met before (P3) It felt good to be able to make eye contact with our mentor and friends during the training (P5) **Direction to research** Thanks to PBL, my desire to pursue research increased. I better understood how to conduct research (P4) **Providing interactive education opportunities** I loved the interactive training; it was like a rehearsal for the work I will do in 6 years (P10) **Supporting self-learning** In PBL, we shape our own learning, which is very productive. We do not have this opportunity in lecture hall classes (P6)	**Difficulty accessing educational resources** I had difficulty accessing some of the educational resources. Therefore, I was not well prepared for some learning objectives (P7) While some teachers shared very detailed training resources, others did not. I needed more help with research (P5) **Organizational problems** There were problems with sound insulation in some classrooms. This sometimes prevented us from getting the results we wanted from the course (P7) I couldn't study very well because it coincided with my Summative exam. I wish the PBL time was not close to the exam (P9) PBL time seemed short to me, but the sessions were more productive than I thought. The duration of sessions can be increased (P6) The number of PBLs should be increased. The study time between PBL sessions should be increased (P8) **Increasing the attractiveness of scenarios** I think we should choose scenarios before training. Thus, it can arouse more curiosity (P2) I was not very motivated in the first session. The first session was not productive. I could not internalize the scenario (P9) **PBL scoring revision** I want the contribution of the PBL score to the summative exam to be increased. We worked with great pleasure and worked hard for the PBL. I think we deserved more points (P1)
PBL: Problem-based learning, P1,2,3,...: Participant 1,2,3,...	

samples from students were coded as participants 1,2,3... (P1,2,3...).

The scale was found to be highly reliable (Cronbach's alpha: 0.944) and valid (exploratory factor analysis, KMO: 0.926; and Bartlett's test: 973.602; confirmatory factor analysis, RMSE: 0.733).

According to the Kirkpatrick level 2 evaluation results, term 1 students received an average of 35 points out of 39 based on performance evaluations made in 3 separate PBL sessions. The overall success score was calculated as the median. Minimum and maximum scores are 5 and maximum score is 39. It was determined that there was a significant difference between the success scores of the students before and after the training and that the post-test scores were higher than the pre-test scores (p<0.001) (Table 4).

In the evaluation conducted using the logic model, the resources used for training, activities performed, program outputs, and results were examined (Table 5).

Discussion

Kirkpatrick level 1 evaluation measures satisfaction with PBL training. This evaluation was conducted through student and educator surveys and focus group studies. According to the survey results, the students stated that a positive educational atmosphere was created, and the modules were well organized. Similar to our study, AlHaqwi (11) emphasized the importance of educators in PBL at their two medical faculties. In their studies, the authors stated the importance of the trainer in training motivation and creating a friendly training environment (11). In a study where Akdogan et al. (12) expressed the opinions of students in PBL, they stated

Table 4. Term 1 students' pre- and post-test results

	Pre-test	Post-test	z-value	p-value
Achievement score	7 (3-13)	12 (7-16)	-9.993	<0.001*

*p<0

Table 5. Logic model evaluation

Inputs/Resources	Activities	Output	Outcomes
Sixteen instructors(faculty members)	Pre-training meetings approximately 2 hours	Twelve trainers attended the face-to-face meetings prior to training. An online meeting was held with 2 instructors	Modification of attitudes and perceptions
16 PBL hall	3 sessions x2 hours in total, and 6 hours of scenario training	The PBL training was conducted with 16 instructors and 176 first-term students	Acquisition of knowledge and skills
2 Educational secretaries	Post-training meetings approximately 1 hour	All instructors and two medical educators attended the face-to-face meetings after the training.Verbal feedback was received at the meeting	Behavioral change
1 manager responsible for organization	Student surveys for educational evaluations	119 of the 176 students answered the post-training survey	Changes inorganizational and educational practices
1 vice dean (responsible for undergraduate medical education)	Instructor survey for training evaluation	11 of the 16 instructors answered the post-training survey	Benefits to patients and relatives
Sufficient stationery	Focus group discussions to evaluate student satisfaction	A focus group interview was held with 10 randomly selected students. Two medical educators attended the meeting	
Various medical education scenarios	Reporting of training and presentation for program evaluation	The faculty member in charge of the PBL training program presented the PBL report to the faculty member in charge of the program evaluation	
2 medical educators responsible for educational organization	Evaluation meetings of managers and staff		
176 term 1 students			

PBL: Problem-based learning

that learning goals were easily achieved with a suitable scenario and the support of instructors. Similarly, in our study, the students stated that they actively participated in the discussions and easily achieved their learning goals. Trainers similarly expressed their satisfaction with the PBL training. However, instructors state that some students arrive to the modules without being sufficiently prepared and therefore cannot achieve their desired performances. Krasne et al. (13) also showed in their study that first-year medical students performed lower than third-year medical students, especially in terms of access to resources and effective educational preparation. Students emphasized important details in their verbal responses to the surveys and focus group discussions. Students say that they like PBL more than lecture halls, that their motivation increases, and that they learn to research. They also stated that with this training, they felt like a doctor for the first time and that they had taken on their own learning responsibilities. There are similar studies in the literature that support our findings. Nandi et al. (14), in their study comparing traditional medical education with PBL, showed that PBL supports self-learning and positively affects students' social skills and motivation. Lee et al. (15) showed that PBL prepared students more professionally for medicine, while Koh et al. (16) showed that it supported social and cognitive skills much better. In the focus group discussion, students mentioned some negative experiences. These are problems with the scenario and problems with the organization. Some students stated that directing students to resources was insufficient. After training, various arrangements were made regarding these problems. When the literature review reveals that there are similar organizational or scenario-related problems with PBL. In their longitudinal study, Okubo et al. (17) mentioned the positive features of PBL as well as organizational problems that can be observed during training. Musal et al. (1) obtained interesting results regarding PBL training that they evaluated through a focus group study. Musal et al. (1) expressed the negative aspects of PBL as problems related to the training hall and training materials.

Kirkpatrick's level 2 assessment evaluates student achievement. In our study, there was a significant increase in the pre- and post-tests, which consisted of the same questions for the students. Additionally, students were evaluated through a method that monitored their class participation, appropriate information gathering, and professional attitudes. In this evaluation, students received an average of 35 of 39 points. Qualitative and quantitative studies in the literature indicate that student success in PBL is high (7).

Evaluation using the logic model is important because it offers people a more systematic evaluation opportunity. In this study, we created a wide-ranging scale for the logic model evaluation. This scale consisted of resources, activities, outputs, and outcomes. Thanks to this table, potential deficiencies in the program can be understood more easily. In the literature, we did not find a program evaluation study that used the logic model in PBL. However, there are many logical model studies on medical education in the literature. Armstrong et al. (18) demonstrated that they achieved the expected outcomes in a logic model study in which they evaluated the success of their faculty development program they created. In this study, we detected positive behavioral improvements in the students at the end of the training. We can say that this is the most important output of the PBL. In surveys and focus group studies, we revealed that students feel that they are learning more effectively than in classical education. In addition, PBL is used by educators and students to develop social skills, improve motivation, and support self-learning. At the end of the evaluation, we made revisions to our training organization and PBL training. Rajashekaraet et al. (19) used the logic model in their studies showing whether 8 basic learning goals were achieved at the end of the training.

Conclusion

In our study, we believe that PBL is a useful training for both instructors and students in general and in many aspects, and we should increase the number of PBL trainings. It can be concluded that in the long term, physicians trained with this PBL training will be much more successful in communication, social accountability, and a positive approach to patient care.

Ethics

Ethics Committee Approval: Ethics Committee approval was obtained from the University of Health Sciences Türkiye, Hamidiye Scientific Research Ethics Committee (approval number: 24/29, date: 19.01.2024).

Informed Consent: Not required.

Foothotes

Authorship Contributions

Surgical and Medical Practices: S.M.A., E.Ç., H.E., Concept: S.M.A., H.E., S.P., Design: S.M.A., S.P., Data Collection or Processing: S.M.A., Analysis or Interpretation: S.M.A., E.Ç., H.E., Literature Search: S.M.A., Writing: S.M.A.

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REFERENCES

1. Musal B, Velipasaoğlu S, Özan S, Tımbıl S. The focus group studies carried out to determine students' opinions on pbl method within the context of program evaluation studies. TED. 2007;25:17-24. [Crossref]
2. Velipaşaoğlu S, Musal B. Probleme dayalı öğrenim süreci, işleyişi ve kazanımlarına ilişkin ölçek geliştirme çalışmaları. TED. 2017;16:5-28. [Crossref]
3. Bate E, Hommes J, Duvivier R, Taylor DC. Problem-based learning (PBL): getting the most out of your students-their roles and responsibilities: AMEE Guide No. 84. Med Teach. 2014;36:1-12. [Crossref]
4. Daley BJ, Torre DM. Concept maps in medical education: an analytical literature review. Med Educ. 2010;44:440-448. [Crossref]
5. Azer SA. Problem-based learning overview. Navigating problem-based learning. 1st ed, Marrickville, N.S.W: Elsevier Australia. 2008. [Crossref]
6. Dolmans DH, De Grave W, Wolfhagen IH, van der Vleuten CP. Problem-based learning: future challenges for educational practice and research. Med Educ. 2005;39:732-741. [Crossref]
7. Imanieh MH, Dehghani SM, Sobhani AR, Haghighat M. Evaluation of problem-based learning in medical students' education. J Adv Med Educ Prof. 2014;2:1-5. [Crossref]
8. Abraham RR, Ramnarayan K, George BM, Adiga I, Kumari GR, Suvarna N, et al. Effects of problem-based learning along with other active learning strategies on short-term learning outcomes of students in an Indian medical school. J. Allied Health Sci. 2012;1:98. [Crossref]
9. Dolmans DH, Schmidt HG. What drives the student in problem-based learning? Med Educ. 1994;28:372-380. [Crossref]
10. Moreno-López LA, Somacarrera-Pérez ML, Díaz-Rodríguez MM, Campo-Trapero J, Cano-Sánchez J. Problem-based learning versus lectures: comparison of academic results and time devoted by teachers in a course on Dentistry in Special Patients. Med Oral Patol Oral Cir Bucal. 2009;14:e583-e587. [Crossref]
11. AlHaqwi AI. Learning outcomes and tutoring in problem based-learning: how do undergraduate medical students perceive them? Int J Health Sci (Qassim). 2014;8:125-132. [Crossref]
12. Akdogan HD, Velipaşaoğlu S, Musal B. Problem-based learning: medical students' points of view TED. 2020;19:54-72. [Crossref]
13. Krasne S, Stevens CD, Wilkerson L. Improving medical literature sourcing by first-year medical students in problem-based learning: outcomes of early interventions. Acad Med. 2014;89:1069-1074. [Crossref]
14. Nandi PL, Chan JN, Chan CP, Chan P, Chan LP. Undergraduate medical education: comparison of problem-based learning and conventional teaching. Hong Kong Med J. 2000;6:301-306. [Crossref]
15. Lee M, Wimmers PF. Validation of a performance assessment instrument in problem-based learning tutorials using two cohorts of medical students. Adv Health Sci Educ Theory Pract. 2016;21:341-357. [Crossref]
16. Koh GC, Khoo HE, Wong ML, Koh D. The effects of problem-based learning during medical school on physician competency: a systematic review. CMAJ. 2008;178:34-41. [Crossref]
17. Okubo Y, Matsushita S, Takakuwa Y, Yoshioka T, Nitta K. Longitudinal PBL in undergraduate medical education develops lifelong-learning habits and clinical competencies in social aspects. Tohoku J Exp Med. 2016;238:65-74. [Crossref]
18. Armstrong EG, Barsion SJ. Using an outcomes-logic-model approach to evaluate a faculty development program for medical educators. Acad Med. 2006;81:483-488. [Crossref]
19. Rajashekara S, Naik AD, Campbell CM, Gregory ME, Rosen T, Engebretson A, et al. Using a logic model to design and evaluate a quality improvement leadership course. Acad Med. 2020;95:1201-1206. [Crossref]

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Early Transient Dysphagia in Acute Brain Stem Infarction

Akut Beyin Sapı İnfarktlarında Erken Geçici Disfaji

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ABSTRACT

Background: Electromyographical techniques are not used to investigate early transient dysphagia in stroke patients with brainstem infarction (BSI). This study aimed to employ electrophysiological methods to determine the presence of swallowing difficulties and the underlying pathophysiology of dysphagia in patients who have experienced an acute brainstem stroke.

Materials and Methods: This prospective study included 20 age-matched healthy individuals and 53 patients with BSI who experienced stroke within nine days of each other. Electrophysiological techniques, including dysphagia limit (DL) and sequential water swallowing (SWS) tests, were employed.

Results: Clinical dysphagia was observed in 21.0% of patients with BSI. Dysphagia, as determined by DL and SWS tests, was present in 52.7% of patients. Patients with cerebellar and medullary infarctions exhibited more severe dysphagia. Subclinical dysphagia was found in 54.7% of patients. Within 4 weeks, two-thirds of patients regained their ability to swallow, while one-third remained dysphagic.

Conclusion: Dysphagia is a severe symptom complex that can be fatal in a significant proportion of stroke cases. This study examined the electrical anomalies associated with swallowing in patients with acute BSI and explored the possible pathophysiological mechanisms underlying swallowing disorders caused by brainstem stroke. The electrophysiological techniques demonstrated in this study are quick, simple to use, noninvasive, and safe for patients, making them valuable for identifying subclinical dysphagia.

Keywords: Brainstem stroke, swallowing tests, electrophysiological methods, sequential water swallowing test, clinical dysphagia

ÖZ

Amaç: Bugüne kadar, beyin sapı infarktı (BSI) olan felçli hastalarda erken geçici disfajiyi araştırmak için elektromiyografik teknikler kullanılmamıştır. Bu çalışma, akut beyin sapı infarktı geçirmiş hastalarda yutma güçlüğünün varlığını ve disfajinin altta yatan patofizyolojisini belirlemek için elektrofizyolojik yöntemler kullanmayı amaçlamaktadır.

Gereç ve Yöntemler: Bu prospektif çalışmaya, yaş uyumlu 20 sağlıklı birey ve dokuz gün içinde inme geçiren beyin sapı enfarktüsü (BSI) olan 53 hasta dahil edildi. Disfaji limiti (DL) ve ardışık su yutma (SWS) testlerini içeren elektrofizyolojik teknikler kullanıldı.

