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# Anatomical dimensions and variances of the foramen ovale in adult human skulls

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**Ethics Committee Approval**

The researchers have stated that all local and international guidelines were followed during the use of cadaveric donors in their anatomical study. □

**Conflict of Interest**

No conflict of interest was declared by the authors. □

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**Abstract**

**Background/Aim:** The foramen ovale (FO) is very important in neurosurgical approaches; however, studies and developments in the literature report that no definite consensus about the cannulation of the FO is available. Therefore, more morphometric information concerning the FO is needed in addition to the previously defined morphological and morphometric features. The aim of this study was to compare the features of the foramen ovale stated in the literature and to analyze the topographic relationship between the FO and the anatomical structures around it to determine its precise location.

**Methods:** The study included 70 sides from 35 dry skulls of unknown age and gender. Skulls with any deformity or pathology that would affect the measurements were not included in the study. All skulls were placed in the horizontal plane with the external occipital protuberance facing posteriorly, the piriform aperture facing anteriorly, and the skull base pointing upwards at a 90° angle after which it was photographed vertically with the length scale. A Nikon D5300 Digital Camera was used for the photography, and digital image processing software (Image J) was used for foramen ovale measurements. In addition, the shape of the foramen ovale was classified as oval, almond, D-shaped, slit-shaped, round, and irregular. SPSS 21.0 was used for the statistical analysis.

**Results:** The mean anteroposterior diameter length of the FO was 6.144 mm, and the transverse diameter length was 2.885 mm. When the distribution of the shape of the FO was examined, oval and almond shapes were most common shapes (34.29%). In addition, round (12.85%), D-shaped (10%), and slit-shaped (8.57%) were obtained. According to Pearson's correlation analysis, the highest correlation was between the distance from the carotid canal to the foramen ovale and the shortest distance from the foramen ovale to the midline (FO-CC and the FO-ML, respectively;  $r = 0.427$ ).

**Conclusion:** The morphology of the FO is important in terms of surgical and interventional approaches. In the literature, no significant differences between the right and left sides for the foramen ovale were found in contrast to our study. When the FO shape percentages were examined in most previous studies, it was seen that most of them were oval. In this study, the ratios of oval and almond shapes were the same. Morphometric measurements can give different results in every race due to the structure of the bones, which may vary according to the population. We think that presenting data on the Turkish population in this study will set an example for conducting future studies.

**Keywords:** Foramen ovale, Cranial base, Morphometry, Anatomy

**Introduction**

The foramen ovale (FO) is located on the infratemporal surface of the greater wing of the sphenoid bone and is very important for the middle cranial fossa. It is located posterolaterally to the foramen rotundum (FR) and anteromedially to the foramen spinosum (FS), lateral to the foramen lacerum (FL) [1]. The FO connects the middle cranial fossa to the infra-temporal fossa and the mandibular nerve (a mandibular division of the trigeminal nerve), the lesser petrosal nerve (a branch of the glossopharyngeal nerve), and accessory meningeal branch of the maxillary artery. Also, the venous plexus passing through the FO connects the pterygoid venous plexus in the infratemporal fossa and the cavernous sinus [2].

In the literature, although the morphology of the FO is mostly described as oval, it is quite diverse in terms of morphological and morphometric features compared to other foramina (Khan). In addition to its oval shape, “almond”, “D-shape”, elongated oval”, “oval”, “round”, semicircular, “slit”, with irregular borders, bordered by bony spurs, spines, and tubercles are also used to describe it, and it has also been expressed in very different terms, such as “pear” and “truly oval” [3].

The importance of the skull base foramina, which contains information about various neoplastic processes and trigeminal neuralgia related to the FO, has been emphasized in the literature [4].

The variation in number and morphometric and morphological features of the foramina located in the skull base are clinically in the view of delicate neurovascular structures [5]. Also, the variations, location, and anatomical features are important for clinicians, surgeons, anatomists, forensic scientists, and anthropologists [6]. The precise location in addition to morphological and morphometric features of the FO are of vital significance during certain diagnostic procedures, such as the cannulation of the foramen, microvascular decompression by percutaneous trigeminal rhizotomy, electroencephalographic analysis, and percutaneous biopsy of cavernous sinus tumors in addition to in the prevention of trigeminal nerve injuries during clinical approaches [7]. The FO is very important in neurosurgical approaches; however, despite the studies and developments reported in the literature, no definite consensus about the cannulation of the FO is available. Therefore, more morphometric information is needed in addition to its previously defined morphological and morphometric features [8].

The aim of this study was to compare the features of the FO stated in the literature and to analyze the topographic relationship between the FO and the anatomical structures around it to determine its precise location.

**Materials and methods**

The study included 70 sides of 35 dry skulls of unknown age and gender, which belonged to the Anatomy Laboratory of Çukurova University Faculty of Medicine. The authors declare that the study was conducted in accordance with the 1964 Declaration of Helsinki. The study did not include human/animal experimentation. Skulls used in this study are used as student course material in the Laboratory of the

Department of Anatomy. Skulls with any deformities or pathologies that would affect the measurements were not included in the study. All skulls were placed in the horizontal plane with the external occipital protuberance facing posteriorly, the piriform aperture facing anteriorly, and the skull base pointing upwards at a 90° angle after which the skulls were photographed vertically using the length scale. A Nikon D5300 Digital Camera was used for photography, and digital image processing software (Image J) was used for FO measurements. Measurements made on the skulls are shown in Figure 1, and their definitions are given in Table 1. In addition, the shapes of the FO were classified as oval, almond, D-shaped, slit-shaped, round, and irregular (Figure 2).

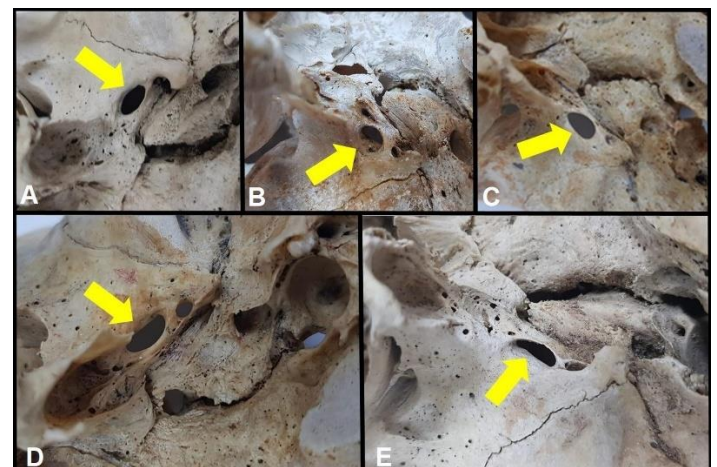
Table 1: Definitions of measurements made on the skull

Measurements	Definitions
APFO	Anteroposterior diameter of foramen ovale
TFO	Transverse diameter of foramen ovale
FO-ML	The shortest distance between foramen ovale and midline
FO-FS	The shortest distance between foramen ovale and foramen spinosum
FO-CC	The shortest distance from the carotid canal to the foramen ovale
FO-FL	The shortest distance from the foramen lacerum to the foramen ovale
FO-TRZ	The shortest distance from the foramen ovale to the tubercle of root of zygoma

Figure 1: Morphometric measurements made on the skulls; 1 = APFO, 2 = TFO, 3 = FO-ML, 4 = FO-FS, 5 = FO-CC, 6 = FO-FL, 7 = FO-TRZ.



Figure 2: The shapes of the foramen ovale (FO): A = Oval, B = Round, C = Almond, D = D-Shaped, E = Slit Shaped



All measurements were made by a single investigator and intraclass correlation coefficients ([ICC] with 95% confidence intervals [CI]) were used for reliability testing. When the interobserver reliability was examined for all measurements, the ICC value was found to be between 0.91 and 0.95, and the interobserver reliability of all measurements was excellent.

**Statistical Analysis**

The suitability of the data for consideration as a normal distribution was evaluated with the Kolmogorov–Smirnov test and graphical examinations. The descriptive analysis was performed to obtain means, standard deviations, and ranges (minimum and maximum values). A paired sample t-test was used for the right and left side data comparison that showed normal distribution. The relationship between quantitative variables was analyzed by correlation analysis, and the Pearson’s correlation coefficient was used to determine the level of relationship. The SPSS (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) program was used for statistical analysis. Statistical significance was accepted as  $P < 0.05$ .

**Results**

Descriptive statistics of the FO are shown in Table 2. The mean anteroposterior diameter length of the FO (APFO) was 6.144 mm, and the transverse diameter length (TFO) was 2.885 mm. When the distribution of the shape of the FO was examined, it was found that oval and almond shapes were most common (34.29%). In addition, round 12.85%, D-Shaped 10%, and slit-shaped 8.57% were reported (Table 3).