Bulgular: Hastaların %21'inde klinik disfaji gözlendi. DL ve SWS testleri ile belirlenen disfaji, hastaların %52,7'sinde mevcuttu. Serebellar ve medüller enfarktüsü olanlarda daha şiddetli disfaji görüldü. Hastaların %54,7'sinde subklinik disfaji saptandı. Dört hafta içinde hastaların üçte ikisi yutma yeteneğini yeniden kazandı, üçte birinde disfaji devam etti.

Sonuç: Disfaji, inme olgularının önemli bir kısmında ölümcül olabilen ciddi bir semptom kompleksidir. Bu çalışma, akut beyin sapı infarktlı hastalarda yutmayla ilişkili elektriksel anomalileri incelemekte ve beyin sapı infarktının neden olduğu yutma bozukluğunun altında yatan olası patofizyolojik süreçleri araştırmaktadır. Bu çalışmada gösterilen elektrofizyolojik teknikler hızlıdır, kullanımı basittir, invaziv değildir ve hastalar için güvenlidir; bu da onları subklinik disfajiyi tanımlamada değerli kılar.

Anahtar Kelimeler: Beyin sapı infarktı, yutma testleri, elektrofizyolojik yöntemler, ardışık su yutma testi, klinik disfaji

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Introduction

Dysphagia is a recognized complication of both acute and hemorrhagic stroke, with 37.0-78.0% of patients with acute stroke experiencing difficulties in swallowing (1). The prevalence of dysphagia varies depending on the timing and method of evaluation (2). It is more common in patients with acute stroke than in those often presumed to have the condition, even when they do not exhibit apparent symptoms related to deglutition. Aspiration pneumonia, with an incidence ranging from 13.0% to 33.0%, is more common among stroke patients with dysphagia (3,4,5). Impaired swallowing is associated with a three-fold increase in mortality risk, primarily due to pneumonia (6). Early identification of dysphagia in patients with acute stroke significantly reduces the risk of aspiration pneumonia, a potentially fatal but preventable complication (7). Although dysphagia often resolves within a few days to a week after stroke (8), studying the early physiological changes in oropharyngeal swallowing is crucial for early diagnosis using bedside examinations and noninvasive screening methods (7,9,10). Nevertheless, 2-12% of stroke patients continue to experience dysphagia in the first month, and 7% may still struggle with swallowing 3 months after the stroke (11,12,13,14). Mild dysphagia is observed in nearly all patients with stroke (15). The stroke region plays a significant role in the prevalence of dysphagia, with dysphagia being highly prevalent in patients with carotid artery involvement (8). Approximately 25% of strokes are caused by brainstem lesions, of which dysphagia is a frequent consequence (16). In brainstem stroke (BSS) patients, dysphagia tends to be more severe and less likely to resolve spontaneously compared with those with hemispheric stroke. Although lateral medullary infarction (LMI) has been studied in relation to dysphagia, few studies have explored dysphagia in other brainstem regions (17,18). This study aimed to investigate voluntary swallowing in patients with acute BSS using electrophysiological techniques to identify the pathophysiological changes associated with neurogenic oropharyngeal dysphagia, to elucidate the spectrum and prevalence of both subclinical (acute transient dysphagia) and overt dysphagia in relation to the involvement of various brainstem regions, and to determine whether acute temporary dysphagia, as identified through clinical procedures, resolves within a week or persists beyond hospital discharge.

Materials and Methods

We examined 53 patients (34 males, 19 females) with brainstem infarction (BSI) affecting unilateral regions. The mean age of the patient sample was 64.9 years (range 37-84). This study included patients presenting to our Neurology department with an acute first stroke occurring between 1 and 9 days before presentation (mean duration five days). All patients were conscious and medically stable. We categorized patients into the following three groups:

Group A: Patients without signs or symptoms related to swallowing since stroke onset.

Group B: Patients with dysphagic complaints and symptoms from stroke onset that were completely resolved by hospital discharge.

Group C: Patients with clinical dysphagia observed at stroke onset that persisted until hospital discharge.

Groups A and B remained hospitalized for 3 weeks, whereas group C was discharged after 4 weeks. Patients who were confused or comatose were excluded. We also included 20 healthy volunteers (18 females, 2 males) without neurological, cardiovascular, cerebrovascular, or oropharyngeal disorders as a control group. The mean age of the control group was 63.9 years (range 56-75). All control subjects were selected from hospital staff and underwent normal neurogenic examinations. We performed a neurological evaluation of each patient to confirm the stroke diagnosis, clinical syndrome, pathological subtype, and functional effects using the Functional Independence Measurement score and the Level of Cognitive Functioning score.

Magnetic resonance imaging was used consistently to confirm stroke diagnosis, examine lesion location, and identify stroke type (ischemic or hemorrhagic). Enrollment was limited to patients with acute BSI. At admission, clinical and biochemical markers were assessed to evaluate dietary and hemodynamic conditions. A detailed neurological examination of the face, tongue, mouth, pharynx, and larynx was performed for each patient, and the patients were thoroughly questioned regarding dysphagia and aspiration. Within 2 days of hospitalization, a neurologist conducted a clinical bedside test to evaluate swallowing abnormalities. Dysphagia severity (DD) was ranked as follows (19):

Grade I (DD-I): No clinical or reported dysphagia.

Grade II (DD-II): The patient did not report dysphagia, but clinical examination revealed very mild dysphagia, including inappropriate voluntary cough and dysarthria.

Grade III (DD-III): The patient reported dysphagia but managed swallowing with non-oral feeding. Additional clinical indications included wet voice, cough during trial swallows, and dysphonia.

Grade IV (DD-IV): Evident clinical dysphagia requiring non-oral feeding and associated with aspiration.

Assessment of Voluntary Swallowing Electrophysiologically

Patients were instructed to sit in a chair and maintain an upright, neutral head position throughout the examination. Surface silver chloride electrodes were placed on both sides of the midline under the chin at a distance of 1 cm to record the activity of the submental muscle (SM) complex, including the mylohyoid, geniohyoid, and anterior digastricus muscles. Activities were recorded using a four-channel electromyograph (EMG) instrument (Nicolet Viking-V11.0). The analysis duration was 20 s. After filtering (100 Hz to 10 kHz), the signals were amplified, rectified, and integrated. Concurrently, a respiratory signal was acquired using a nasal cannula (Sleep Sense SLP Tel Aviv Israel) placed at the nasal entrance and linked to an airflow sensor transducer. The two EMG channels were connected to the breathing sensor output. The direction of the airflow was recorded using positive and negative polarities for expiration and inspiration, respectively. For respiratory recordings, EMG filters were set at a bandpass frequency of 0.2-30 Hz. The entire analysis time was 20 s.

Simultaneously, electrocardiogram data were captured using silver chloride cup electrodes, with one electrode positioned on the second left intercostal region and the other on the dorsum of the hand. The signals were amplified and filtered (band pass 0.2 Hz to 30 Hz).

Dysphagia Limit (DL)

The DL technique was previously described (19). This study employed the same electrophysiological methods to investigate the "DL", which is sensitive and specific for tracking neurogenic dysphagia. The DL is based on the physiological phenomenon where an oral bolus of a large liquid volume is split into two or more portions and effectively swallowed. Normally, individuals can swallow a 20 mL bolus of water in a single swallow. However, those with reduced swallowing ability may require two or more swallows for a bolus of less than 20 mL, referred to as piecemeal deglutition. Piecemeal deglutition at a volume of 20 mL is considered abnormal and indicates dysphagia. The DL is the volume of water below 20 mL at which piecemeal deglutition occurs. Electrophysiological recordings can detect swallowing difficulties of various etiologies.

Participants received 3, 5, 10, 15, and 20 mL of water in steps. The examiner instructed the subjects to immediately swallow each bolus. A graduated syringe was used to progressively deliver water into the mouth behind the incisors; swallows were initiated with water on the tongue and the tip of the tongue touching the upper incisors. Rapid rearward-directed water delivery was avoided to prevent the early escape of water flow to the pharynx and possible gag response. At the examiner's command, oscilloscopic traces were initiated for swallowing. If piecemeal deglutition or any indication of subglottic aspiration (e.g., wet voice or coughing) was observed, the examination was halted. The subjects were asked to speak between each test. If fragmented deglutition was suspected, the process was repeated and documented using the same volume of water. The term "normal DL" refers to piecemeal deglutition occurring in healthy individuals when swallowing at or above a water volume of 20 mL. Otherwise, a water volume of 20 mL was considered abnormal (21) (Figure 1).

Sequential Water-Swallowing (SWS)

All patients and control group members underwent the "SWS" test as previously described (22,23). Participants were instructed to sip 50 mL of water continuously from a cup as they would in daily life. The water temperature was 25°C. EMG traces appeared on the screen for a few seconds before the start command for SWS was given. The analysis took 20s. Each subject completed three repetitions of the SWS test, with the third trial being considered the most accurate measurement. The following variables were recorded:

Number of swallows occurring while drinking water.
Total time spent drinking 50 mL of water continuously.
Total duration of apnea during the 50 mL SWS.

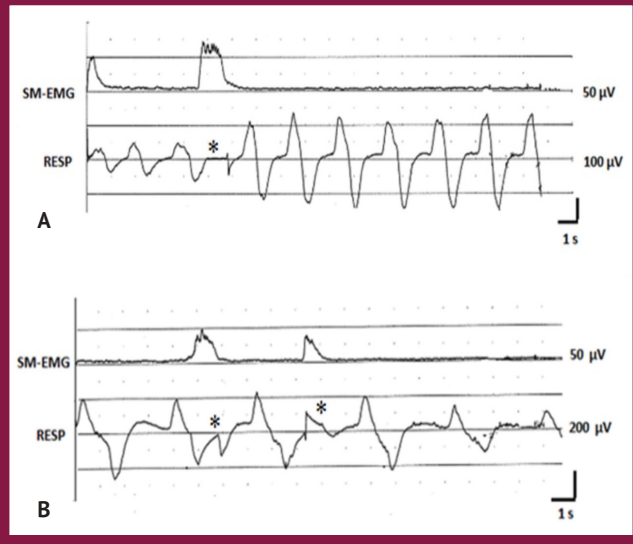

Figure 1. A) Five milliliters of water swallowed by a patient with mesencephalic infarction. B) DL of 5 mL discrete swallows in a patient with pontin infarction who swallowed water twice in a short interval
**Apnea during water swallowing, DL: Dysphagia limit, SM: Submental muscle, EMG: Electromyograph, RESP: Respiration*

During SWS, the number of swallows was determined by counting the periodic motions of the SM-EMG. The total duration of SWS was calculated from the start of the first swallow burst at the end of the final swallow burst using SM-EMG traces. The swallowing apnea duration was measured at the end of the previous respiratory cycle until the reappearance of the first respiratory cycle. Patients provided written informed consent, and the study was approved by the institutional research ethics review board. The study was approved by the İzmir Kâtip Çelebi University Faculty of Medicine Clinical Research Ethics Committee (approval number: 75, date: 07.05.2014).

Statistical Analysis

Descriptive summary statistics were reported as mean ± SD, minimum, and maximum, depending on data distribution. Categorical variables were assessed using chi-square tests and Fisher's exact test. Groups were compared using Kruskal-Wallis and Mann-Whitney U tests for continuous variables, depending on the data distribution. Post hoc comparison testing was completed using Bonferroni correction. All analyses were two-tailed, and significance was set at 5%. The statistical analysis was conducted using SPSS 15.0 for Windows.

Results

Imaging analyses confirmed that all patients had ischemic stroke and no prior cerebrovascular disease. Among the 53 patients, 30 (56.6%) had pontine infarcts, 13 (24.6%) medullary infarcts (7 lateral, 6 medial), 5 (9.4%) mesencephalic infarcts, and 5 (9.4%) cerebellar infarcts. Of the 53 BSS patients, 11 (21%) exhibited clinical dysphagia, with infarcts located in the medulla oblongata (6), pons (4), and cerebellum (1). The remaining 42 (79%) BSS patients reported no difficulty swallowing.

DL

The DL was >20 mL of water in all normal subjects, whereas it was definitively pathological and 20 mL in 5 of 11 (45%) BSS patients with Grade II clinical dysphagia (ranging from 3-15 mL of water). Forty-two patients (79%) were clinically non-dysphagic, but a pathological DL was recorded in 15 of these 42 patients (35.7%), indicating subclinical dysphagia, with DL values ranging between 1 and 20 mL. Overall, among the 53 patients with and without clinical swallowing complaints, a total of 20 patients (37.7%) demonstrated pathological DL. The highest prevalence of pathological DL was observed in patients with cerebellar infarction (3 out of 5 patients), followed by those with medullary infarction (5 out of 13 patients) and pontine infarction (10 out of 30 patients).

SWS

The total duration of swallowing ($p<0.001$), swallowing apnea ($p<0.001$), and the number of swallows ($p<0.05$) were significantly prolonged in all BSS patients compared with the normal subjects (Table 1). Figure 2 illustrate the SWS values in patients with pontine infarction and healthy subjects. The duration of swallowing was significantly longer in patients with pontine infarcts than in other brainstem locations ($p<0.05$). Similarly, the duration of swallowing apnea was significantly prolonged in patients with pontine infarction ($p<0.05$). Although the duration of swallowing apnea was longer in subjects with other brainstem involvements than in healthy subjects, the correlation did not reach a significant level. The total number of swallows did not significantly differ between patients with BSS and healthy subjects (Table 2).

During the 50 mL SWS, two healthy participants (10%) demonstrated compensatory respiration cycles (CRC), particularly between the last successive swallow intervals of SWS. CRCs were recorded in 27 patients (52.9%) and observed more than once, appearing not only during the last inter-swallow interval but also during the middle inter-swallow interval of SWS. Figure 3 illustrates CRC in a patient with medial medullary infarction (MMI). In patients with BSS, subclinical dysphagia was frequently observed in the SWS test. Increased duration of swallowing time,

Table 1. Comparison of the total duration of swallowing, swallowing apnea, and number of swallows in all BSS patients and normal subjects

		Mean± SD	Minimum	Maximum	p-value
Total swallowing duration	Normalsubjects	6.91±1.36	4.2	9.5	**p<0.001**
	Patients	10.24±3.37	4.5	17	
Swallowingapnea	Normal subjects	6.89±1.49	3.8	9.5	**p<0.001**
	Patients	8.97±3.31	3.5	16	
Number of swallows	Normal subjects	5.00±0.97	4	7	**p<0.05**
	Patients	5.86±2.16	3	12	

BSS: Brainstem stroke, SD: Standard deviation

swallow apnea, increased CRC, and to a lesser extent, an increased number of swallows were found in 21 patients (50%) without clinical dysphagia. When the pathological values of the electrophysiological tests (either DL, SWS, or both) were calculated for the clinically normal patients (42 patients), 23 out of 42 BSS patients (54.7%) presented with subclinical dysphagia (Figure 4A).

Conversely, in the 11 patients with BSS, clinical dysphagia was evident at the onset of the stroke. However, four of these patients showed clinical improvement in the end of their hospital stay. Furthermore, three patients were found to be electrophysiologically normal despite mild clinical symptoms related to oropharyngeal dysphagia. The last patient, who was electrophysiologically pathologically diagnosed with dysphagia, demonstrated recovery both clinically and electrophysiologically upon a second examination (Figure 4B).

The remaining seven patients were clinically dysphagic from onset until hospital discharge. Four of these patients were also electrophysiologically dysphagic (one with pontine, two with medullary, and one with cerebellar infarction). Three other patients with medullary infarction were clinically dysphagic, but their electrophysiological test results were within normal limits. Figure 5 illustrates the clinical course of dysphagia in these three groups of patients.

In summary, when comparing all individual pathological findings between patients with BSI and healthy subjects, clinical assessment revealed dysphagia in 21.5% of patients, pathological DL in 37.7%, and SWS abnormalities in 49%. When combining the electrophysiological findings (DL+SWS) for all patients, 52.7% of the BSI patients investigated in the first week had pathological results.

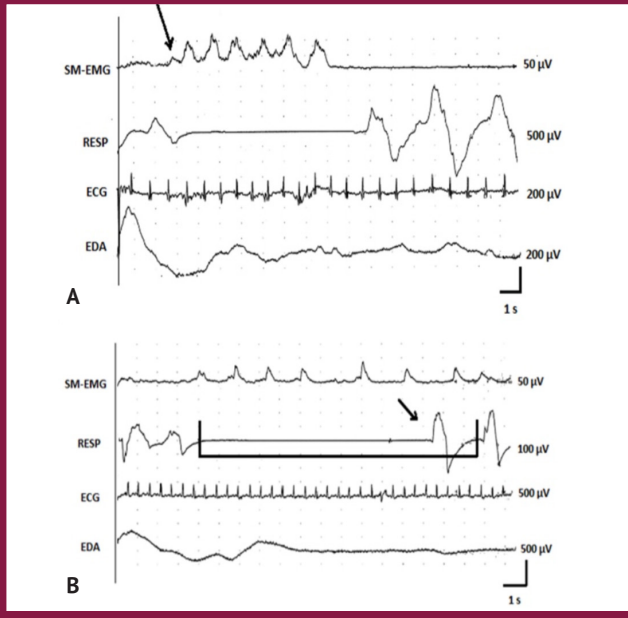

Figure 2. A) The total duration of swallowing, swallowing apnea, and the number of swallows were prolonged in a normal subject and the "foreburst" occured before the apnea interval in the same patient.B) The duration of apnea was significantly prolonged in a patient with pontine infarction who also demonstrated a compensatory respirator cycle
SM: Submental muscle, EMG: Electromyograph, ECG: Electrocardiogram, RESP: Respiration, EDA: Electrodermal activity

Table 2. Comparison of the total duration of swallowing, swallowing apnea, and number of swallows among all BSS patients

50 mL SWS	Group	Mean± SD	Minimum	Maximum	p-value
Total swallowing duration	Pons	11.27±3.49	5	17	**0.042[a]**
	Mesencephalon	8.90±2.88	6	12	
	Bulbus	8.65±2.80	4.5	13,5	
	Cerebellum	8.86±2.51	6.3	12	
Swallowing apnea	Pons	9.94±3.45	4	16	**0.031[b]**
	Mesencephalon	6.80±2.77	3.5	9.5	
	Bulbus	8.11±2.85	5	13.5	
	Cerebellum	7.20±1.96	5.5	10	
Number of swallows	Pons	6.34±2.18	4	12	**0.201[c]**
	Mesencephalon	4.80±1.79	3	7	
	Bulbus	5.36±2.50	3	11	
	Cerebellum	5.20±0.84	4	6	

[a]p (pons vs. bulbus)=0.02; [b]p (pons vs. mesencephalon)=0.046; [c]p (pons vs. mesencephalon)=0.041, BSS: Brainstem stroke, SD: Standard deviation, SWS: Sequential water swallowing

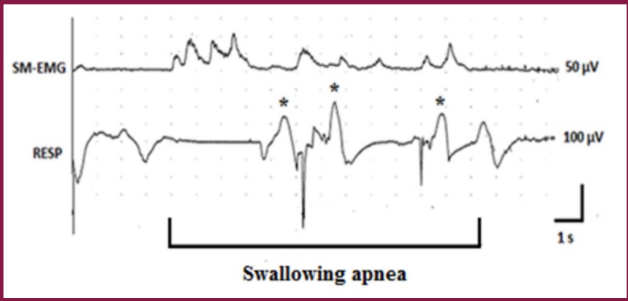

Figure 3. Compensatory respirator cycles (*) in a patient with medial medullary infarction
SM: Submental muscle, EMG: Electromyograph, RESP: Respiration

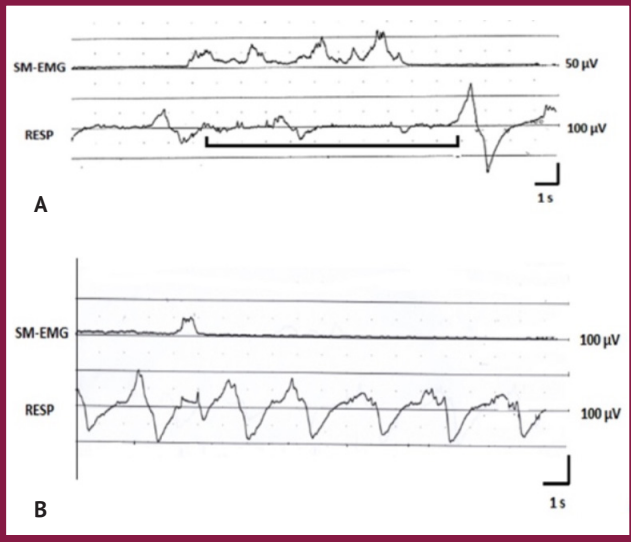

Figure 4. A) DL in 10 mL discrete swallow and prolonged apnea duration in a patient with pontine infarction. B) The second examination showed that the patient had recovered both clinically and electrophysiologically
DL: Dysphagia limit, SM: Submental muscle, EMG: Electromyograph, RESP: Respiration

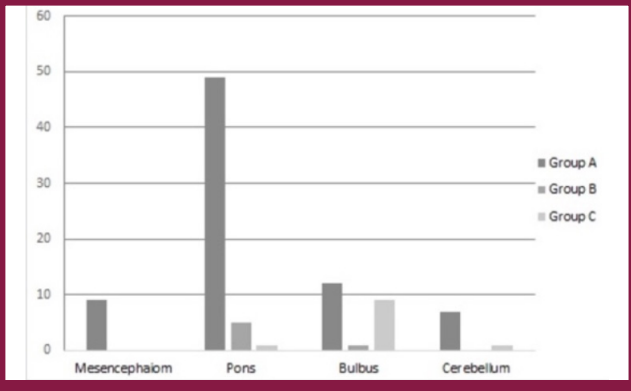

Figure 5. Clinical course of dysphagia in three groups of patients

Discussion

This study primarily aimed to investigate the incidence and characteristics of dysphagia in patients with acute BSS using electrophysiological techniques. Our findings indicate that even in patients with mild-to-moderate BSS, there is a high incidence of dysphagia that can be detected using straightforward and secure electrophysiological methods. Notably, more than half of the patients exhibited subclinical or mild dysphagia by the ninth day after stroke onset, highlighting the sensitivity of these techniques in the early detection of concealed swallowing issues.

Dysphagia is a significant concern in stroke patients, particularly because it occurs in approximately 50% of ischemic stroke cases (9). Early detection of dysphagia is crucial for reducing the risk of aspiration-related complications, such as pneumonia, which underscores the need for diligent bedside examinations and simple screening tests (6,7,8,10). In recent studies, it was stated that delayed dysphagia adversely affects the improvement of dysphagia in patients with stroke and needs to be identified early (11). Our study contributes to this body of knowledge by demonstrating that neurophysiological methods, specifically the DL and SWS tests, are effective tools for identifying both clinical and subclinical dysphagia in patients with BSS. The severity of dysphagia in patients with stroke varies depending on the location of the infarct. Our findings showed that although dysphagic symptoms are minimal in cases of mesencephalic infarction, they are significantly more severe in patients with pontobulbar involvement. This can be attributed to the impact on critical swallowing centers and networks, such as the central pattern generator (CPG), nucleus tractus solitarii, and nucleus ambigus (24,25). In contrast, neurogenic oropharyngeal dysphagia is less frequent and less severe in hemispheric strokes, likely due to early neuroplasticity in the non-affected hemisphere that aids recovery (26).

The exact nature of transient dysphagia in BSS remains unclear. However, in LMI, early-stage regional disconnection between two swallowing networks may result in severe pharyngeal dysphagia, similar to chronic Wallenberg syndrome (27,28). Dysphagia in LMI is more common in patients with rostral lesions, with cortical connections potentially aiding neuroplasticity (29). Our study found a higher incidence of dysphagia in patients with LMI (71%) than in those with MMI cases (33%). However, due to the small sample size of patients with medullary infarction, our electrophysiological findings did not show significant differences in the oropharyngeal effects between MMI and LMI.

Both LMI and MMI cases often exhibited abnormalities in DL and SWS, with only one normal case in each group (6 out of 7 vs. 5 out of 6 pathological). A high incidence of subclinical or mild dysphagia is expected given the involvement of the swallowing CPG in the lateral medullary region and the corticobulbar and corticospinal tracts in the medial medullary region. Pontine infarction was the most common in our patient group (56% of all cases), with all cases being unilateral. Severe clinical dysphagia, like quadriparesis, is observed in patients with bilateral pontine infarcts (28). In contrast, our pontine cases were clinically mild but still showed signs of dysphagia, particularly the prolonged duration of swallowing 50 mL of water during SWS. This is likely due to the involvement of the pontobulbar trigeminal system, especially if oropharyngeal input to the pontobulbar trigeminal afferent pathway is compromised. Sensory input to the pontobulbar area comes from the vagal, glossopharyngeal, and trigeminal-maxillary nerves, which innervate the oropharyngeal muscles. Any sensory impairment in this system may lead to dysphagia and aspiration (30,31). Thus, in pontine infarction, the trigeminal system may be partially damaged. Additionally, unilateral facial paresis in some pontine lesions can modestly contribute to dysphagia (32). Abnormal conduction in the afferent and efferent swallowing pathways, rather than a core anomaly in the medullary CPG, is likely responsible for early transient dysphagia, particularly in patients with pontine infarction.

It was surprising to find a high number of swallowing problems in cerebellar infarction despite the few cases. Oropharyngeal dysphagia is rarely observed in chronic neurological disorders with severe cerebellar syndrome. However, in this study, cerebellar infarction may have distended and compressed the lower brainstem structures related to deglutition, or the inferior cerebellar peduncle (corpus restiform), which is anatomically connected to the lateral medullary region, may have been involved. The early transient dysphagia observed in cerebellar infarction cases could be attributed to the indirect involvement of the CPG in the medullary region. Neuroimaging studies have shown that experimentally induced swallowing in healthy individuals can produce hyperdense fields within the cerebellum (33). Early transient dysphagia in patients with BSS can be explained by the data obtained from the DL. If a patient has overt or silent dysphagia, they cannot swallow water volumes above the 20 mL bolus and must resort to piecemeal deglutition with less than 20 mL of water. In our cohort, this type of defective swallowing was detected in approximately 39% of all patients investigated.

Piecemeal deglutition is essentially a compensatory and protective mechanism for oropharyngeal swallowing. However, it also indicates subclinical and clinical dysphagia in neurological patients, even in the absence of clinical complaints, as reported previously (20,34). Finally, DL has been recognized as a reliable, non-invasive quantitative test with high sensitivity (92%) and specificity (91%) for detecting and monitoring both clinical and subclinical dysphagia (20). Thus, in our study, early transient dysphagia appeared to be a benign process; while patients may be clinically non-dysphagic, the DL can still indicate previous dysphagia states after the "overt dysphagia" days have passed. As a more recent screening test, SWS offers a physiological approach to diagnosing dysphagia, making it a valuable tool. In our study, 49% of BSS patients exhibited clear abnormalities in the 50 mL SWS test, with a significant increase in the duration of swallowing and swallowing apnea compared with age-matched controls. Patients also showed a change in the regularity and rhythmicity of their swallowing pattern, often resulting in an irregular, arrhythmic pattern. Such abnormalities, which were previously reported in the literature, suggest that the brainstem CPG is involved in arrhythmic swallowing and compensatory respiration (23,35). The impaired regularity of the swallowing pattern, coupled with compensatory respiration, further supports the notion that early transient dysphagia in BSS patients may be linked to CPG dysfunction. Given the high incidence of early transient dysphagia, which is detected in 52.7% of BSS patients, combining electrophysiological methods for comprehensive evaluation. These non-invasive, simple-to-apply techniques are especially suited for use in acute stroke patients and can be employed in various clinical settings, including intensive care. Any detected electrophysiological abnormality should prompt close monitoring of the patient in the subsequent days and months.

This study has several limitations that should be considered when interpreting the results. First, the sample size, particularly for patients with specific types of BSIs, such as medullary infarction, was relatively small, which may limit the generalizability of our findings. Additionally, although the electrophysiological methods used in this study are non-invasive and straightforward, they may not fully capture the complexity of dysphagia, especially in patients with subtle or transient symptoms. Furthermore, the cross-sectional study design did not allow for the assessment of long-term outcomes related to dysphagia in these patients. Future studies with larger sample sizes and longitudinal follow-up are needed to confirm these findings and to provide a more comprehensive understanding of dysphagia in stroke patients.

Study Limitations

The small sample size and the small number of male patients are the limitations of our study.

Conclusion

In conclusion, this study highlights the importance of early detection and monitoring of dysphagia in patients with acute BSS. The use of electrophysiological methods, such as DL and SWS, is a sensitive and reliable method for identifying both clinical and subclinical dysphagia, even in patients with mild to moderate BSS. The high incidence of dysphagia detected in this study underscores the need for diligent screening and follow-up in this patient population to prevent complications such as aspiration pneumonia. Given the simplicity and non-invasive nature of these methods, they can be effectively employed in both acute and chronic care settings. Further research is warranted to explore the long-term impact of these findings and to refine the use of electrophysiological techniques in the management of dysphagia in stroke patients.