Table 2: Descriptive statistics of measurements of the foramen ovale in mm

Measurements	Mean (SD)	Minimum	Maximum	SEM
APFO	6.144 (0.913)	4.327	7.981	0.109
TFO	2.885 (0.565)	1.440	4.559	0.067
FO-ML	19.147 (1.887)	15.214	23.713	0.225
FO-FS	2.471 (0.803)	1.086	4.305	0.095
FO-CC	10.757 (1.992)	7.248	16.507	0.238
FO-FL	6.260 (1.307)	3.793	9.514	0.156
FO-TRZ	26.688 (2.170)	23.376	32.892	0.259

n = 70, SD: Standard deviation, SEM: Standard Error of Mean

Table 3: Distribution according to the shape of the foramen ovale

Shape	Right (n=35)	Left (n = 35)	Total (n = 70)
Oval	14 (40%)	10 (28.57%)	24 (34.29%)
Round	4 (11.43%)	5 (14.28%)	9 (12.85%)
3333Almond	11 (31.43%)	13 (37.14%)	24 (34.29%)
D-Shaped	3 (8.57%)	4 (11.43%)	7 (10%)
Slit Shaped	3 (8.57%)	3 (8.57%)	6 (8.57%)

The comparison between the measurements of the side difference (right and left side) of FO in the skull is shown in Table 4. When the measurements were examined, a statistically significant difference between the right and left sides only in the anteroposterior diameter of the FO (APFO) measurement (6.292 versus 5.995 mm;  $P = 0.004$ ) was shown, while no right and left side differences in terms of other measurements were found ( $P > 0.05$ ).

Table 4: Differences between the right and left sides of the foramen ovale (mm)

Measurements	Right (n = 35)	Left (n = 35)	Mean difference	SEM	T value	P-value
	Mean (SD)	Mean (SD)				
APFO	6.292 (0.150)	5.995 (0.157)	0.297	0.096	3.076	0.004*
TFO	2.942 (0.097)	2.828 (0.094)	0.113	0.101	1.129	0.267
FO-ML	19.356 (0.324)	18.939 (0.315)	0.416	0.252	1.650	0.108
FO-FS	2.375 (0.132)	2.565 (0.138)	-0.190	0.112	-1.703	0.098
FO-CC	10.599 (0.350)	10.914 (0.325)	-0.314	0.155	-2.025	0.051
FO-FL	6.191 (0.229)	6.328 (0.214)	-0.136	0.111	-1.234	0.226
FO-TRZ	26.763 (0.361)	26.612 (0.377)	0.151	0.207	0.733	0.469

SD: Standard deviation, SEM: Standard Error of Mean

The correlation between the measurements of the FO is shown in Table 5. While a statistically significant positive correlation between APFO measurement and TFO, the distance from the carotid canal to the foramen ovale (FO-CC), and the foramen ovale to the tubercle of root of zygoma (FO-TRZ) measurements, a statistically significant negative correlation was found in terms of the shortest distance between the foramen ovale and foramen spinosum (FO-FS) measurement ( $r = 0.390$ ,  $r = 0.334$ ,  $r = 0.253$ , and  $r = 0.292$ , respectively). In addition, a statistically significant and positive correlation was obtained between TFO measurement and the shortest distance from the foramen ovale to the midline (FO-ML), FO-CC, and FO-TRZ measurements ( $r = 0.242$ ,  $r = 0.315$ , and  $r = 0.331$ , respectively). In addition, a statistically significant and positive correlation was found between FO-ML and FO-CC, FO-FS and FO-FL, FO-CC, and FO-TRZ, and FO-FL and FO-TRZ ( $r = 0.427$ ,  $r = 0.394$ ,  $r = 0.383$ , and  $r = 0.346$ , respectively).

The comparison of the length and width measurements of the FO and the distribution data of the shapes obtained in our study with the studies in the literature is shown in Table 6.

**Discussion**

This study provides information about the shape of the FO and its relationship with the other cranial base structures in the Turkish population. The FO plays an important role because it connects the intracranial and extracranial structures of the skull. Therefore, it is widely used in various surgical interventions and diagnostic procedures [9]. For this reason, the relationship of the FO with the neighboring structures in the region is important.

In the literature, there are studies on the structure and topography of the foramen ovale conducted on different races. In a study conducted in the Japanese population by Yagani, the mean length and width of the FO were 7.48 and 4.17 mm, respectively, from 220 adult skulls [10]. In another study conducted in Nepal with 35 skulls, the mean length of the FO was reported as 7.46 (1.41) mm, and the mean width of the FO was 3.21 (1.02) mm on the right side. On the left side, the mean length and width were 7.01 (1.41) and 3.29 (0.85) mm, respectively [11]. Also, according to Lang et al.’s study conducted in New York, the mean length of FO was 7.2 mm. It was 6.9 mm on the right side and 6.8 mm on the left. The mean width of the FO in adult skulls was 3.7 mm [12]. In Somesh’s study, the maximum widths of FO were 7.5 and 8.0 mm on right and left sides, respectively, and the minimum width was 3.0 mm on the right and left sides. The mean width was 5.128 (0.827) mm on the right side and 5.244 (0.950) mm on the left side, and no side differences were found [13]. In these studies, no statistically significant differences between the right and left sides were noted although millimetric differences were detected. In our study, the mean maximum length of the FO was 6.29 mm on the right side and 5.99 mm on the left side. The mean width of the FO was 2.94 mm and 2.83 mm for the right and left sides, respectively.

Table 5: Comparison between the present and previous studies

Authors	Doğan et al. [4] 2014	Karthikeyan et al. [5] 2017	Patil et al. [7] 2013	Daimi et al. [9] 2011	Das et al. [14] 2019	Ajrish George & Thenmozhi [15] 2019	Ravinthar [16] 2015	Srikantaiah & Shetty [17] 2019	Sridhar et al. [18] 2014	Present study	
Shape (%)	Others	-	-	-	-	-	-	-	28.3%	-	
	Slit shaped	-	-	-	-	-	-	-	6.7%	8.57%	
	D-shaped	-	-	-	-	3.94%	-	-	-	10%	
	Round	-	-	-	-	21.05%	-	-	6.7%	12.85%	
	Almond	-	-	-	-	21.05%	-	-	10%	34.29%	
	Oval	-	-	-	-	53.94%	-	-	48.3%	34.29%	
TFO (Mean [SD])	Right	4.32 (1.41)	3.99 (1.80)	5.0 (0.42)	70 (0.81)	3.49 (0.54)	3.56 (0.73)	3.56 (0.73)	6.0 (1.7)	4.46 (0.83)	2.94 (0.10)
	Left	4.06 (0.66)	4.6 (1.40)	4.70 (0.91)	3.34 (0.77)	3.73 (0.83)	4.28 (0.83)	4.28 (0.83)	5.6 (1.4)	4.40 (0.94)	2.83 (0.10)
APFO (Mean [SD])	Right	7.18 (1.78)	7.45 (1.10)	7.0 (2.17)	6.60 (1.06)	7.17 (1.31)	6.77 (1.65)	6.77 (1.65)	7.45 (3.1)	7.17 (1.46)	6.29 (0.15)
	Left	7.29 (0.94)	7.61 (1.15)	6.8 (1.40)	6.26 (1.23)	7.26 (1.91)	5.74 (1.79)	5.74 (1.79)	6.8 (1.5)	7.41 (1.67)	5.99 (0.16)

In a study by Ray et al. [11] in which the authors used 70 sides from 35 adult skulls, 43 (22R, 21L) were typically oval shaped, 24 (11R, 13L) were almond shape, two (1R, 1L) were round, and one side resembled a slit-like shape. In Somesh's study [13] with 82 adult dry skulls, 56.70% (48R, 45L) had an oval shape, 28.65% (24R, 23L) had an almond shape, 10.97% (8R, 10L) had round shape, and 3.65% (2R, 4L) were irregular. In our study using the same number of skulls, the oval (14R, 10L) and almond shaped (11R, 13L) skulls had the same number out of 70 sides. Seven out of 70 sides (3R, 4L) were D-shaped, and six (3R, 3L) were slit-shaped. The mean FO values reported in other studies are shown in Table 5 [4, 5, 7, 9, 14–18].

Burdan et al. [19] stated that the mean maximum length of the FO was 6.070 mm for males and 5.793 mm for females on the right side. On the left side, they reported values of 5.913 mm for males and 5.817 mm for females. The mean width of the FO was 3.477 mm on the right side and 3.650 mm on the left side for the males. In females, the mean width of the FO was 3.050 mm on the right side and 3.200 mm on the left side in the Polish population. They also stated that that no side differences were found.