Ethics

Ethics Committee Approval: The study was approved by the İzmir Kâtip Çelebi University Faculty of Medicine Clinical Research Ethics Committee (approval number: 75, date: 07.05.2014).

Informed Consent: Patients provided written informed consent.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: N.G.B., Concept: N.G.B., Y.B., Ş.A., N.G., T.K.İ., Design: N.G.B., Y.B., Ş.A., Data Collection or Processing: N.G.B., Ş.A., Analysis or Interpretation: N.G.B., N.G., T.K.İ., Literature Search: N.G.B., Writing: N.G.B.

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REFERENCES

1. Martino R, Foley N, Bhogal S, Diamant N, Speechley M, Teasell R. Dysphagia after stroke: incidence, diagnosis, and pulmonary complications. Stroke. 2005;36:2756-2763. [Crossref]
2. Edmiaston J, Connor LT, Steger-May K, Ford AL. A simple bedside stroke dysphagia screen, validated against videofluoroscopy, detects dysphagia and aspiration with high sensitivity. J Stroke Cerebrovasc Dis. 2014;23:712-716. [Crossref]
3. Falsetti P, Acciai C, Palilla R, Bosi M, Carpinteri F, Zingarelli A, et al. Oropharyngeal dysphagia after stroke: incidence, diagnosis, and clinical predictors in patients admitted to a neurorehabilitation unit. J Stroke Cerebrovasc Dis. 2009;18:329-335. [Crossref]
4. Langdon PC, Lee AH, Binns CW. Dysphagia in acute ischaemic stroke: severity, recovery and relationship to stroke subtype. J Clin Neurosci. 2007;14:630-634. [Crossref]
5. Smithard DG, Smeeton NC, Wolfe CD. Long-term outcome after stroke: does dysphagia matter? Age Ageing. 2007;36:90-94. [Crossref]
6. Donovan NJ, Daniels SK, Edmiaston J, Weinhardt J, Summers D, Mitchell PH, et al. Dysphagia screening: state of the art: invitational conference proceeding from the State-of-the-Art Nursing Symposium, International Stroke Conference 2012. Stroke. 2013;44:24-31. [Crossref]
7. Sørensen RT, Rasmussen RS, Overgaard K, Lerche A, Johansen AM, Lindhardt T. Dysphagia screening and intensified oral hygiene reduce pneumonia after stroke. J Neurosci Nurs. 2013;45:139-146. [Crossref]
8. Okubo PC, Fábio SR, Domenis DR, Takayanagui OM. Using the National Institute of Health Stroke Scale to predict dysphagia in acute ischemic stroke. Cerebrovasc Dis. 2012;33:501-507. [Crossref]
9. Galovic M, Leisi N, Müller M, Weber J, Abela E, Kägi G, et al. Lesion location predicts transient and extended risk of aspiration after supratentorial ischemic stroke. Stroke. 2013;44:2760-2767. [Crossref]
10. Ickenstein GW, Riecker A, Höhlig C, Müller R, Becker U, Reichmann H, et al. Pneumonia and in-hospital mortality in the context of neurogenic oropharyngeal dysphagia (NOD) in stroke and anew NOD step-wise concept. J Neurol. 2010;257:1492-1499. [Crossref]
11. Shimizu A, Fujishima I, Maeda K, Murotani K, Ohno T, Nomoto A, et al. Delayed dysphagia may be sarcopenic dysphagia in patients after stroke. J Am Med Dir Assoc. 2021;22:2527-2533. [Crossref]
12. Barer DH. The natural history and functional consequences ofdysphagiaafter hemispheric stroke. J Neurol Neurosurg Psychiatry. 1989;52:236-241. [Crossref]
13. Teasell RW, Bach D, McRae M. Prevalence and recovery of aspiration poststroke: a retrospective analysis. Dysphagia. 1994;9:35-39. [Crossref]
14. Kidd D, Lawson J, Nesbitt R, MacMahon J. The natural history and clinical consequences of aspiration in acute stroke. QJM. 1995;88:409-413. [Crossref]
15. Mann G, Hankey GJ, Cameron D. Swallowing disorders following acute stroke: prevalence and diagnostic accuracy. Cerebrovasc Dis. 2000;10:380-386. [Crossref]
16. Kruger E, Teasell R, Salter K, Foley N, Hellings C. The rehabilitation of patients recovering from brainstem strokes: case studies and clinical considerations. Top Stroke Rehabil. 2007;14:56-64. [Crossref]
17. Teasell R, Foley N, Doherty T, Finestone H. Clinical characteristics of patients with brainstem strokes admitted to a rehabilitation unit. Arch Phys Med Rehabil. 2002;83:1013-1016. [Crossref]
18. Oshima F, Yokozeki M, Hamanaka M, Imai K, Makino M, Kimura M, et al. Predilection of dysphagia severity: An investigation of the dysphagia patterns in patients with lateral medullary infarction. Intern Med. 2013;52:1325-1331. [Crossref]
19. Ertekin C, Aydogdu I, Yüceyar N, Kiylioglu N, Tarlaci S, Uludag B. Pathophysiological mechanisms of oropharyngeal dysphagia in amyotrophic lateral sclerosis. Brain. 2000;123:125-140. [Crossref]
20. Aydogdu I, Kiylioglu N, Tarlaci S, Tanriverdi Z, Alpaydin S, Acarer A, et al. Diagnostic value of "dysphagia limit for neurogenic dysphagia: 17 years of experience in 1278 adults. Clin Neurophysiol. 2015;126:634-643. [Crossref]

21. Ertekin C, Aydogdu I, Yüceyar N. Piecemeal deglutition and dysphagia limit In normal subjects and in patients with swallowing disorder. J Neurol Neurosurg Psychiatry. 1996;61:491-496. [Crossref]
22. Aydogdu I, Tanriverdi Z, Ertekin C. Dysfunction of bulbar central pattern generator in ALS patients with dysphagia during sequential deglutition. Clin Neurophysiol. 2011;122:1219-1228. [Crossref]
23. Gürgör N, Arıcı Ş, Kurt Incesu T, Seçil Y, Tokuçoğlu F, Ertekin C. An electrophysiological study of the sequential water swallowing. J Electromyogr Kinesiol. 2013;23:619-626. [Crossref]
24. Bougousslavsky J, Caplan LR. Stroke syndromes. 2nd ed. 2001. [Crossref]
25. Ertekin C, Aydogdu I. Neurophysiology of swallowing. Clin Neurophysiol. 2003;114:2226-2244. [Crossref]
26. Huckabee ML, Prosiegel M. Wallenberg syndrome (WS). In: Jones HN, Rosenbek JC, eds. Dysphagia in rare conditions. An Encyclopedia. 1st ed. San Diego: Plural Publishing; 2010: 639-646. [Crossref]
27. Aydogdu I, Ertekin C, Tarlaci S, Turman B, Kiylioglu N, Secil Y. Dysphagia in lateral medullary infarction (Wallenberg's syndrome): an acute disconnection syndrome in premotor neurons related to swallowing activity? Stroke. 2001;32:2081-2087. [Crossref]
28. Kim H, Chung CS, Lee KH, Robbins J. Aspiration subsequent to a pure medullary infarction: lesion sites, clinical variables, and outcome. Arch Neurol. 2000;57:478-483. [Crossref]
29. Paliwal VK, Kalita J, Misra UK. Dysphagia in a patient with bilateral medial medullary infarcts. Dysphagia. 2009;24:349-353. [Crossref]
30. Aviv JE, Martin JH, Sacco RL, Zagar D, Diamond B, Keen MS, et al. Supraglottic and pharyngeal sensory abnormalities in stroke patients with dysphagia. Ann Otol Rhinol Laryngol. 1996;105:92-97. [Crossref]
31. Aviv JE, Sacco RL, Thomson J, Tandon R, Diamond B, Martin JH, et al. Silent laryngopharyngeal sensory deficits after stroke. Ann Otol Rhinol Laryngol. 1997;106:87-92. [Crossref]
32. Seçil Y, Aydogdu I, Ertekin C. Peripheral facial palsy and dysfunction of the oropharynx. J Neurol Neurosurg Psychiatry. 2002;72:391-393. [Crossref]
33. Ertekin C. Electrophysiological Evaluation of Oropharyngeal Dysphagia in Parkinson's Disease. J Mov Disord. 2014;7:31-56. [Crossref]
34. Prigent H, Lejaille M, Terzi N, Annane D, Figere M, Orlikowski D, et al. Effect of a tracheostomy speaking valve on breathing-swallowing interaction. Intensive Care Med. 2012;38:85-90. [Crossref]
35. Bariohay B, Tardivel C, Pio J, Jean A, Félix B. BDNF-TrkB signaling interacts with the GABAergic system to inhibit rhythmic swallowing in the rat. Am J Physiol Regul Integr Comp Physiol. 2008;295:1050-1059. [Crossref]

ORIGINAL ARTICLE

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Pituitary MRI Findings of Pediatric Patients with Growth-Hormone Deficiency and Biologically Inactive Growth-Hormone

Büyüme Hormonu Eksikliği ve Biyoinaktif Büyüme Hormonu Tanılı Çocuk Hastalarda Hipofiz MRI Bulguları

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ABSTRACT

Background: Growth hormone (GH)-related short stature is a rare but important problem during pediatric follow-up. The determination of pituitary anatomy via pituitary magnetic resonance imaging (MRI) is an important tool in the diagnosis of GH disorders and acquired pituitary diseases. Pituitary dimensions in children vary according to age, and clear limits are not known. In this study, we investigated the relationship between pituitary MRI findings and GH in patients with GH deficiency (GHD) and bioinactive GH.

Materials and Methods: A total of 306 pediatric patients with GHD and bioinactive GH were analyzed. Pituitary MRI was performed in all patients, and the diagnoses were divided into 3 groups: severe GHD, mild-moderate GHD, and bioinactive GH.

Results: According to pituitary size, 63.4% of patients had a normal pituitary MRI scan, 27.5% were hypoplastic, and 0.3% were hyperplastic. Pituitary height and volume were lower in patients with severe GHD than in the mild-moderate group ($p<0.05$). The most effective measurement of pituitary volume was the height of the pituitary gland. A significant correlation was observed between the height standard deviation score and pituitary height ($r=0.824$, $p<0.001$). The relationship between peak GH level and pathologic MRI was analyzed. Cut-off 14.5 area under the curve (AUC) (95%): 0.59 (0.52-0.67), sensitivity 97%, specificity 95% ($p=0.007$).

Conclusion: There was a strong correlation between GH and pituitary size measured by MRI for the estimation of pituitary volume. Pituitary height measurement alone is an important supportive finding for the diagnosis of isolated GHD in children with slow growth.

Keywords: Bioinactive growth hormone, growth hormone deficiency, magnetic resonance imaging

ÖZ

Amaç: Büyüme hormonu (BH) ilişkili boy kısalığı nadir olmakla beraber çocuk izleminde önemli bir sorundur. Hipofiz manyetik rezonans görüntülemesi (MRG) ile hipofiz anatomisinin belirlenmesi, BH bozuklukları ve edinsel hipofiz hastalıklarının tanısında önemli bir araçtır. Çocuklarda hipofiz boyutları yaşa göre değişkenlik göstermektedir ve net sınırları bilinmemektedir. Bu çalışmada, BH eksikliği (BHE) ve biyoinaktif BH tanılı hastalarda hipofiz MRG bulguları ile BH arasında ilişki olup olmadığı araştırıldı.

Gereç ve Yöntemler: BHE ve biyoinaktif BH tanılı 306 çocuk hasta incelendi. Tüm hastalara hipofiz MRG çekildi ve tanılar 3 gruba ayrıldı: Ağır BHE, hafif-orta BHE ve biyoinaktif BH.

Bulgular: Hipofiz büyüklüğüne göre hastaların %63,4'ünün hipofiz MRG taraması normal, %27,5'inin hipoplastik ve %0,3'ünün hiperplastikti. Ağır BHE olan hastalarda hipofiz yüksekliği ve hacmi, hafif-orta gruba göre daha düşüktü ($p<0,05$). Hipofiz hacmini

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ÖZ

tahmin etmede en etkili ölçümün, hipofiz boyu olduğu görüldü. Boy standard sapma skoru ile hipofiz yüksekliği arasında anlamlı bir korelasyon gözlendi (r=0,824, p<0,001). Pik BH düzeyi ile patolojik MRG ilişkisi incelendi. Cut-off 14,5 eğrinin altındaki alan (%95): 0,59 (0,52-0,67), sensitivite %97, spesifite %95 saptandı (p=0,007).

Sonuç: BH ve hipofiz hacminin tahmini için MRG ile ölçülen hipofiz boyu arasında güçlü bir ilişki vardır. Yavaş büyüyen çocuk hastalarda tek başına hipofiz yükseklik ölçümü izole BHE tanısı koymada önemli destekleyici bulgudur.

Anahtar Kelimeler: Biyoinaktif büyüme hormonu, büyüme hormonu eksikliği, manyetik rezonans görüntüleme

Introduction

Short stature is a common problem in the follow-up of children. A height below 2 standard deviations score (SDS) is defined as a short stature. Most variants are variants of normal. Growth hormone (GH)-related causes are rare (1). GH deficiency (GHD) is an important endocrine cause with a frequency of 1/3500-10000 (2). Unfortunately, there is no gold standard for the diagnosis of GHD. In addition to compatible auxologic findings, the issues of low growth rate, delayed bone age, and low insulin-like growth factor-1 (IGF-1) levels have continued to be discussed. Stimulated GH levels support the diagnosis. Drugs commonly used for stimulation include L-dopa, clonidine, glucagon, and insulin. For stimulated GH, values >10 ng/mL are considered normal (3). However, it is also believed that a reference value should be determined according to the stimulating agent used (4). Most cases of GH deficiency are idiopathic, and only 20% are due to organic causes, including congenital central nervous system abnormalities, tumors, and other acquired pathological conditions involving the pituitary-hypothalamic axis (5). Pituitary imaging is normal in 20-70% of patients with isolated GHD (IGHD) (6,7,8,9).

In a short child with a low serum IGF-1 level, if the stimulated GH level is normal, a decrease in GH effect is considered. The GH-IGF axis may be impaired. If classical GH insensitivity (Laron syndrome) is not observed, then Kowarski syndrome (bioinactive GH) is considered (10).

Neuroimaging, particularly magnetic resonance imaging (MRI) of the pituitary anatomy, is an important tool in GH disorders, congenital malformations, and acquired pituitary disease (11). Imaging of the pituitary gland anatomy is also important for monitoring multiple pituitary hormone deficiencies (MPHD). In the presence of an abnormal pituitary gland, other pituitary hormones are likely to be affected (12). Normal values are presented for each part of the pituitary gland in adults (11). However, in children, values vary with age, and no clear cutoff values are known (12). For the pituitary stalk, values 1 mm are considered thin (13).

In our study, we analyzed the MRI findings of the pituitary gland in pediatric patients with GHD and bioinactive GH who were initiated on GH therapy.

Material and Methods

Our study was a retrospective, single-center analysis of 306 pediatric patients diagnosed with GHD and bioinactive GH between May 2021 and February 2023. We obtained ethical approval from the Scientific Research Ethics Committee of Health Sciences University Türkiye, Başakşehir Çam and Sakura City Hospital (approval number: 2023-35, date: 25.01.2023) and recorded the patients' sociodemographic information. Patients with familial and structural short stature and syndromic patients were excluded. The body weight and height of all participants were measured, and the child metrics program was used to calculate the height and body weight SDSs based on published normal values (14,15). All patients underwent puberty staging using Tanner staging (16,17).

The study evaluated each patient using a GH provocation test, in which GH levels were measured at 30-60-90-120-150 minutes after the administration of L-dopa, clonidine, or glucagon. Patients who exhibited a peak GH value below 5 ng/mL were considered to have severe GHD, whereas those with a peak GH value of 5-9,99 ng/mL were considered to have moderate-mild GHD (18,19,20). Patients who had normal GH provocation test results but low IGF-1 levels (⩽2 standard deviation) were subjected to an IGF-1 generation test. Synthetic somatropin GH was administered subcutaneously for four consecutive days at a dose of 0.1 mg/kg/day. A significant increase in IGF-1 levels above 15 ng/mL compared to baseline was used to diagnose bioinactive GH (4,21). No molecular studies were conducted on the patients.

A total of 306 individuals underwent MRI using a 3T MRI machine (Ingenia; Philips Medical Systems; Best, Netherlands). The hypophysis MRI protocol was standard and encompassed sagittal T2-weighted (T2-W) turbo spin echo (TSE) [repetition time (TR): 3000 milliseconds (ms), echo time (TE): 80 ms, slice thickness (st): 2.5 mm, field of

view (FOV): 150 mm]. The brain imaging scans used included sagittal T1-weighted (T1-W) TSE (TR: 557 ms, TE: 7 ms, st: 2.5 mm, FOV: 150 mm, matrix: 216x156 mm, gap: 1), coronal T2-W TSE (TR: 3000 ms, TE: 80 ms, st: 2.5 mm, FOV: 130 mm, matrix: 188x163 mm, gap: 1), and coronal T1-W TSE (TR: 557 ms, TE: 7.5 ms, st: 2.5 mm, FOV: 120 mm, matrix: 200x146 mm, gap: 1). Post-contrast imaging included coronal dynamic T1-W TSE (TR: 12 ms, TE: 884 ms, st: 2.5 mm, FOV: 125 mm, matrix: 156x110 mm, gap: 1), and sagittal T1-W TSE (TR: 507 ms, TE: 7 ms, FOV: 150 mm, matrix size: 232x179, interslice gap: 1 mm), and coronal T1-W TSE (TR: 557 ms, TE: 7.5 ms, st: 2.5 mm, FOV: 120 mm, matrix size: 200x159, interslice gap: 1 mm) MRI images were retrospectively evaluated by a 9-year experienced pediatric radiologist.

The anterior pituitary dimensions were measured in three dimensions: height (mm), anteroposterior diameter (mm), and mediolateral width (mm). The height of the pituitary gland was measured at the midline in the coronal T2-W. The anteroposterior diameter of the adenohypophysis was measured in the sagittal T1-W sequence to avoid neurohypophysis measurement. The mediolateral width of the pituitary gland was measured in the delayed post-contrast coronal T1-W sequence to avoid measuring the cavernous sinuses (Figure 1).

The anterior pituitary height, coronal width, and volume were measured according to sex and age. Patients were classified as "normal pituitary", "hypoplasic pituitary", or "hyperplasic pituitary" using a reference range from a previous study (22). Pituitary volume was calculated according to the ellipsoid formula (pituitary height x pituitary anteroposterior diameter x pituitary width/2) using the values of pituitary height, pituitary anteroposterior diameter, and pituitary width (23). Anatomical anomalies, including pars intermedia cyst, Rathke's cleft cyst, and ectopic neurohypophysis, were recorded.

Statistical Analysis

The study data were analyzed using SPSS 24.0 (SPSS Inc., Chicago, Illinois). Descriptive statistics are presented as mean ± SD and frequency (%). The Kolmogorov-Smirnov test was used to assess the normal distribution of continuous variables between groups. Parameters that fit the normal distribution were compared using Student's t-test, and those that did not fit the normal distribution were compared using the Mann-Whitney U test. Categorical variables were compared between groups using the chi-squared test. Pearson's correlation analysis was performed according to the distribution of variables. p-value <0.05 was considered statistically significant. The diagnostic sensitivity of pituitary measurements was determined using receiver operating characteristic (ROC) curve. The cut-off point for the curve was set at the highest sensitivity and specificity. From there, the data were recoded and positive predictive values and negative predictive values were calculated. Confidence intervals for these values were obtained using the syntax in SPSS software. This study analyzed the correlations between pituitary height, anteroposterior diameter, width, and volume and puberty.

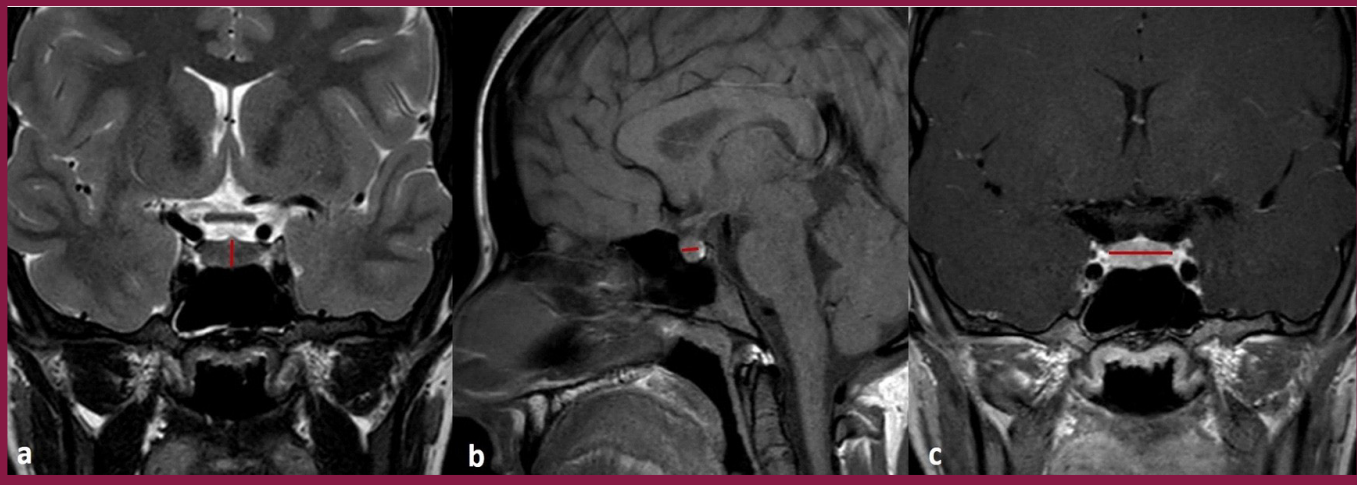

Figure 1. In a 14-year-old female patient with mild-moderate GHD, coronal T2-W (a), sagittal T1-W (b), and post-contrast coronal T1-W (c) sequences revealed a pituitary gland of normal size, with a measured height of 6.1 mm (a), anteroposterior diameter of 5.5 mm (b), and mediolateral diameter of 14.6 mm (c). Pituitary gland measurements were performed as follows: height was measured from the midline in the coronal T2-W sequence, anteroposterior diameter of the anterior pituitary was measured in the sagittal T1-W sequence, and mediolateral width was measured in the post-contrast coronal T1-W sequence (red lines)

GHD: Growth hormone deficiency, T2-W: T2-weighted, T1-W: T1-weighted

Results

One hundred and sixty-five (53.9%) male and 141 (46.1%) female patients were analyzed. The mean age was 9.96±3.25 years [minimum (min.)=0.7 years, maximum (max.)=16.9 years]. The mean height was 123.73±17.44 cm (min.=57 cm, max.=159 cm), height SDS value was -2.47±0.79 (min.=-6.8, max.=-0.43), body weight was 27.66±12.22 kg (min.=6.1 kg, max.=79 kg), body weight SDS value was -1.71±1.1 (min.=-5.9, max.=2.2), body mass index SDS value was -0.42±1.1 (min.=-3.9, max.=3.4). When puberty status was analyzed, 200 patients (65.4%) were prepubertal and 106 patients (34.6%) were pubertal. Fourteen patients (4.6%) had hypothyroidism (4 patients had central hypothyroidism). Three patients had panhypopituitarism and 1 patient had a history of brain gamma-knife treatment due to a congenital malformation.

All patients underwent GH stimulation tests. Those who had a peak GH level below 10 ng/mL during the initial test underwent a second stimulation test. Of the patients, 63.1% (n=193) were diagnosed with mild-moderate GHD and 27.1% (n=83) were diagnosed with severe GHD. Patients with a normal response to either of the two stimulation tests were subjected to an IGF-1 generation test. Nine point eight percent of all patients (n=30) were diagnosed with bioinactive GH by the IGF-1 generation test. GHD and bioinactive GH were diagnosed in 89.7% and 10.3% of the males, respectively. On the other hand, GHD and bioinactive GH were diagnosed in 90.8% and 9.8% of female patients, respectively. Notably, there was no significant difference between the genders in terms of diagnoses (p=0.75).

Pituitary MRI was performed in all patients, and the diagnoses were divided into three groups: severe GHD, mild-moderate GHD, and bioinactive GH. The MRI images were then compared. Based on pituitary size, 63.4% (n=194) of the patients exhibited normal pituitary MRI scans, 27.5% (n=84) were hypoplastic, and 0.3% (n=1) were hyperplastic. The table (Table 1) illustrates pituitary MRI and pathological findings in the examined regions. Thirty-two point seven percent (n=54) of boys and 22% (n=31) of girls had pathological MRI scans. MRI pathology was more prevalent in males than females (p=0.032). Patients with GHD had a higher incidence of pathologic MRI (29%) than those with bioinactive GH (16.7%). However, no significant difference was observed between the groups (p=0,15). The prevalence of pathologic MRI was 36,1% (n=30) in patients with severe GHD and 25.9% in those with mild-moderate GHD (p=0.059). Figure 2 presents an example of a patient's pathology.

There were no significant differences in pituitary volume and height between patients with and without GHD. In patients with severe GHD, pituitary height and volume were lower than those with mild-moderate GHD (p=0.04) (Table 2). Likewise, the width and anteroposterior diameter measurements did not differ significantly between the groups (Table 3). The pituitary volume increased significantly with the progression of puberty (Table 4).

The pituitary volume of individuals with pars intermedia cyst measured 139.85±62.9 mm^3, which was greater than that of other patients (p=0.045). Due to the limited number of patients, it is unclear whether this finding affected GHD or not.

Table 1. MRI findings of all patients

MRI finding	Severe GHD (n=83)	Mild-moderate GHD (n=193)	Bioinactive GH (n=30)	Total number of patients n (%)
Normal	48	125	21	194 (63.4%)
Hypoplasic pituitary	29	50	5	84 (27.5%)
Hyperplasic pituitary	0	1	0	1 (0.3%)
Ectopic neurohypophysis	2	0	0	2 (0.7%)
Arachnoid cyst	0	1	0	1 (0.3%)
Encephalomalacia	0	2	0	2 (0.7%)
Agenesis of the corpus callosum	0	0	1	1 (0.3%)
Microadenoma	0	2	0	2 (0.7%)
Pars intermedia cysts	4	7	2	13 (4.2%)
Rathke's kleft cyst	0	3	1	4 (1.3%)
The pituitary gland central region is thin		1	0	1 (0.3%)
Enlarged sella	0	1	0	1 (0.3%)

MRI: Magnetic resonance imaging, GHD: Growth hormone deficiency, GH: Growth hormone, n: Number of patients

The most effective measurement for estimating pituitary volume was determined to be height (r=0.824, p<0.001). Subsequent correlation analysis indicated that the factors with the greatest impact on volume were height, anteroposterior diameter, and width. When examining pituitary height, volume, and peak responses in the GH stimulation test, we found no correlation between volume and peak GH values (r=0.096, p=0.093). However, peak GH values increased with increasing height (r=0.133, p=0.02).