In the study of Akcay et al. [20] on 40 Anatolian dry skulls, the average length of the FO on the right side was 7.09 (1.07) mm and 7.06 (1.01) mm on the left side. The mean width was 4.16 (0.79) mm on the right side and 4.15 (0.5) mm on the left side. Out of 80 skulls, 70.0% (28R, 28L) had an oval shape, 18.75% (7R, 8L) had an almond shape, 5% (2R, 2L) had a round shape, and 6.25% (3R, 2L) were split-shaped. The distance between the posterior point of the CC and the FO was 18.89 (2.03) mm on the right and 18.82 (1.74) mm on the left side. Özalp et al. [21] claimed that the mean distance between the FO and the CC was 12.57 (1.56) mm in skulls and 12.45 (1.34) mm on computed tomography (CT) images. In our study, the distance between the FO and the CC was 10.599 (0.350) mm on the right side and 10.914 (0.325) mm on the left side.

It is seen that the present study yielded low values when compared to other studies except for the study by Burdan et al. [19]. The present study also had similar results, but it was not possible to compare them because of the lack of specific gender of the skulls. Also in the present study, a side difference in the mean maximum length of the FO was noted, and the right left side had a higher value than the right side. When the FO shape percentages were examined in most previous studies, it was seen that the shape was mostly oval. In the present study, the oval and almond shapes of the FO ratios were the same (34.29%), which we think affected the average values of the FO.

Most studies in the literature present findings regarding the maximum width and length of the FO for morphometry. In the study, the relationship of the FO with other adjacent bone structures, such as the FS, FL, and CC, were evaluated morphometrically. When we evaluated the correlation between variables, we did not encounter a variable with a high correlation coefficient. The highest correlation was between the FO-CC and the FO-ML ( $r = 0.427$ ). Also, we tried to produce a formula with a regression analysis to estimate the location of the FO, but this attempt was not successful.

The bone structures differ between populations due to genetic and environmental factors, such as gender, geography, and nutrition [21]. It is worth mentioning the numbers of different shapes of the FO because of its bilateral symmetry. Most of the major brain anomalies involve asymmetrical deformities of the cranial bones; therefore, it is important to understand anatomical structure and their morphometry [20].

The morphology of the FO is important in terms of surgical and interventional approaches. The measurements made in this region and the neighboring areas and relationship of the structures with each other are especially important for surgeons, radiologists, and anatomists to understand. Morphometric measurements can yield different results in every race due to the structure of the bones, which may vary according to the population. We think that our study will set an example for ways to conduct future studies.

### Limitations

The most important limitation of our study was the low number of intact skulls due to the strict inclusion criteria and the lack of age and gender data on the skulls. Further multicenter studies using these data and larger samples can be planned to investigate the Turkish population in more detail.

### Conclusion

The FO is one of the major anatomical structures on the cranial base. The morphology of the skull differs between populations because of genetics and environment. Its variations, location, anatomical features, and relationship with the other important neighboring structures are important for clinicians, surgeons, anatomists, forensic scientists, and anthropologists to understand.

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# Pediatric healthcare professionals' opinions, attitudes, and vaccine hesitancy toward personal and children's COVID-19 vaccination

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**Ethics Committee Approval**

This study was approved by Erciyes University,  
Ethical Committee on Noninvasive Clinical  
Research (Date: 03.02.2021, Number: 2021/99).  
All procedures in this study involving human  
participants were performed in accordance with  
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**Conflict of Interest**

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**Abstract**

**Background/Aim:** Pediatric healthcare professionals are at the forefront of both facilitating an increase vaccine acceptability and reduction in vaccine hesitancy and play a vital role in eliminating vaccine hesitancy of families. In this context, it was thought that the individual pediatric healthcare professional's vaccine hesitancy could affect successful administration of the coronavirus 2019 (COVID-19) vaccination. This study aimed to determine the opinions and attitudes of pediatricians and pediatric nurses toward the COVID-19 vaccination and the reasons for vaccine hesitancy. The study also aimed to identify their views and attitudes toward COVID-19 vaccination in children.

**Methods:** The survey was carried out as a cross-sectional study between February and May 2021. The study sample consisted of 83 pediatricians and 79 pediatric nurses. Necessary permission was obtained before the study began. Data were collected using questionnaires that had been prepared by researchers. Data were analyzed using descriptive statistical methods and a chi-squared test.

**Results:** Almost all pediatricians and more than half of the pediatric nurses reported that they considered getting vaccinated/were vaccinated; however, a greater proportion of nurses were vaccine-hesitant ( $P = 0.001$ ). Reasons for not being vaccinated/being hesitant among healthcare professionals included harmful ingredients in the COVID-19 vaccines, thinking that vaccines were developed too quickly, vaccine development studies in different phases did not yield conclusive outcomes, hearing from the social media that vaccines are harmful, believing it is not necessary to receive a vaccine that is not included in the routine immunization schedule, and lack of knowledge about vaccines. The majority of the physicians and nurses who participated in the study reported that, if COVID-19 vaccines were available for children, they would not consider advising it or were unsure ( $P = 0.003$ ). When asked about the reasons for hesitancy, a greater proportion of nurses reported they thought that vaccines had been developed too quickly ( $P < 0.001$ ) and that the outcomes of vaccine development studies in different phases were not conclusive ( $P = 0.008$ ).

**Conclusion:** Healthcare workers serve as role models for vaccination acceptance in the community. Identifying the reasons for vaccine hesitancy among healthcare professionals is key to encouraging vulnerable populations to accept and take the vaccine. Vaccine hesitancy may be countered by comprehensive in-service trainings on vaccine development processes and phases of trials relating to COVID-19 vaccines.

**Keywords:** COVID-19, Pediatrician, Nurses, Opinion, Attitude, Vaccine hesitancy

## Introduction

Coronavirus disease 2019 (COVID-19) is a severe acute respiratory syndrome caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 disease was first identified in Wuhan, Hubei Province of the People's Republic of China in December 2019 and became a pandemic in April 2020 [1, 2]. While all countries across the world are making individual efforts to contain the spread of SARS-CoV-2, the World Health Organization (WHO) is conducting a global campaign of prevention, early detection, and medical treatment. In addition to ongoing measures, including mask-wearing, social distancing, and hygiene measures intended for flattening the curve of infections, development of an effective vaccine against COVID-19 has become a priority for global health organizations. With a large number of clinical vaccine trials underway, the timeline for public distribution of a safe and effective vaccine is projected to be between the end of 2020 and 2022 [3]. Increasing rates of mortality and significant morbidity due to the COVID-19 pandemic accelerated vaccine development in different countries and led to vaccines being administered through emergency use authorization based on phase 3 trials [4]. However, vaccine hesitancy remains an obstacle to herd immunity against highly contagious diseases, such as COVID-19. Indeed, WHO has characterized vaccine hesitancy as "one of the top ten threats to global health" [5].

Healthcare workers are disproportionately exposed to infectious diseases and play a role in hospital-acquired transmission; thus, these workers are an important target group for vaccination. Although several countries promote vaccination for healthcare workers, vaccination rates vary [6–8]. Healthcare workers, even when asymptomatic, can transmit the virus to patients. In addition, being at risk for contracting infections from their patients often causes them to be viewed as a source of vaccine-preventable nosocomial infections that seem particularly threatening during the COVID-19 pandemic [9, 10]. A previous study that evaluated and substantiated this information [11] compared centers that advised or did not advise vaccination for their healthcare workers and found that all-cause mortality was lower in centers in which healthcare professionals were vaccinated against influenza. Another study conducted during a season when only 15% of healthcare personnel were vaccinated against influenza found 19 cases and one death in an outbreak of nosocomial influenza reported from a neonatal intensive care unit [12]. Pediatric patients, one of the most vulnerable groups, also play a key role in the spread of the epidemic and deserve particular attention. These reports suggest that vaccination of healthcare professionals is critical not only for their own health but also for the health of the patients for whom they care.

Pediatric healthcare professionals administering vaccines are the most experienced group in terms of understanding the effects, efficacy, and side effects of vaccines. Healthcare professionals serve as role models and thus contribute to the success of vaccination campaigns, particularly at a time that is characterized by increasing distrust of vaccines and dominated by discussions about the safety of vaccines rather than about their efficacy. So, given the critical nature of pediatric healthcare professionals' acceptance of the COVID-19

vaccination, it is important to investigate vaccination rates and reasons for vaccine hesitancy among these professionals to protect vulnerable populations and promote vaccination in the community [9, 10]. Against this background, this study was conducted to determine the rates of COVID-19 vaccination among pediatricians and pediatric nurses and to reveal their opinions and attitudes toward vaccinating children in addition to the reasons for vaccine hesitancy.

## Materials and methods

Our research, designed as a cross-sectional study, was carried out between February and May 2021. The study population consisted of 250 physicians and nurses working at a children's hospital in a province in the Central Anatolian Region. To determine the minimum number of required study participants, the formula  $n = N \times t^2 \times \sigma^2 / d^2 (N - 1) + t^2 \times \sigma^2$  was used. The sample size calculated 5% acceptable error, 95% confidence level, and 1.96 degrees of freedom. The minimum sample size was calculated as 152 participants. After exclusion of healthcare professionals who were on maternity leave, were in self-quarantine because of testing positive for COVID-19, or refused to participate in the study, the study sample comprised a total of 162 participants (83 pediatricians and 79 pediatric nurses) who volunteered to participate in the study.

The study received approval from the scientific research board of the ministry of health, institution. This study was approved by Erciyes University, Ethical Committee on Noninvasive Clinical Research (Date: 03.02.2021, Number: 2021/99). Data were collected using an online survey as part of the infection control measures against the pandemic. Participants were informed about the purpose of the study and the confidentiality of the data on a note included at the beginning of the online survey and was asked to provide informed consent. The second part of the online form consisted of a questionnaire that was prepared by the researchers based on a literature review and that collected information about demographic characteristics of pediatricians and pediatric nurses, such as age, sex, number of children, and questionnaires inquiring views and attitudes towards COVID-19 vaccination [13–15]. Data were collected through online questionnaires shared with online groups.

### Statistical analysis

Data were analyzed using the statistical software suite IBM SPSS Statistics 25.0 (IBM Corp., Armonk, New York, USA). Descriptive statistics were expressed in unit number (n) and percentage (%), and the relationship between categorical variables was evaluated using a chi-squared test. Statistical significance was set at  $P < 0.05$ .

## Results

In this study 38.9% of the healthcare professionals who participated in the study were in the 22–30-year-old age group, and 81.5% of them were female. Almost three-quarters (71.6%) of the participants were married, and 62.3% had children. Just over half (51.2%) were pediatricians, and 48.8% were pediatric nurses (Table 1).



Table 1: Demographic characteristics of pediatricians and pediatric nurses (n = 162)

Characteristics	Number (n)	Percent (%)
Age		
22–30 years	63	38.9
31–40 years	63	38.9
41 years and older	36	22.2
Gender		
Female	132	81.5
Male	30	18.5
Marital status		
Married	116	71.6
Single	46	28.4
Educational status		
Undergraduate	82	50.6
Masters	47	29.0
Doctorate	33	20.4
Profession		
Physician	83	51.2
Nurse	79	48.8
Having children		
Yes	101	62.3
No	61	37.7

In all, 91.6% of the physicians and 69.6% of the nurses reported that they thought it necessary to be vaccinated against COVID-19. In this study, 6% of the physicians and 29.1% of the nurses were found to be hesitant about COVID-19 vaccination or about whether it was necessary ( $P = 0.001$ ). Pediatricians and pediatric nurses listed healthcare workers, people over 65 years of age, and women in the 15–49-year-old age group as priority

groups for vaccination, but both groups placed pregnant women and children at the end of the list. However, a statistically significant difference between physicians and nurses in mentioning healthcare workers as a priority group for vaccination ( $P = 0.005$ ) was found. When asked if the country of origin of the vaccine is important, 42.2% of the physicians and 62% of the nurses gave a positive answer ( $P = 0.011$ ). When asked, “If you had a choice, which vaccine (in terms of country of origin) would you prefer?”, 39.8% of the physicians said they would prefer vaccines originating from Germany, and 41.8% of the nurses said they would prefer vaccines produced in Turkey ( $P = 0.004$ ),

In all, 90.4% of the pediatricians and 65.8% of the pediatric nurses reported that they considered getting vaccinated/were vaccinated, which showed a higher rate of vaccine hesitancy among nurses ( $P = 0.001$ ). The most common reasons for not being vaccinated/being hesitant among both groups of healthcare professionals included several factors: (1) thinking that vaccines were developed too quickly ( $P = 0.520$ ), (2) thinking that the results of vaccine development studies in different phases were inconclusive ( $P = 0.236$ ), and (3) lack of

Table 2: Pediatricians’ and pediatric nurses’ opinions and attitudes toward coronavirus 2019 (COVID-19) vaccination

Characteristics	Physician (83) n %		Nurse (79) n %		$\chi^2$	P-value
Thinking COVID-19 vaccination should be received/is necessary during the pandemic						
Yes	76	91.6	55	69.6	15.182	0.001
No	2	2.4	1	1.3		
Unsure	5	6.0	23	29.1		
Which group do you think should be vaccinated first*						
Healthcare workers	75	90.4	57	72.2	7.729	0.005
Children	9	10.8	5	6.3	0.551	0.458
Pregnant women	7	8.4	3	3.8	0.808	0.369
Women 15–49 years of age	9	10.8	13	16.5	0.661	0.416
People over 65 years of age	48	57.8	39	49.4	0.851	0.356
Whether the country of origin of COVID-19 vaccines is an important factor in vaccination						
Yes	35	42.2	49	62.0	6.392	0.011
No	48	57.8	30	38.0		
If you had a choice (in terms of country of origin), our vaccine choice would be						
Turkey	14	16.9	33	41.8	15.144	0.004
Germany	33	39.8	17	21.5		
China	14	16.9	14	17.7		
It doesn't matter	8	9.6	3	3.8		
Other	6	7.2	7	8.9		
No idea	8	9.6	5	6.3		
Considering vaccination/vaccination status as healthcare workers						
Yes	75	90.4	52	65.8	14.423	0.001
No	3	3.6	9	11.4		
Hesitant	5	6.0	18	22.8		
Reason for not being vaccinated and being hesitant*						
I believe COVID-19 vaccines contain harmful ingredients	1	12.5	5	18.5	1.716	0.190
I think I have a lack of knowledge about vaccines	3	37.5	9	33.3	2.526	0.112
I think vaccines were developed very quickly	6	75.0	9	33.3	0.413	0.520
I think the results of the studies in different phases are inconclusive	5	62.5	10	37.0	1.404	0.236
I've heard from the television and the Internet that vaccines are harmful.	0	0.0	1	3.7	1.443	0.488
My family doesn't want me to get this vaccine	0	0.0	1	3.7	1.443	0.488
I think that healthcare institutions have not provided sufficient information about vaccines.	0	0.0	2	7.4	2.899	0.236
I do not believe it is necessary to receive a vaccine that is not included in the routine immunization schedule.	0	0.0	3	11.1	1.462	0.114
I don't think any vaccine is safe or protective. I won't get this as I haven't received other vaccinations.	0	0.0	2	7.4	2.899	0.236
Based on my religious beliefs, I believe that vaccines contain inadvisable substances.	1	12.5	0	0.0	1.343	1.000
I'm concerned about potential side effects	4	50.0	7	25.9	0.504	0.361

\*More than one option has been selected.

Table 3: Comparison of healthcare professionals’ views and attitudes towards COVID-19 vaccination in children

Characteristics	Physician (83) n %		Nurse (79) n %		$\chi^2$	P-value
Whether they would recommend vaccination if COVID 19 vaccines were available for children						
Yes	9	10.8	22	27.8	11.385	0.003
No	44	53.0	24	30.4		
Hesitant	30	36.2	33	41.8		
Reason for hesitancy*						
I believe COVID-19 vaccines contain harmful ingredients	1	3.3	3	9.1	1.176	0.278
I think vaccines were developed very quickly	5	16.7	23	69.7	15.522	<0.001
I think the results of the studies in different phases are inconclusive	8	26.7	17	51.5	7.005	0.008
I've heard from the television and the Internet that vaccines are harmful.	0	0.0	1	3.0	1.443	0.488
I think that healthcare institutions have not provided sufficient information about vaccination in children.	2	6.7	7	21.2	3.373	0.066
I do not believe it is necessary to receive a vaccine that is not included in the routine immunization schedule.	1	3.3	1	3.0	0.001	0.972
I'm concerned about potential side effects	13	43.3	11	33.3	1.285	0.257
I think it can cause neurological diseases like autism	0	0.0	2	6.1	2.899	0.236

\*More than one option has been selected.

knowledge about vaccines ( $P = 0.112$ ). A greater proportion of physicians (50%) than nurses were concerned about potential side effects (Table 2).

More than two-thirds of the physicians and nurses (53% and 36.2% for physicians; 30.4% and 41.8% for nurses) who participated in the study reported that they did not consider recommending COVID-19 vaccination if it were available for children or were hesitant about making such a recommendation ( $P = 0.003$ ). Reasons for hesitancy were different between physicians and nurses. A greater proportion of nurses versus physicians thought that vaccines were developed too quickly ( $P < 0.001$ ) and that the results of vaccine development studies in different phases were inconclusive ( $P = 0.008$ ). Other reasons for hesitancy mentioned by the physicians included several factors: (1) thinking that healthcare institutions did not provide sufficient information about vaccination in children, (2) concern about potential side effects, and/or (3) COVID-19 vaccination not listed in the routine vaccination schedule. Nurses were also hesitant because they thought that COVID-19 vaccines contained harmful substances ( $P = 0.278$ ) and that vaccines may cause neurological diseases, such as autism ( $P = 0.236$ ) as shown in Table 3.