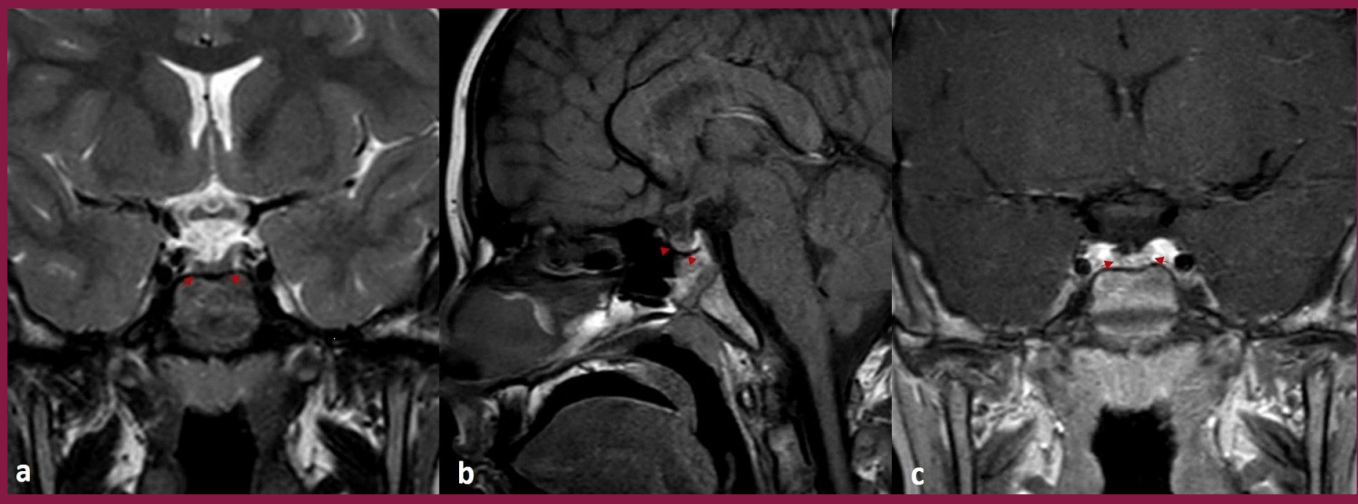

Figure 2. In an 11-year-old male patient with severe GHD, coronal T2-W (a), sagittal T1-W (b), and post-contrast coronal T1-W (c) sequences reveal a hypoplastic pituitary gland that is thinner than the normal gland for the age. The pituitary gland height was 1.8 mm, anteroposterior diameter was 4.7 mm, and mediolateral diameter was 10.8 mm. The pituitary gland, shown between red arrows, was measured in height from coronal T2-W, anteroposterior from sagittal, and width from coronal sequences

GHD: Growth hormone deficiency, T2-W: T2-weighted, T1-W: T1-weighted

Table 2. Relationship between pituitary volume, pituitary height, and diagnosis

Diagnosis	Pituitary volume (mm³)	Pituitary height (mm)	p (95% confidence interval)
GHD (severe and mild to moderate GHD) (n=276)	103.8±64.79	3.48±1.08	0.88 (volume) 0.57 (height)
Bioinactive GH (n=30)	102.42±47.21	3.36±1.26	0.19 (volume) 0.07 (height)
Severe GHD (n=83)	89.04±48.14	3.05±1.12	**0.004 (volume)** **0.004 (height)**
Mild-moderate GHD (n=193)	110.15±69.91	3.5±1.3	0.44 (volume) 0.94 (height)

GHD: Growth hormone deficiency; GH: Growth hormone; n: Number of patients

Table 3. Relationship between pituitary measurement and diagnosis

Diagnosis number of patients (n): SD standard error					
Pituitary height (mm)	Bioinactive GH	30	3.4867	1.08524	0.19814
	GHD	276	3.3678	1.26460	0.07612
Pituitary width (mm)	Bioinactive GH	30	11.4500	1.64940	0.30114
	GHD	276	11.5308	1.94438	0.11704
Pituitary anterior-posterior diameter (mm)	Bioinactive GH	30	5.0300	0.95381	0.17414
	GHD	276	5.1069	1.05905	0.06375
Pituitary volume (mm³)	Bioinactive GH	30	102.42580	47.217026	8.620610
	GHD	276	103.80915	64.791440	3.899986

GHD: Growth hormone deficiency, GH: Growth hormone, n: Number of patients, SD: Standard deviation

A significant correlation was observed between SDS and pituitary height (r=0.096, p=0.012), but no similar correlation was found between other pituitary measurements.

ROC analysis was conducted to examine the association between GHD and pituitary height, with a cut-off value of 3.55% area under the curve (AUC) (95% confidence interval: 0.46, 0.56), sensitivity of 40.6%, and specificity of 40% (p=0.51) (see Figure 3). Additionally, we investigated the relationship between peak GH levels and pathologic MRI using a cutoff of 14.5 AUC (95% confidence interval: 0.59, (0.52-0.67), sensitivity of 97%, and specificity of 95% (p=0.007) (see Figure 4).

Table 4. Relationship between stage of puberty and pituitary volume

Puberty stage	Number of patients	Pituitary volume (mm^3)		p
		Mean	SD	
1	200	83.45	37.18	
2	46	108.75	46.41	0.001
3	34	139.75	101.45	0.003
4	8	154.21	53.48	0.007
5	18	224.69	66.88	0.000

SD: Standard deviation

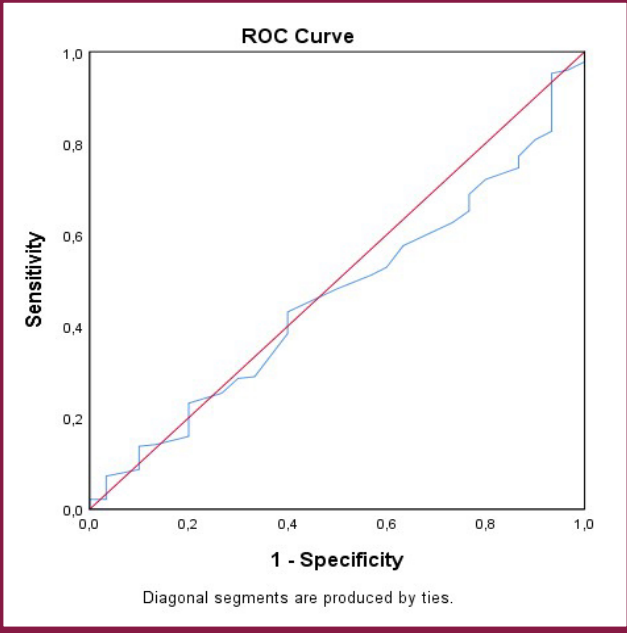

Figure 3. ROC curve analysis of GHD and pituitary height
ROC: Receiver operating characteristic, GHD: Growth hormone deficiency

DISCUSSION

GHD results in short stature during childhood, slow growth rate, and significantly reduced adult height. Diagnosis is based on auxologic data, detailed physical examination, and GH stimulation testing. The decision to perform stimulation testing is based on clinical findings and auxologic analysis. Our study involved the application of stimulation tests and pituitary MRI in all patients. The agents typically used in GH stimulation tests include clonidine, arginine, and glucagon (24). For our study, we used L-dopa, clonidine, and glucagon.

A correlation between peak GH levels obtained via GH stimulation testing and sagittal and coronal pituitary heights in children with GHD has been reported (25). In our study, an increase in pituitary height was observed with increasing peak GH, but there was no effect on volume.

MRI is the optimal method for identifying pituitary abnormalities. The radiologist's expertise is crucial in executing MRI evaluations. T1-W sequences reveal the brightness of the rear pituitary gland, which the radiologist must observe in terms of appearance and location. Our research focused on adenohypophysis. To avoid neurohypophysis measurement, we measured the anteroposterior diameter using sagittal T1-W sequences. In addition, the mediolateral width was measured using post-contrast coronal T1-W images, excluding the cavernous sinuses, which have similar intensity to the pituitary gland

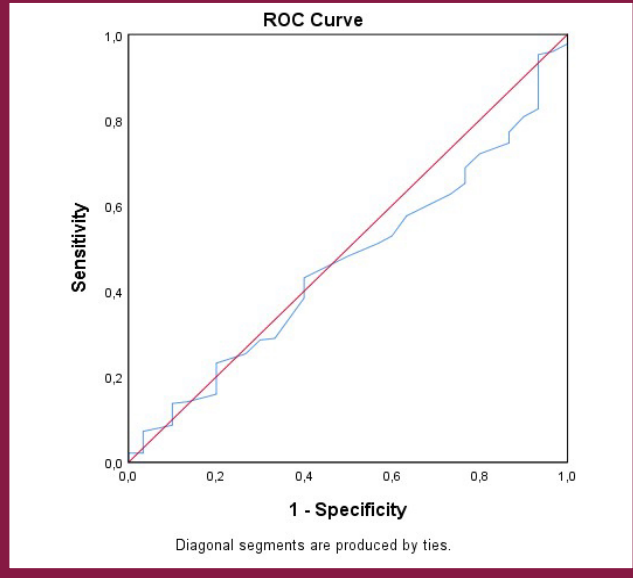

Figure 4. ROC analysis of peak GH and pathological MRI findings
ROC: Receiver operating characteristic, GHD: Growth hormone deficiency, MRI: Magnetic resonance imaging

in T2-W. The height of the pituitary gland was measured at the midline in the coronal T2-W. The width of the pituitary gland was measured in the delayed post-contrast coronal T1-W sequence to avoid measuring the cavernous sinuses.

A meta-analysis found sellar and parasellar abnormalities in 58% of patients with non-acquired GHD. Patients with MPHD were found to have a higher rate of pathology. Furthermore, patients with a peak stimulated GH level of 5 ng/mL had a higher frequency of severe MRI pathology (26). In a separate study, the incidence of abnormal MRI in patients with a peak GH level ⩽5 ng/mL was 36.9%, which was significantly higher than that in the other groups (groups with a peak GH level >5 ng/mL). The incidence of MRI pathology was also high in MPHD (27). In our study, the frequency of MRI pathology in patients with GHD was 29%. However, the rate was higher in patients with severe GHD (36.1%). The frequency of MRI abnormalities was higher in individuals with severe GHD than in the other groups, although not significantly.

Although the use of MRI for the diagnosis of IGDH is not recommended, current guidelines recommend pituitary MRI in all cases of GHD without discrimination. Tillmann et al. (11) reported that MRI is highly specific and predictive in the presence of sessile ectopic neurohypophysis and hypoplastic anterior pituitary in the diagnosis of GHD. Abnormal pituitary anatomy has been demonstrated at a rate of 50% in patients with idiopathic GHD (12). In congenital GHD, abnormal pituitary anatomy and concomitant pituitary hormone deficiency may be observed. Pituitary stalk interruption, thin pituitary stalk, ectopic neurohypophysis, and pituitary hypoplasia are important MRI findings of congenital GHD (28). Sharma et al. (29) reported pituitary hypoplasia as the most important MRI marker of disease severity in children with congenital GHD (66% IGHD, 34% MPHD). The finding that significantly predicted MPHD was pituitary hypoplasia (29).

Because most patients in our study had IGHD, we could not draw a definitive conclusion on this issue. However, 3 patients with MPHD had pituitary hypoplasia. One of these patients had congenital GHD.

A previous study revealed that ectopic neurohypophysis and interrupted pituitary stalk occurred in 48.6% of patients with IGHD and 93.5% of patients with MPHD (30). Another neuroimaging-oriented study showed that pituitary MRI was normal in 67% of patients with IGHD. Since no MPHD cases displayed isolated anterior pituitary hypoplasia, the conclusion reached was that IGHD should be considered in such cases (31). In the present study, 28.6% of patients with GHD exhibited anterior pituitary hypoplasia. Patients with severe GHD had a significantly lower pituitary volume than those in the other groups.

In this study, the average pituitary height of 49 patients with IGHD was significantly lower than that of the control group (70 patients). Additionally, in the same study, pituitary height was observed to be lower during the pre-pubertal period (32). Another study compared 69 pediatric patients with IGHD to those with idiopathic short stature and healthy controls, and the results revealed lower pituitary volume in the GHD group (33). There was no control group in this study, but we evaluated it based on a previous study that established the normal range for pituitary measurements (22). Comparing the severe GHD group with the other groups, we found significantly lower pituitary height and volume. Furthermore, we observed that pituitary volume increased as puberty progressed.

It is uncertain whether pituitary microadenoma contributes to the etiology of GHD. In our study, only 2 patients had microadenomas, a notably lower rate than in previous studies. It is important to consider the experience of the radiologist in such cases.

ROC analysis was performed to compare abnormal MRI findings with peak GH levels, and the results revealed AUCs of 0.614% and 0.728 for IGHD and MPHD, respectively (27). In our study, we found a cut-off value of 14.5 AUC (95%): 0.59 (0.52-0.67), a sensitivity of 97%, and a specificity of 95% for the relationship between peak GH level and pathological MRI. As previously reported in the literature, the frequency of pathology detection increased with decreasing GH levels. However, no relationship was observed between peak GH levels and pituitary height.

Pars intermedia cysts or Rathke cleft cysts are not expected to result in endocrine disorders unless they are exceptionally large and do not require special follow-up (34). Our study found that patients with pars intermedia cysts did not exhibit low pituitary volume. Additionally, 3.9% of patients with GHD had a pars intermedia cyst, although it was unclear whether it contributed to the etiology of GHD given the limited number of patients in our study.

Pituitary imaging is typically normal in patients with bioinactive GH, also known as Kowarski syndrome (35). However, our study found that 5 out of 30 patients with bioinactive GH (16.6%) had pituitary hypoplasia. In one patient, a rathke left cyst was present with a size of 11 mm, while the other pituitary hormones were in the normal range. This unexpected finding requires further support, as it contradicts the existing literature on the subject.

Study Limitations

This study has several limitations, including its retrospective nature, potential selection bias, and limited number of patients. The findings may be generalizable to

some populations, and more extensive prospective studies are needed to confirm these results. In addition, not having a control group is a limitation.

Conclusion

In patients with severe GHD, MRI is more effective in identifying pituitary pathology. Imaging of the pituitary gland is necessary for severe GHD and MPHD. In the diagnosis of a slowly growing child with IGHD, pituitary volume measurement via MRI can be beneficial. The most reliable measure of pituitary volume is the pituitary height. Height measurement alone is the most significant supportive finding for diagnosing GHD. Although current MRI technology has proven helpful in detecting large structural lesions, there is optimism that further improvements in imaging techniques will offer greater benefits to clinical practice.

Ethics

Ethics Committee Approval: This study obtained ethical approval from the Scientific Research Ethics Committee of Health Sciences University Türkiye, Başakşehir Çam and Sakura City Hospital (approval number: 2023-35, date: 25.01.2023).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.H.A.K., N.G.A., Z.K.S., A.Ö., H.Ö., Concept: E.H.A.K., Design: E.H.A.K., Data Collection or Processing: E.H.A.K., N.G.A., Z.K.S., A.Ö., H.Ö., Analysis or Interpretation: E.H.A.K., M.Ş., Literature Search: E.H.A.K., N.G.A., Z.K.S., A.Ö., H.Ö., M.Ş., Writing: E.H.A.K., N.G.A., Z.K.S., M.Ş.

Conflict of Interest: No conflict of interest was declared by the authors.