## Discussion

Vaccines can provide protection against a great number of infectious diseases. The tremendous success of vaccination campaigns that prevent exposure to the devastating effects of vaccine-preventable diseases have paradoxically resulted in people fearing the side effects of vaccines more than those vaccine-preventable diseases themselves [16–18]. The COVID-19 pandemic has severely affected people and healthcare systems globally. Increasing rates of mortality and significant morbidity have made the development of a COVID-19 vaccine a priority goal. COVID-19 vaccines started to be administered in the phase 3 of trials through emergency use authorization. Despite high mortality rates resulting from COVID-19 disease, there has been significant vaccine hesitancy in the community [16].

To help vaccination campaigns succeed, healthcare professionals should set an example of accepting vaccines and becoming vaccinated, especially at a time characterized by increased distrust of vaccines and dominated by concerns about safety of vaccines rather than by efficacy [6, 19–21]. The reason this study involved pediatricians and pediatric nurses is because most vaccines included in the national immunization program in Turkey are delivered during childhood. Pediatricians and pediatric nurses know more than other healthcare professionals about the protective effects, efficacy, and side effects of vaccines. For this reason, determining the rationale for vaccine hesitancy in this group could be instructive. This study was conducted to reveal pediatricians' and pediatric nurses' views and attitudes toward the COVID-19 vaccination, to determine whether they advised vaccination in children, and reasons for vaccination hesitancy.

This study found that physicians and nurses held different views about vaccination against COVID-19 during the pandemic. Physicians were more likely than nurses to believe in the necessity of vaccines and to consider getting vaccinated, whereas pediatric nurses were more hesitant than pediatricians.

Previous studies have found that nurses have lower vaccine acceptance and higher vaccine hesitancy compared to physicians [3, 22, 23]. In one of these studies, the vaccine acceptance rate among 2047 healthcare workers in France was found to be 76.9%; doctors (92%) and physiotherapists (96%) were among the groups with the highest acceptance rates, while nurses (65%) and assistant nurses (60%) were among those with the lowest acceptance rates [24]. These results were attributed to low levels of health literacy, defined as receiving medical information as part of their interaction with the healthcare system [25]. Based on this definition, it can be suggested that future studies should investigate the relationship between health literacy and vaccination.

Most common reasons for not being vaccinated/being hesitant among both pediatricians and pediatric nurses included several factors: (1) thinking that vaccines were developed too quickly, (2) that the results of vaccine development studies in different phase are inconclusive, and/or (3) lack of knowledge about vaccines. Vaccine hesitancy can originate from several causes. Dube et al. [17] reviewed 22 qualitative studies that used the socioecological framework and found that vaccine hesitancy was influenced by previous experiences, emotions, ways of thinking, sources of information, family and friends, perceptions of disease risk, and trust in healthcare systems. A study conducted during influenza A/H1N1 and Ebola outbreaks, which can lead to pandemic, such as the COVID-19 pandemic, identified seven key points that influenced vaccine hesitancy or acceptance: (1) demographic features that affect vaccination, (2) vaccine availability and cost, (3) precautionary measures based on the decision to be vaccinated, (4) personal responsibility and perceptions of risk, (5) level of confidence in healthcare authorities and vaccines, (6) safety and efficacy of new vaccines, and/or (7) lack of information or misinformation about vaccines [18]. Similar to this study, Fakonti et al. [26] found COVID-19 vaccination acceptance to be related to nurses' and midwives' knowledge of vaccination. Gönüllü et al. [27] found pediatricians' concerns were caused by insufficient knowledge about new vaccines and especially by the lack of information on long-term side effects. Dara et al. [28] found results similar to those in our study and listed several main reasons for healthcare professionals not accepting vaccines: (1) insufficient information on safety of vaccines, (2) concerns about potential side effects of vaccination, (3) lack of sufficient data on safety, and (4) lack of data from clinical trials involving chronic diseases and COVID-19 vaccines. Another study reported that safety of vaccines influenced willingness to be vaccinated [29]. Studies have also shown that vaccine hesitancy may be influenced by several other factors, including the rapid development of COVID-19 vaccines globally, thinking that vaccines have not been used and tested for a sufficient period of time, thinking that a new vaccine is not needed, and limited public knowledge and misinformation [3, 30].

This study found that the country of origin of vaccines was a factor involved in vaccine-related decisions. Acı et al. [30] found that vaccine myths and prejudices about the country in which the vaccine was developed influence vaccination decisions. In line with our results, the same study reported that some participants were biased toward the country of origin of the

vaccine and would prefer waiting for a domestic vaccine. It has been hypothesized that healthcare professionals' confidence in vaccines is affected by the COVID-19 pandemic's impact on the whole world and negative information that has spread quickly on social media and prejudice. A study by Motta [31] concluded that Americans would be more inclined to accept vaccines if they were produced in the United States rather than in China, a finding that could be attributed to suspicions that the Chinese government was involved in the "creation" or "spread" of the virus. Based on these results, we can hypothesize that producing vaccines locally, if possible, could increase vaccine acceptance.

Most physicians and more than two-thirds of the nurses participating in the study reported that they did not consider advising or were hesitant to advise the COVID-19 vaccine for children if such a vaccine was available for them. When asked about the reasons for hesitancy, a greater proportion of nurses reported that they thought vaccines were developed too quickly and that the results of vaccine development studies in different phases were inconclusive. Vaccines, which save the lives of millions of children by preventing infectious diseases and related complications, are seen as one of the most effective ways of fighting infectious diseases today [32]. Studies on COVID-19 vaccination for children have mostly been conducted with parents who have reported the following reasons for hesitancy: (1) children are at a lower risk of contracting a disease, (2) concerns about safety, efficacy, and (3) rapid development of vaccines, (4) low education levels of parents, and/or (5) distrust of information available on the web/social media and vaccination policies [33, 34]. Vaccination prevents complications that might be caused by diseases and thus allows children to become more productive adults in the future eventually contributing to the welfare and development of the community. A report from the World Health Organization's (WHO's) Commission on Macroeconomics and Health qualified health interventions as "techniques for economic recovery and poverty reduction" and vaccination as "investment in human capital" [35]. Based on these findings, this study is important as it reveals pediatric healthcare professionals' hesitancy to advise vaccination, suggesting the need for trainings and interventions to protect and improve child health and contain the pandemic.

#### Limitations:

This study is a single center, time-limited study. The study involved only pediatricians and pediatric nurses; thus, the findings can only be generalized to this group.

#### Conclusion

Healthcare workers serve as role models for vaccination acceptance in the community. Identifying the reasons for vaccine hesitancy among healthcare professionals is key to protecting vulnerable populations and promoting vaccination in the community. Thus, we can recommend comprehensive in-service trainings on vaccine development processes and trial phases relating to COVID-19 vaccines, COVID-19 vaccination in children, and other training and interventions to counter vaccine hesitancy. It can be recommended that vaccines be produced domestically, if possible, as this process can contribute to vaccine confidence and acceptance.

#### Proposal for future research

The impact of educational studies on vaccine hesitancy can be addressed as education may contribute to vaccine trust and acceptance. Similarly, the impact of vaccination literacy on the vaccination status of pediatric healthcare professionals and their recommendation for vaccination to pediatric patients may be the subject of another study.

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# Timing of cesarean delivery for women with four or more previous cesarean sections

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**Ethics Committee Approval**

Ethics Committee approval was taken from the Bursa Yuksek Ihtisas Training and Research Hospital Ethics Committee, 2011-KAEK-25/2021/12-06.

All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

**Conflict of Interest**

No conflict of interest was declared by the authors.

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**Abstract**

**Background/Aim:** The number of recurrent cesareans is increasing worldwide, but the optimal timing for delivery in women who have had previous cesareans is controversial. The aim of this study is to determine the optimal timing of elective cesarean delivery in women with a history of four or more cesarean sections (CSs).

**Methods:** This retrospective cohort study was conducted in a tertiary hospital; 195 patients with a history of four or more CSs were grouped according to their gestation weeks on operation day and analyzed in terms of demographic features and clinical data as well as maternal and neonatal outcomes. Gestation weeks were grouped as 37-38 weeks and 39 weeks. Logistic regression analysis was used to determine the effect of independent variables on maternal and fetal outcomes.

**Results:** Of the 195 patients, 118 had CS between 37-38 weeks and 77 at 39 weeks. Clinical and demographic characteristics were similar among groups. The overall maternal complication did not differ between the groups (16.1% vs 16.9%,  $P = 0.885$ ). The 1<sup>st</sup> and 5<sup>th</sup> minute APGAR scores were significantly lower in the 37-38<sup>6</sup> weeks group ( $P = 0.013$  and  $P = 0.04$ , respectively). Logistic regression analysis found that neonatal 5<sup>th</sup> minute APGAR score was associated with a model including maternal age, number of previous CS, anesthesia type, gestational week at delivery, and neonatal birth weight.

**Conclusion:** Timing CS at 39 weeks in patients with a history of four or more CSs was found not to worsen maternal outcomes. Additionally, planning at 39 weeks could improve newborn outcomes.

**Keywords:** Cesarean section, Timing, Maternal outcome, Neonatal outcome

## Introduction

Cesarean section (CS) is a common procedure worldwide, and its rate has increased [1]. Previous CS appears to be the most common medical indication for cesarean delivery [2]. In this case, it could be stated that the number of recurrent CSs is gradually increasing. In developing countries, four or more repeated CSs could be encountered. However, the optimal timing for delivery in women who have had multiple previous CSs is controversial. Both neonatal and maternal risks should be considered together when deciding on the appropriate timing. While early intervention may increase neonatal morbidity, maternal risks may arise in case of delay [3, 4]. In addition to these risks, patient and physician convenience could be regarded as influencing factors for timing, albeit less important.

In general, it is recommended that elective CS not be performed before 39 weeks of pregnancy due to the risk of neonatal respiratory morbidity [5]. On the other hand, planning of CS at 39 weeks is also reported to increase the probability of onset of labor and the possibility of emergency delivery [6]. In addition, elective repeat CS planned at 39 weeks has also been shown to lead to adverse maternal outcomes versus scheduled delivery at 38 weeks [7]. Women with multiple prior low uterine transverse incisions show a particular trend towards an increased risk of rupture versus a single previous CS [8]. Some clinicians may prefer the timing of elective CS earlier than 39 weeks in women with a high number of previous CS to avoid maternal risks such as the onset of uterine contractions, the development of uterine rupture, and the necessity of emergency delivery. However, some have advocated that planned repeat CS should be performed in 39 weeks in patients who have had multiple previous CSs [9]. Thus, there is no consensus on best practice. These contradictory data makes it difficult to plan the timing of four or more repetitive CSs.

Therefore, this study aimed to compare the outcomes of CSs performed before and after 39 weeks in women who had 4 or more previous CS. and to determine the optimal timing of CSs in patients.

## Materials and methods

This retrospective study was performed in a tertiary education and research hospital. After obtaining local ethics committee approval (Bursa Yuksek Ihtisas Training and Research Hospital Ethics Committee, 2011-KAEK-25/ 2021/12-06), patients who had a history of four or more previous CSs and who delivered by CS in our hospital between January 2019 and December 2021 were examined from the medical records. Demographic data, medical history, laboratory tests, anesthesia data, as well as maternal and neonatal findings of the patients were recorded. The gestational week at which the patients had CS was calculated according to the crown-lump length (CRL). Subjects aged between 20-45 years, those with a history of four or more CSs, singleton pregnancies, and those whose medical records were fully obtainable were included. Multiple pregnancies, CSs before 37 weeks, those with a history of CS with classical uterine incision, those with a history of uterine rupture, those who have a history of COVID-19 infection during

pregnancy, major fetal anomalies, and premature rupture of membranes were excluded.

Cesarean delivery timing is planned on week 38 or 39 of gestation at our hospital. Our hospital is a tertiary referral center, and thus it was not always be possible to perform CSs on these planned days. The timing might change 2-3 days before or after the target date. Thus, the patients were divided into two groups according to their CS dates: 37<sup>0</sup>-38<sup>6</sup> weeks and  $\geq 39^0$  weeks. The maternal and neonatal data were compared between these groups. Primary outcome was composite maternal outcome, and secondary outcome was adverse neonatal outcome. Those who had CS with fetal distress and active labor indications were defined as emergency CS, and those who had scheduled CS were defined as elective CS. Uterine dehiscence was defined as separation of the lower uterine segment up to the serosa. Uterine rupture was defined as full-thickness separation of uterine wall including the serosa. Gestational diabetes was diagnosed with at least two abnormal results in the 75 g/100 g glucose tolerance tests. Those who were given antihypertensive treatment or those with preeclampsia after the 20<sup>th</sup> gestational week were defined as gestational hypertension disease.

### Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 21 (SPSS Inc., Chicago, IL, USA). The normality of the data was determined via the Shapiro Wilk test. Categorical data were calculated with the Chi-square test, and non-parametric data were calculated with the Mann Whitney U test. The results were presented as frequency and percentages for qualitative variables and mean (SD) or median (min-max) for quantitative variables. Multivariate logistic regression analysis was performed to detect the independent effects of variables on outcomes.  $P < 0.05$  was considered statistically significant.

## Results

There were 23,392 women who gave birth of which 8,695 were via CS (37.1%). After considering the inclusion/exclusion criteria, 195 patients were enrolled. Of the 195 patients, 118 had CS between 37-38<sup>6</sup> week and 77 at  $\geq 39^0$  weeks. There was no patient in the  $\geq 39^0$ -week group with a delivery date at 40 weeks or more. The median gestational week was 39<sup>3</sup> in that group and ranged between 39<sup>0</sup>- 39<sup>6</sup>. The clinical characteristics of the groups are given in Table 1. There were no differences between the groups in terms of age, number of previous CSs, and comorbid diseases (Table 1).

Table 1: Demographic and clinical characteristics of the groups

	37 <sup>0</sup> -38 <sup>6</sup> weeks (n = 118)	39 <sup>0</sup> weeks (n = 77)	P-value
Maternal age (years)*	34 (23-44)	33 (24-42)	0.148
Parity*	4 (4-6)	4 (4-7)	0.992
Cesarean Type			
Elective (n=167)	101 (85.6)	66 (85.7)	
Emergency (n=28)	17 (14.4)	11 (14.3)	0.981
Pregestational diabetes	2 (1.7)	3 (3.9)	0.342
Gestational diabetes	5 (4.2)	3 (3.9)	0.907
Hypertension in pregnancy	6 (5.1)	3(3.9)	0.699

Values are given n (%) and Chi square test was performed unless otherwise specified. \*Values are given as median (min-max), Mann Whitney U test was performed.

When the groups were analyzed in terms of maternal outcomes, the overall complication did not differ between the groups (Table 2). There were no differences in terms of bladder injury, uterine atony, abruptio placenta, and infectious morbidity.

However, the rate of uterine dehiscence was significantly high in the 39-week group (10.4% vs 3.4%,  $P = 0.04$ ) (Table 2). There was no uterine rupture diagnosed in either of the groups. The groups were similar in terms of blood loss or blood transfusion. The time to discharge did not differ between the groups. In addition, none of the patients had intestinal laceration or post-operative ileus.

Table 2: Maternal and neonatal outcomes of the groups according to cesarean timing

	37 <sup>0</sup> -38 <sup>6</sup> weeks (n = 118)	39 <sup>0</sup> weeks (n = 77)	P-value
Anesthesia			
General (n=77)	29 (24.6)	15 (19.5)	0.405
Regional (n=118)	89 (75.4)	62 (80.5)	
Maternal overall complications	19 (16.1)	13 (16.9)	0.885
Uterine Dehiscence	4 (3.4)	8 (10.4)	0.047
Bladder injury	3 (2.5)	1 (1.3)	0.549
Uterine atony	2 (1.7)	5 (6.5)	0.078
Postpartum Hysterectomy	9 (7.6)	0 (0)	0.013
Abruptio placenta	3 (2.5)	2 (2.6)	0.981
Surgical site infection	8 (6.8)	3 (3.9)	0.394
Blood transfusion	13 (11)	9 (11.7)	0.885
Preoperative Hb *(mg/dL)	11.23 (1.20)	11.45 (1.45)	0.408
Postoperative Hb *(mg/dL)	10.58 (1.38)	10.59 (1.40)	0.764
Postoperative HTC (%)*	32.05 (3.93)	32.14 (3.77)	0.858
Duration of hospitalization* (days)	2.57 (1.08)	2.49 (0.77)	0.765
Birth weight (gr)*	2944.06 (487.20)	3205.84 (401.69)	<0.001
APGAR score (1 min)	9 (0-9)	9 (4-9)	0.013
APGAR score (5 min)	10 (5-10)	10 (7-10)	0.040
NICU admission, n(%)	7 (5.9)	3 (3.9)	0.529
Perinatal mortality, n(%)	0 (0)	0 (0)	N/A

Hb: Hemoglobin, HTC: hematocrit, NICU: neonatal intensive care unit, N/A: not applicable. Values are given n (%) and median (min-max). Chi square test was performed unless otherwise specified. \* Values are given mean (SD), Mann Whitney U test was performed.

Regional anesthesia rather than general anesthesia was used in most patients (60.5% vs 39.4%). There was no difference between the groups in terms of anesthesia type (Table 2). No anesthesia-related complications were encountered in any of the patients.