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REFERENCES

1. Günöz H. Boy kısalıkları. İçinde: Neyzi , Ertuğrul T (ed). Pediatri (3rd ed) Cilt 1. İstanbul: Nobel Tıp Kitabevleri. 2002:120-131. [Crossref]
2. Graber E, Rapaport R. Growth and growth disorders in children and adolescents. Pediatr Ann. 2012;41:e1-9. [Crossref]
3. Webb EA, Dattani MT. Diagnosis of growth hormone deficiency. Endocr Dev. 2010;18:55-66. [Crossref]
4. Grimberg A, DiVall SA, Polychronakos C, Allen DB, Cohen LE, Quintos JB, et al. Guidelines for growth hormone and insulin-like growth factor-I treatment in children and adolescents: growth hormone deficiency, idiopathic short stature, and primary insulin-like growth factor-I deficiency. Horm Res Paediatr. [Crossref]
5. Naderi F, Eslami SR, Mirak SA, Khak M, Amiri J, Beyrami B, et al. Effect of growth hormone deficiency on brain MRI findings among children with growth restrictions. J Pediatr Endocrinol Metab. 2015;28:117-123. [Crossref]
6. Maghnie M, Triulzi F, Larizza D, Preti P, Priora C, Scotti G, et al. Hypothalamic-pituitary dysfunction in growth hormone-deficient patients with pituitary abnormalities. J Clin Endocrinol Metab. 1991;73:79-83. [Crossref]
7. Abrahams JJ, Trefelner E, Boulware SD. Idiopathic growth hormone deficiency: MR findings in 35 patients. AJNR Am J Neuroradiol. 1991;12:155-160. [Crossref]
8. Argyropoulou M, Perignon F, Brauner R, Brunelle F. Magnetic resonance imaging in the diagnosis of growth hormone deficiency. J Pediatr. 1992;20:886-891. [Crossref]
9. Hamilton J, Chitayat D, Blaser S, Cohen LE, Phillips JA 3rd, Daneman D. Familial growth hormone deficiency associated with MRI abnormalities. Am J Med Genet. 1998;80:128-132. [Crossref]
10. Storr HL, Chatterjee S, Metherell LA, Foley C, Rosenfeld RG, Backeljauw PF, et al. Nonclassical GH insensitivity: characterization of mild abnormalities of GH action. Endocr Rev. 2019;40:476-505. [Crossref]
11. Tillmann V, Tang VW, Price DA, Hughes DG, Wright NB, Clayton PE. Magnetic resonance imaging of the hypothalamic-pituitary axis in the diagnosis of growth hormone deficiency. J Pediatr Endocrinol Metab. 2000;13:1577-1583. [Crossref]
12. Tsai SL, Laffan E, Lawrence S. A retrospective review of pituitary MRI findings in children on growth hormone therapy. Pediatr Radiol. 2012;42:799-804 [Crossref]
13. Delman BN. Imaging of pediatric pituitary abnormalities. Endocrinol Metab Clin North Am. 2009;38:673-698. [Crossref]
14. Demir K, Konakçı E, Özkaya G, Kasap Demir B, Özen S, Aydın M, et al. New features for child metrics: further growth references and blood press-sure calculations. J Clin Res Pediatr Endocrinol. 2020;12:125-129. [Crossref]
15. Neyzi O, Bundak R, Gökçay G, Günöz H, Furman A, Darendeliler F, et al. Reference values for weight, height, head circumference, and body mass index in Turkish children. J Clin Res Pediatr Endocrinol. 2015;7:280-293. [Crossref]
16. Marshall WA, Tanner JM. Variations in the pattern of pubertal changes in boys. Arch Dis Child. 1970;45:13-23. [Crossref]
17. Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. Arch Dis Child. 1969;44:291-303. [Crossref]
18. Wagner IV, Paetzold C, Gausche R, Vogel M, Koerner A, Thiery J, et al. Clinical evidence-based cutoff limits for GH stimulation tests in children with a backup of results with reference to mass spectrometry. Eur J Endocrinol. 2014;171:389-397. [Crossref]
19. Collett-Solberg PF, Ambler G, Backeljauw PF, Bidlingmaier M, Biller BMK, Boguszewski MCS, et al. Diagnosis, genetics, and therapy of short stature in children: a growth hormone research society international perspective. Horm Res Paediatr. 2019;92:1-14. [Crossref]
20. S2e-Leitlinie 174/002 Aktualisierte Leitlinie. Diagnostik des Wachstumshormonmangels im Kindes- und Jugendalter. Kurzfassung Stand. 2014. [Crossref]
21. Coutant R, Dörr HG, Gleeson H, Argente J. Diagnosis of endocrine disease: limitations of the IGF1 generation test in children with short stature. Eur J Endocrinol. 2012;166:351-357. [Crossref]
22. Sari S, Sari E, Akgun V, Ozcan E, Ince S, Saldir M, et al. Measures of pituitary gland and stalk: from neonate to adolescence. J Pediatr Endocrinol Metab. 2014;27:1071-1076. [Crossref]
23. Fink AM, Vidmar S, Kumbla S, Pedreira CC, Kanumakala S, Williams C, et al. Age-related pituitary volumes in prepubertal children with normal

endocrine function: volumetric magnetic resonance data.J Clin Endocrinol Metab. 2005;90:3274-3278. [Crossref]

24. Rosenfeld RG, Albertsson-Wikland K, Cassorla F, Frasier SD, Hasegawa Y, Hintz RL, et al. Diagnostic controversy: the diagnosis of childhood growth hormone deficiency revisited. J Clin Endocrinol Metab. 1995;80:1532-1550. [Crossref]
25. Chen J, Wang X, He C, Wei S. MRI Findings of pituitary gland in growth hormone-deficient children and their correlation with growth hormone peak during growth hormone stimulation tests. Contrast Media Mol Imaging. 2022;2022:3111585. [Crossref]
26. Hwang J, Jo SW, Kwon EB, Lee SA, Chang SK. Prevalence of brain MRI findings in children with nonacquired growth hormone deficiency: a systematic review and meta-analysis. Neuroradiology. 2021;63:1121-1133. [Crossref]
27. Mamilly L, Pyle-Eilola AL, Chaudhari M, Henry RK. The necessity of magnetic resonance imaging in the evaluation of pediatric growth hormone deficiency: Lessons from a large academic center. Growth Horm IGF Res. 2021;60-61:101427. [Crossref]
28. Beukhof CM, Lequin MH, Drop SLS. The classic triad and variants. Deal C (red). MRI in congenital hypopituitarism. Remedica. 2007:69-80. [Crossref]
29. Sharma H, Purwar N, Kumar A, Sahlot R, Garg U, Sharma B, et al. Pituitary hypoplasia is the best MRI predictor of the severity and type of growth hormone deficiency in children with congenital growth hormone deficiency. J Pediatr Endocrinol Metab. 2021;34:851-858. [Crossref]
30. Jagtap VS, Acharya SV, Sarathi V, Lila AR, Budyal SR, Kasaliwal R, et al. Ectopic posterior pituitary and stalk abnormality predicts severity and coexisting hormone deficiencies in patients with congenital growth hormone deficiency. Pituitary. 2012;15:243-250. [Crossref]
31. Tsai SL, Laffan E. congenital growth hormone deficiency-a review with a focus on neuroimaging. Eur Endocrinol. 2013;9:136-140. [Crossref]
32. Dumrongpisutikul N, Chuajak A, Lerdlum S. Pituitary height at magnetic resonance imaging in pediatric isolated growth hormone deficiency. Pediatr Radiol. 2018;48:694-700. [Crossref]
33. Kessler M, Tenner M, Frey M, Noto R. Pituitary volume in children with growth hormone deficiency, idiopathic short stature and controls. J Pediatr Endocrinol Metab. 2016;29:1195-1200. [Crossref]
34. Mahdi ES, Webb RL, Whitehead MT. Prevalence of pituitary cysts in children using modern magnetic resonance imaging techniques. Pediatr Radiol. 2019;49:1781-1787. [Crossref]
35. Sprynchuk N, Bolshova O. Syndrome of biologically inactive growth hormone-features of diagnosis and treatment. Endokrynologia. 2023;28:82-89. [Crossref]

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Surgical Approach to Cases with Sternal Dehiscence After Sternotomy

Sternotomi Sonrası Sternal Dehisens Gelişen Olgulara Cerrahi Yaklaşım Yöntemlerimiz

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ABSTRACT

Background: Sternotomy is the most commonly used method of cardiovascular surgery. Sternal instability and infection in the region that develops after sternotomy are serious complications. Reoperation is often required to ensure sternal stability. In this study, we aim to presentthe surgical methods used incases of sternal dehiscence.

Materials and Methods: Between December 2020 and July 2023, 632 patients who underwent sternotomy due to coronary artery disease and/or valve replacement were retrospectively analyzed at Tekirdağ Dr. İsmail Fehmi Cumalıoğlu City Hospital Hospital.

Results: Surgical intervention was performed in 23 (3.6%) cases with sternal dehiscence. The mean age was 62±8.7 years (range: 40-77) and the majority were male (n=18, 78.3%). The operation types were steel wire removal, steel wire reuse, the Robicsek technique, sternal plate use, and sternal clip use. Two patients who underwent surgery due to sternal dehiscence underwent revision surgery due to recurrent sternal instability. No morbidity or mortality was observed in any patient who underwent surgery due to dehiscence.

Conclusion: Sternal dehiscence is a complication that can cause serious morbidity and mortality, and its intervention is important. We prefer the application of sternal clips as the most appropriate and physical support material for ensuring stability.

Keywords: Sternotomy, sternal dehiscence, sternal clip

ÖZ

Amaç: Kalp ve damar cerrahisinde sternotomi en sık kullanılan yöntemdir. Sternotomi sonrası gelişen sternal insitabilite ve bölgenin enfeksiyonu ciddi bir komplikasyondur. Sternal stabiliteyi sağlamak için sıklıkla reoperasyon gerekmektedir. Bu çalışmada, sternal dehisens gelişen olgulara uyguladığımız cerrahi yöntemleri sunmayı hedefledik.

Gereç ve Yöntemler: Tekirdağ Dr. İsmail Fehmi Cumalıoğlu Şehir Hastanesi'nde, Aralık 2020 ile Temmuz 2023 tarihleri arasında koroner arter hastalığı ve/veya kapak replasmanı nedenli sternotomi uygulanan 632 hasta retrospektif olarak analiz edildi.

Bulgular: Sternal dehisens gelişen 23 (%3,6) olguya cerrahi müdahale yapıldı. Yaş ortalaması 62±8,7 yıl (aralık: 40-77) iken büyük çoğunluğu erkek idi (n=18, %78,3). Operasyon tipleri; çelik tel çıkartılması, tekrar çelik tel kullanımı, Robicsek tekniği, sternal plak kullanımı ve sternal klips kullanımı idi. Sternal dehisens nedenli operasyon gerçekleştirdiğimiz hastalardan iki tanesi tekrarlayan sternal instabilite nedenli revizyon operasyona alınmıştır. Dehisens nedeni ile cerrahi yapılan hiçbir olguda morbidite ve mortalite izlenmedi.

Sonuç: Sternal dehisens ciddi morbidite ve mortalite yaratabilecek bir komplikasyondur ve müdahalesi önem arz etmektedir. Stabilite sağlanması açısından en uygun ve fiziksel destekleyici materyal olarak sternal klips uygulamasını tercih etmekteyiz.

Anahtar Kelimeler: Sternotomi, sternal dehisens, sternal klips

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Introduction

Sternotomy is the primary approach in cardiovascular surgery. Despite a median wound infection incidence of 1% among patients undergoing median sternotomy, the associated morbidity and mortality rates remain notably elevated, ranging from 14% to 47%, as reported in the literature (1). There is currently no universally agreed-upon surgical method for managing complex cases of median sternotomy. Essential procedural steps include wound debridement and foreign material removal.

In cases of type I mediastinitis, closed mediastinal irrigation may yield successful outcomes, whereas patients with type II-V mediastinitis likely benefit most from major reconstructive surgery. Advances in diagnostic tools and ongoing evaluation of primary sternal fixation's advantages suggest its potential use alongside reconstructive procedures in type I-III mediastinitis, aiming to enhance outcomes in these high-mortality complications (1).

The patient-related risk factors were obesity, smoking history, hypertension, diabetes, septicemia after sternotomy, use of the bilateral internal mammary artery for coronary bypass, chronic obstructive pulmonary disease, and prolonged use of mechanical ventilation in the postoperative period. In cases of acute infection, treatment includes early debridement, antibiotic therapy, and, in some patients, the use of a pectoralis or omentum flap to improve vascularization. However, in some of these patients, the condition is characterized by stitch opening and chronic wounds. Some separations can only be corrected by debridement and approximation of the edges until the tissues involved are in better condition. Although there are various sternal closure methods, the use of flaps is a standardized method in some modalities. The selection of flap is based on the wound type, and the most important indicator is the amount of tissue loss (2,3).

In this study, we aimed to present the methods and results of sternal dehiscence cases.

Material and Methods

We retrospectively examined patients who underwent surgery due to sternal dehiscence during the follow-up period and who underwent 632 stereotomies for 518 coronary artery diseases, 71 mitral valve replacements, and 43 aortic valve replacements between December 2020 and July 2023 at Tekirdağ Dr. İsmail Fehmi Cumalıoğlu City Hospital. During the postoperative outpatient clinic follow-up, the development of sternal dehiscence was diagnosed by clinical examination at different time points. Thorax computed tomography was performed for mediastinal area examination and evaluation of existing steel wires. The acute-phase reactant values were controlled by laboratory investigations.

Close outpatient follow-up of the cases in our clinic and accessibility of the patients to their primary surgeons at all times can facilitate early diagnosis and acceleration of the treatment plan. Due to early diagnosis, no serious infections were observed in this series. After diagnosis, the patients were hospitalized, and intravenous antibiotherapy was started after consultation with the Department of infectious diseases. Perioperative images were discussed with the Department of Infectious Diseases, and antibiotherapy treatment was extended if necessary during the postoperative period.

The fact that the materials used for sternal stabilization are of foreign origin has created access difficulties during the COVID-19 pandemic. In addition, working in a peripheral hospital creates transport difficulties. For this reason, in the first cases, the dislocated steel wires were removed to prevent infection if the risk of recurrence due to a lack of equipment was taken into consideration or if partial field stabilization was relied upon.

During surgery, the infected tissues were debrided, and the dislocated steel wires were removed. Sternal tissue was debrided if necessary. Culture was collected from the infected area, and postoperative antibiotherapy was extended as necessary. Because the risk of sternal dehiscence is high in patients withosteoporotic bone structure, the Robicsek technique was used based on a perioperative decision. The Robicsek technique consists of placing bilateral peristernal double rows of wire sutures and then reconnecting the separated sternal parts with transverse sutures supported by two double axial suture lines (4). The use of sternal clips among locally produced sternal stabilization equipment has increased in our clinic due to the increased accessibility of sternal clips. The surgical methods are presented as radiological imaging and perioperative images in Figure 1.

IBM SPSS Statistics Version 26 software was used. The descriptive results of this study are presented as frequencies with corresponding percentages for nominal or ordinal variables. Continuous variables are presented as mean and standard deviation. Permission for the study was obtained from Tekirdağ Dr. İsmail Fehmi Cumalıoğlu City Hospital Clinical Research Ethics Committee (approval number: 14/2022, date: 16.12.2022). Informed consent forms were obtained.