There were nine patients who underwent postpartum hysterectomy. All nine patients were between 37<sup>0</sup>-38<sup>6</sup> weeks. Five of them were diagnosed with placenta accreta spectrum (PAS) and were scheduled for hysterectomy. Of the other four patients, three were referred to our hospital for delivery with the diagnosis of PAS. The remaining one patient underwent hysterectomy as a result of unsuccessful intrauterine balloon tamponade due to atony. Apart from this, there were six other patients diagnosed with atony across the whole study group. The intrauterine balloon tamponade system was used in five of the patients, and compression sutures were performed in one of them. These were treated successfully.

The results specific to newborns are shown in Table 2. As expected, birth weights were different between groups according to their weeks. The birth weight of the 37-38<sup>6</sup>-week group was lower than that of the 39-week group. Additionally, the 1<sup>st</sup>- 5<sup>th</sup>-minute APGAR scores were also significantly lower in that group. However, there was no difference between the groups in terms of neonatal intensive care unit (NICU) admission and no perinatal mortality (Table 2).

Logistic regression analysis was used to define the association between the timing of repeat CSs and neonatal 5<sup>th</sup> min APGAR score. Maternal age (< 35 years or ≥ 35 years), number of previous CSs (4 or > 4), gestational week at delivery, anesthesia type (general or regional), and neonatal birth weight were included as covariates. This model was found to be associated with neonatal 5<sup>th</sup>-minute APGAR scores ( $P = 0.001$ ,  $R^2 = 0.542$ ).

## Discussion

We compared the outcomes of CSs performed before and after 39 weeks to detect the most appropriate timing for women who had four or more previous cesarean deliveries. The maternal overall outcomes showed no significant advantage to planning the CS before 39 weeks in these patients. However, uterine dehiscence was significantly more common when CS was performed beyond 39 weeks. The presence of dehiscence was not associated with emergency CS in the 39-week group; only 18.2% (2/11) of emergency CS cases had dehiscence. In this case, the timing of CS before 39 weeks of gestation would likely not have an additional benefit in terms of maternal outcomes.

Contrary to our results, Helwick et al. [10] recommended that those with more than two previous CSs should be planned at 37 weeks of gestation because it improves maternal outcomes. That study had fewer patients than ours, and the exact maternal outcomes were not clearly stated. Unlike Helwick et al., Tita et al. [11] reported that composite maternal outcomes were increased in recurrent CSs in the early term period and recommended planning repetitive CSs at the 39<sup>th</sup> gestational week. However, four or more previous CSs were not evaluated separately in Tita et al.

Similar to our data, a recent review about more than two previous CSs stated that early term delivery (delivery at 37-38 weeks) for recurrent CS does not induce maternal benefit [12]. In addition, Mohammed et al. [13] found that repetitive CSs performed at ≥ 39 weeks had a higher risk of emergency CS than those at < 39 weeks (16.6% vs 10.6%, respectively,  $P < 0.05$ ). While our rate of emergency CS in all patients are higher than Mohammed et al. (14.3% vs 12.3%), we did not detect a difference among our study groups in terms of emergency CS rate. Mohammed et al. [13] also added that uterine rupture was more common in emergency CSs than elective CSs (3.8% vs 0.8% respectively,  $P < 0.05$ ), which contradicts our data. However, they did not declare a difference between groups of CS at < 39 weeks and ≥ 39 weeks in terms of uterine rupture. They had two complete ruptures and two uterine dehiscence cases. We observed no complete uterine rupture.

Neonatal outcomes were also evaluated. Although NICU hospitalization was similar between groups, the birth weight and APGAR scores were higher in the ≥ 39<sup>0</sup>-week group. We concluded that performing repetitive CS at 39 weeks induces neonatal benefits. In agreement with the present study, Hamadneh et al. [14] mentioned that CSs performed at 37 weeks had a higher risk of neonatal respiratory morbidity versus those at 38 weeks. The risk of stillbirth in later gestational weeks is an important factor in deciding the appropriate timing for an elective CS at term. Prior studies reported no increase in stillbirths after 39 weeks of gestation [15, 16]. We had no stillbirth regardless of the timing of CS.

A retrospective study in which 9.4% (83/886) of the patients had four or more cesarean sections reported no significant differences in terms of maternal outcomes between CSs performed at 37 and 38 weeks [14];

A retrospective study, in which 9.4% (83/886) of the patients had four or more cesarean sections, reported that there was no difference in terms of maternal outcomes between CSs performed at 37 and 38 weeks [14]; however, there was a

difference between the groups in terms of anesthesia type when maternal complications were reviewed. General anesthesia rates were higher in CSs at 37 weeks compared to those at 38 weeks (43.4% vs 34.1%,  $P = 0.005$ ) [14]. The authors mentioned that this may be related to the high rate of emergency CS at 37 weeks. We found no difference between the groups in terms of CS type and anesthesia type. Furthermore, 78.6% (22/28) of emergency CSs were given regional anesthesia.

Still another study compared repeat cesarean deliveries at 38 and 39 weeks; they found that neonatal respiratory morbidity decreased at 39 weeks versus 38 weeks, and there was no change in maternal complications between these groups [17]. Although the rate of unscheduled CS at 39 weeks was higher than that at 38 weeks, the authors recommended elective timing at 39 weeks regardless of the number of previous cesarean sections due to neonatal benefits. Our results were similar, but the number of patients with four or more previous CSs was not explicitly stated in that prior work. The same study added that the number of previous CSs was not associated with adverse neonatal outcomes [17].

To our knowledge, this is the first study to investigate maternal fetal outcomes in women with a history of four or more CSs to define the optimal timing for elective CS. The strengths of the study are that the study included only four or more cesarean section results and the relatively high number of patients enrolled relative to the existing literature. The groups were also quite similar in terms of demographic features and comorbid diseases. The fact that the majority of the patients (60.5%) received regional anesthesia—thus minimizing the effect of anesthesia on maternal and neonatal outcomes—increases the power of the study. On the other hand, some possible limitations to the study are as follows: a) all cases came from a single center and b) elective and emergency CSs were evaluated along with patients with PAS.

### Conclusion

In conclusion, the timing of CS at 39 weeks does not appear to worsen maternal outcomes in patients with a history of four or more CSs. In fact, planning at 39 weeks instead of 37-38<sup>6</sup> weeks could improve neonatal outcomes in this subset of patients. Prospective studies with a larger number of patients are needed to support this interpretation.

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## Outcomes of osteoporotic intertrochanteric fractures treated with cement-augmented proximal femoral nail

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**Ethics Committee Approval**

The study was approved by Istanbul Aydın University Clinical Researches Ethics Committee (approval number:2022-050.06.04/132).

All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

**Conflict of Interest**

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### Abstract

**Background/Aim:** Implant failure due to poor bone quality in osteoporotic intertrochanteric fractures increases mortality and morbidity, leading to secondary surgery and complications in patients. Our study aims to evaluate the early functional and radiologic outcomes and complications of osteoporotic intertrochanteric fractures using a cement-augmented proximal femoral nail design.

**Methods:** This case series included 24 patients AO (Arbeitsgemeinschaft für Osteosynthesefragen type 31-A2.2 in 10 patients, A2.3 in 7 patients, 31-A3.1 in 4 patients, and A3.2 in 3 patients). Proximal femoral nail cement augmentation was invariably accomplished by injecting polymethylmethacrylate (PMMA) cement into the femoral head. The clinical outcome was rated using the Harris Hip Score (HSS) at the time of the final follow-up. The results were recorded as excellent (score >90), decent (score 89–70), and poor (score 70–0). Radiographs were reviewed for implant failure and union. Implant failure was defined as lag screw cut-out or perforation.

**Results:** The average age of our sample was 73.8 (6.9) years, and the mean follow-up time was 13.6 months. In all patients, union was accomplished. Implant failure and cut-out were not observed in any of the patients. The average Harris score at the final follow-up was 80.6. According to the HSS, four patients had excellent, 15 had good, and 5 had poor functional results.

**Conclusion:** Cement-augmented femoral nails can be used safely with a low complication rate in osteoporotic intertrochanteric femur fractures. In future studies, controlled studies should be conducted for this nail design.

**Keywords:** Cement augmented proximal femoral nail, Osteoporosis, Trochanteric

## Introduction

Intertrochanteric fractures are common orthopedic injuries, most of which occur in elderly patients [1-3]. As the population ages and severe osteoporosis becomes more prevalent, the incidence of intertrochanteric fractures is expected to increase further [2-3]. The surgical treatment of intertrochanteric fractures aims to achieve early mobilization and restore functional capacity [1]. Management of this common injury is often challenging and controversial [1, 4]. Proximal femoral nail (PFN) fixation has long been considered an option for intertrochanteric fractures [4, 5]. Although PFN may be an attractive treatment method for unstable fractures in elderly patients, fixation with a nail in this age group is prone to complications due to osteoporosis, such as failure of fracture fixation and screw cut-out [4-7]. Poor bone quality results in insufficient mechanical stability [7]. Bone cement augmentation procedures effectively treat osteoporotic intertrochanteric fractures [8-9]. Cement-augmented fixation devices, including dynamic hip screw and on a nail have been used as a solution in unstable intertrochanteric fractures.