Results

A total of 632 median stereotomies were performed, and 23 (3.6%) of them underwent surgical intervention due to the development of sternal dehiscence. The mean age

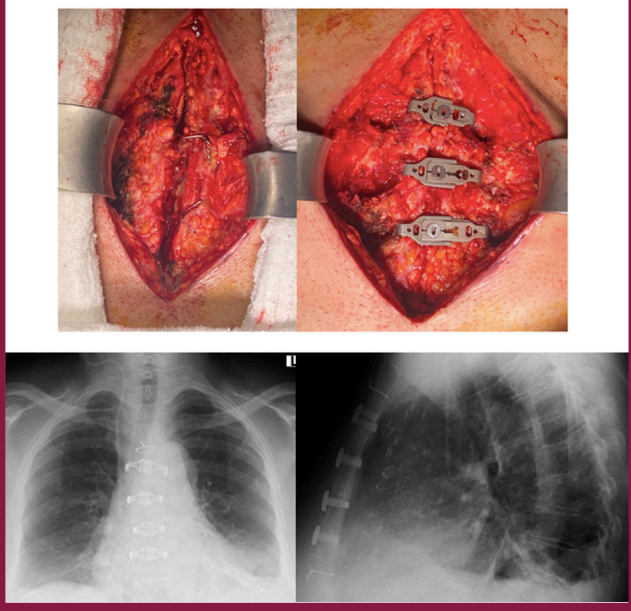

Figure 1. Sternal clips

was 62±8.7 years (range: 40-77). There were 18 (78.3%) males and 5 (21.7%) females. Comorbidity was detected in 15 (65.2%) patients. Hypertension was found in 6 (26.1%) patients, chronic obstructivepulmonary disease in 3 (13%), diabetes mellitus in 2 (8.7%), congestive heart failure in 2 (8.7%), asthma in 1 (4.3%), and chronic renal failure in 1 (4.3%).The demographic features of the cases are shown in Table 1.

Local infection was observed in 2 cases (8.7%) and systemic infection in 4 cases (17.4%). Patients with elevated acute-phase reactants were operated after intravenous antibiotic therapy and regression of infection parameters. The types of operation were 4 (17.4%) steel wire removal, 5 (21.7%) steel wire reuse, 4 (17.4%) Robicsek technique, 2 (8.7%) sternal plate use, and 8 (34.8%) sternal clip use. In two patients who underwent surgery again using steel wires due to sternal dehiscence, recurrent sternal instability was observed during the second week of follow-up after discharge. Osteomyelitis due to infection in the sternal tissue caused the steel wires to dislodge again. Intravenous antibiotic treatment and surgery were planned. While a sternal plate was used in one case, a steel wire was used

Table 1. Demographic characteristics of the patients

Patients	Gender	Age	Comorbidities	Infection	Surgical types
1	Male	77	Hypertension	Local	Wire removal
2	Male	59	Asthma	Local	Wire removal
3	Male	66	Heart failure	Systemics	Wire removal
4	Male	50	None	None	Wire removal
5	Male	68	Hypertension	None	Reuse of wire*
6	Male	62	Hypertension	None	Reuse of wire*
7	Male	51	None	None	Reuse of wire
8	Male	58	None	Systemics	Reuse of wire
9	Male	67	Diabetes mellitus	Systemics	Reuse of wire
10	Male	62	Renal failure	None	Robicsek technique
11	Female	73	Hypertension	None	Robicsek technique
12	Male	75	None	None	Robicsek technique
13	Female	56	Heart failure	None	Robicsek technique
14	Male	40	None	None	Plaque technique
15	Male	62	None	Systemics	Plaque technique
16	Male	58	Hypertension	None	Sternal clip
17	Male	53	None	None	Sternal clip
18	Male	65	None	None	Sternal clip
19	Male	66	None	None	Sternal clip
20	Female	61	Hypertension	None	Sternal clip
21	Female	61	None	None	Sternal clip
22	Female	60	Diabetes mellitus	None	Sternal clip
23	Male	74	Chronic obstructive pulmonary disease	None	Sternal clip

*Reoperations are the reuse of the wire and plaque technique

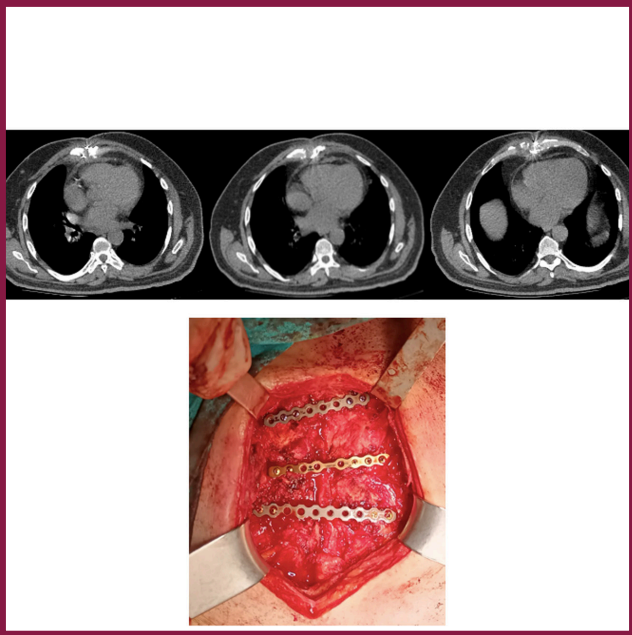

Figure 2. Sternal plate

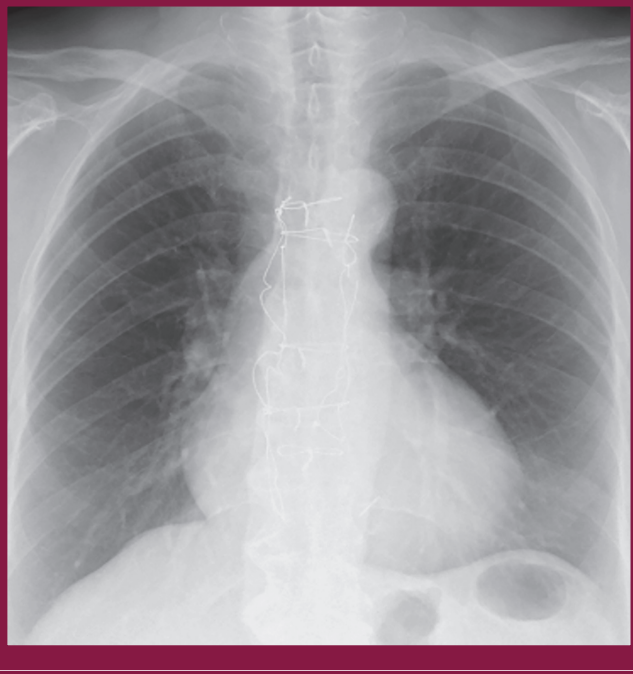

Figure 3. Robicsek technique

again in the other case due to difficulty in accessing the material. No recurrence of sternal instability was detected during follow-up after discharge.

No complications related to the procedure were observed after surgery. During follow-up of the cases, no recurrent sternal instability, hemorrhage, wound infection, or mediastinitis was observed. The patients were followed up in the postoperative ward, and the patients whose antibiotherapy treatment was completed were discharged. No mortality or morbidity events were observed.

Discussion

Sternal dehiscence and mediastinitis after sternotomy, which is preferred for cardiovascular and thoracic surgery, is a complication that negatively affects quality of life and may cause serious morbidity and mortality. Among the complications, the development of mediastinitis is particularly an indicator of poor prognosis. For reference, the classification of mediastinitis is presented in Table 2(1).

In the study by Gucu et al. (5), nitinol thermo-reactive clips were used in patients with sternal dehiscence. This method was found to be safe, easy, and effective for non-infective secondary sternal closure. No recurrent dehiscence or instability was observed in the postoperative period. It has been reported that the advanced shape memory and flexibility of nitinol clips facilitate their use (5).

In the study by Ergene et al. (6), cases of sternal fractures who were admitted to the emergency department because of trauma were analyzed. In 66% of the cases with additional system pathologies, the operation was usually performed on the second post-traumatic day after stabilization was achieved. The radius plate used in radius fractures was reshaped to fit the sternal region perioperatively, and stabilization was provided. The technique using a locked volar distal radius plate was found to be safe and effective. It has been reported that large vessel injuries are avoided with the use of a sternal stabilization system that does not require the mediastinum (6).

Lafci et al. (7) modified the Robicsek technique in their study. The Robicsek technique is based on the principle of strengthening the side by passing a steel wire through intercostal spaces to strengthen the unstable sternal region. In this study, the method was modified. In the bilateral intercostal region, the Robicsek technique was applied, and the sternum strength was doubled using a figure of 8-sutures in the sutures to be applied horizontally. It has been reported that it does not require the use of a plate or clip and therefore does not incur additional costs (7).

In a study by Şahin et al. (8) in 2022, 13 cases were included, and vacuum-assisted closure treatment was applied before secondary closure. The application was performed as 1-10 (Median: 4), and surgical closure was decided if the culture result was negative. In 10 patients, the omentum was removed transdiaphragmatically and placed in the sternal cavity. During follow-up, seroma and local infection recurrence were observed in two patients,

Table 2.Classification of mediastinitis among patients undergoing cardiovascular surgery	
Class	**Description**
Type I	Mediastinitis occurring within 2 weeks after surgery without the presence of additional risk factors
Type II	Mediastinitis appearing between 2 and 6 weeks after surgery without additional risk factors
Type IIIA	Type I mediastinitis with one or more risk factors
Type IIIB	Type II mediastinitis with one or more risk factors
Type IVA	Mediastinitis Types I, II, or III after unsuccessful initial treatment
Type IVB	Mediastinitis Type I, II, or III persisting after more than one unsuccessful treatment attempt
Type V	Mediastinitis more than 6 weeks after surgery, presenting for the first time

and incisional hernia was found in one patient. Thoracic stabilization was achieved in all patients (8).

In a study by Arazi et al. (9) in 2022, modified stenoplasty was used in deep mediastinitis and sternal dehiscence. After freeing the area to the level of the middle clavicular line, the sternum is approximated with horizontal steel wires after the use of sagittal steel wires between the costae. The bilateral pectoral muscle flap is pulled to the area, and closure is performed. Femoral-femoral cardiopulmonary bypass can be performed to release adhesions and to be safe during the sternal re-entry phase. Although an increase in postoperative complications and length of hospitalization was observed, this method was reported to be safer (9).

Sternal dehiscence is a complication that can cause serious morbidity and mortality, and its intervention is important. We prefer the application of sternal clips as the most appropriate and physical support material for ensuring stability. The use of sternal clips among locally produced sternal stabilization equipment has increased in our clinic due to the increased accessibility of sternal clips. Supporting the sternal area from the bilateral lateral area is the best stabilization technique. The reciprocity of bone ends supports osteogenesis and has the advantage of not affecting blood flow in the region. The only disadvantage of this approach is that it slightly increases the access time to the cardiac area in cases requiring urgent re-sternotomy. Sternal stabilization were achieved with the use of sternal plate and Robicsek technique, and we prefer to use the sternal clip technique in our clinic.

Ethics

Ethics Committee Approval: Permission for the study was obtained from Tekirdağ Dr. İsmail Fehmi Cumalıoğlu City Hospital Clinical Research Ethics Committee (approval number: 14/2022, date: 16.12.2022).

Informed Consent: Informed consent forms were obtained.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.Ü., H.A., Concept: M.Ü., Design: M.Ü., Data Collection or Processing: M.Ü., Analysis or Interpretation: M.Ü., Literature Search: H.A., Writing: M.Ü.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. El Oakley RM, Wright JE. Postoperative mediastinitis: classification and management. Ann Thorac Surg. 1996;61:1030-6. [Crossref]
2. Jones G, Jurkiewicz MJ, Bostwick J, Wood R, Bried JT, Culbertson J, et al. Management of the infected median sternotomy wound with muscle flaps. The Emory 20-year experience. Ann Surg. 1997;225:766-776. [Crossref]
3. Anger J, Farsky PS, Almeida AF, Arnoni RT, Dantas DC. Use of the pectoralis major fasciocutaneous flap in the treatment of post sternotomy dehiscence: a new approach. Einstein (Sao Paulo). 2012;10:449-454. [Crossref]
4. Robicsek F, Daugherty HK, Cook JW. The prevention and treatment of sternum separation following open-heart surgery. J Thorac Cardiovasc Surg. 1977;73:267-268. [Crossref]
5. Gucu A, Toktas F, Eris C, Ata Y, Turk T. Nitinol thermoreactive clips for secondary sternal closure in cases of noninfective sternal dehiscence. Tex Heart Inst J. 2012;39:513-516. [Crossref]
6. Ergene G, Tulay CM, Anasız H. Sternal fixation with nonspecific plate. Ann Thorac Cardiovasc Surg. 2013;19:364-7. [Crossref]
7. Lafci G, Yasar E, Cicek OF, Irdem A, Uzun A, Yalcinkaya A. A novel modified Robicsek technique for sternal closure: "Double-check." Asian Cardiovasc Thorac Ann. 2014;22(6):758-760. [Crossref]
8. Şahin MF, Yazıcıoğlu A, Beyoğlu MA, Yekeler E. Succesful method in the treatment of complicated sternal dehiscence and mediastinitis: sternal reconstruction with osteosynthesis system supported by vacuum-assisted closure. Turk J Thorac Cardiovasc Surg. 2022;30:57-65. [Crossref]
9. Arazi M, Grosman-Rimon L, Yehezkeel S, Rimon J, Gohari J, Gleitman S, et al. Predictors of prolonged hospitalization in modified sternoplasty following postoperative mediastinitis. J Card Surg. 2022;37:4726-4731. [Crossref]

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Şenoymak MC, Erbatur NH, Babacanlar N, Yardımcı G, Deniz F, Yönem A. Depression and Anxiety Disorders in Patients with Reported Prolactinoma Using Cabergoline Therapy: A Comparative Analysis with Controls. Hamidiye Med J 2024;5(3):166-171.

The title was changed at the request of the author. The wrong section is shown below:

Depression and Anxiety Disorders in Patients with Reported Prolactinoma Using Cabergoline Therapy: A Comparative Analysis with Controls

The title of the article has been corrected as follows:

Depression and Anxiety Disorders in Patients with Remitted Prolactinoma Using Cabergoline Therapy: A Comparative Analysis with Controls

2024 REFEREE INDEX

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