Our study uses a cement-augmented proximal femoral nail (PFN) design to assess the early functional, radiologic, and complication outcomes in osteoporotic trochanteric fractures.

## Materials and methods

The study was approved by the Istanbul Aydın University Clinical Research Ethics Committee (approval number: 2022-050.06.04/132) and adhered to the principles of the Declaration of Helsinki. Patients treated between September 2020 and December 2021 with cement-augmented PFNs due to intertrochanteric fracture were retrospectively analyzed. Patients under 65 years of age, patients with pathological fractures associated with lower limb fractures, and those without a follow-up for at least 6 months were excluded from the study. The osteoporosis severity of the patients included in the study was determined according to the Singh Index [10]. The Singh Index grades 1, 2, and 3 were included in the sample. The hip fracture types of the patients included in the study were determined according to the AO/OTA classification system. In addition, the database collected the age, gender, operation time, and intraoperative complications.

### Surgical procedure

We used epidural, spinal, or general anesthesia during the surgical procedures. Following successful anesthesia, patients were placed on an orthopedic fracture table in the lateral decubitus position. Typically, internal rotation and longitudinal traction were initially used to attempt closed reduction. In patients who were unable to undergo a closed reduction, a mini-open incision and hook were used to reduce the fracture. A small longitudinal incision was made 5 cm proximal to the greater trochanter. The gluteal fascia was incised, and the gluteus medius was bluntly split longitudinally and reached the tip of the trochanter. The appropriate entry site of the nail was determined with the aid of fluoroscopy, and the guide wire was advanced from the trochanter type to the medulla. A cannulated drill was inserted to prepare the entry of the nail (Tasarım Medical, Istanbul, Turkey) (Figure 1). After the drilled proximal femur,

the nail (130° and 200 mm) was inserted into the femur. With controlling fluoroscopy, lag screw guides were placed as close to the calcar on the anteroposterior radiograph as central on the lateral radiographs. After the appropriate location was determined, the measurement was recorded, and the lag screw was inserted. Afterwards, the fixation was strengthened with an anti-rotation screw, and compression was performed when necessary. The nail was statically locked from the distal with one screw. Polymethylmethacrylate (PMMA) bone cement was mixed and placed in a specialized cement gun (Figure 2). The cement gun contains threads that can adapt to the lag screw, which was inserted into the screw (Figure 3). The cement was injected into the femoral head under fluoroscopy control (Figure 4). After injection, the cement gun was removed, and the hole of the lag screw was closed with a screw. Postoperatively, the patients received standard prophylaxis for deep vein thrombosis. Patients were mobilized with weight bearing, as tolerated.

Figure 1: Design of cemented proximal nail. The white arrow indicates the holes at the tip of the lag screw.



Figure 2: Cement gun and the chamber in which the cement is placed.

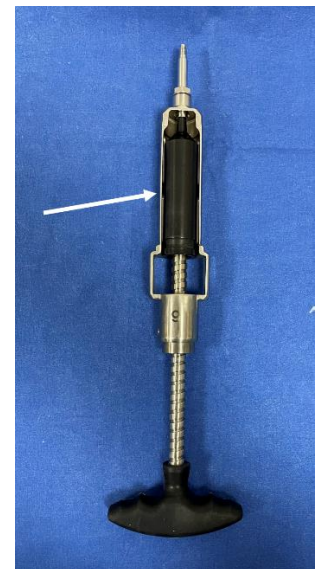


Figure 3: Connection of cement gun with lag screw on nail.



Figure 4: Monitoring cement application with fluoroscopy.



### Radiologic and clinical evaluation

Immediate postoperative radiographs were reviewed to reduction quality and to determine intra-articular leakage of cement. The postoperative reduction quality of the patients was determined as good, acceptable, or poor according to the reduction criteria defined by Baumgaertner et al. [11]. During follow-up, radiographs were reviewed for implant failure and union. Implant failure was defined as lag screw cut-out or perforation.

At the final follow-up, the functional level was estimated using the Harris Hip Score (HSS; <70 = poor, 70–89 = fair/good, and >90 = excellent) [12] and the visual analog scale (VAS) score [13].

### Statistical analysis

SPSS version 23.0 program was used to perform statistical analyses (IBM Corp., Armonk, NY). For continuous variables, descriptive data were reported as mean (standard deviation), or median (min–max), and as number and frequency for categorical variables. The categorical variables were also compared using the chi-square test.

### Results

A cemented augmented PFN was used as a surgical intervention for 34 intertrochanteric fractures. One patient died due to COVID-19 infection on postoperative day 12; 2 patients died due to pulmonary complications at 1 month postoperation; and 1 patient died due to cardiac failure in the third postoperative month. Of the remaining patients, 24 who had at least 6 months of follow-up were included in the study. Fourteen of these patients were female and 11 were male, with a mean (standard deviation) age of 73.8 (6.9) years. The mean follow-up period duration was 13.6 months. The mean time between surgery and admission was 2.3 (1.2) days.

The mean surgical time was 45.5 (12.4) minutes. According to the AO classification; 10 patients had AO 31-A 2.2, 7 had AO 31-A 2.3, 4 had AO31-A3.1, and 3 had AO 31-A3.2 type fractures. According to the Singh Index, the degree of osteoporosis was classified as stage 3 in 11 patients, as stage 2 in 9 patients, and as stage 1 in 4 patients (Table 1).

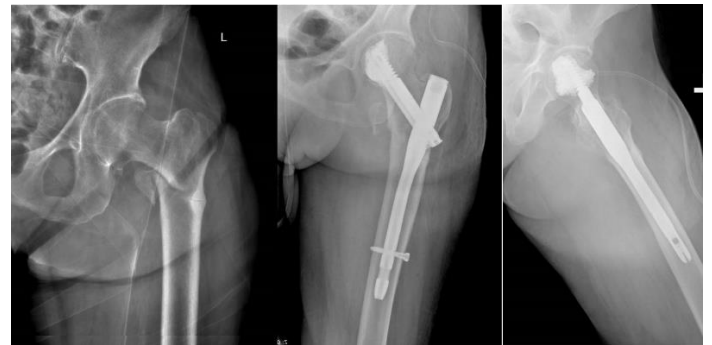
In the intraoperative evaluation, the mean blood loss was determined as 320.4 cc. Intraoperative erythrocyte suspension transfusion was applied to 8 patients. No complications developed in any of the patients during cement injection.

Early postoperative radiographs revealed an excellent reduction of intertrochanteric fracture in 15 patients and a good reduction in 9 patients. Cement leakage was observed in the joint in 1 patient (Figure 5). The average HSS at the final follow-up was 80.6. According to the HHS, 4 patients had excellent, 15 had good, and 5 had poor functional results. The mean VAS was found to be 2.3. In the final radiologic control, no patient had a screw cut out, perforation, or implant failure. Union was achieved in all patients (Figure 6).

Figure 5: Cement leakage in the joint following cement application.



Figure 6: Pre- and postoperative radiologic images of a 69-year-old female patient.



### Discussion

Insufficient fixation strength due to poor bone quality in osteoporotic intertrochanteric fractures remains the leading cause of implant failure [1]. The radiologic and clinical results of high-grade osteoporotic patients with intertrochanteric fractures treated with a novel cement-augmented PFN were the subject of this study. Our results indicate that cement-augmented PFNs can be a valuable option to prevent failure in osteoporotic intertrochanteric fracture.

Surgery to treat osteoporotic and unstable intertrochanteric fractures remains problematic in orthopedic practice [4]. Due to their biomechanical benefits, intramedullary implants are frequently utilized to treat unstable pertrochanteric fractures [2, 5, 14]. Although adequate stabilization is obtained with intramedullary nailing, implant failure, cut-out, and screw penetration are significant complications in osteoporotic patients [7, 14]. Poor bone quality is one of the major causes of mechanical complications [14–16]. Reduction in the mechanical properties of the bone due to osteoporosis predisposes fracture failure [2]. In patients with an osteoporotic bone, achieving adequate strength of the bone–implant construct may not be feasible [7, 17]. To address this problem, cement-augmented nails have become increasingly popular in recent years. In a recent prospective trial, Kammerlander et al. [18] evaluated patients with closed unstable intertrochanteric fractures treated

by proximal femoral nail anti-rotation (PFNA) with and without cement augmentation, finding that non-augmented PFNA may have the potential to prevent re-operations by strengthening the osteosynthesis construct. A biomechanical cadaver study confirmed that cement augmentation with PFNA has higher implant stability than the non-augmented group [19]. Another biomechanical study discovered that femoral heads that had been supplemented showed greater rotational stability and pull-out resistance than femoral heads that had not been augmented [20]. Implant failure and cut-out were not observed in any of the patients in our cohort group, which supports the proposition that cement augmentation increases implant stability in osteoporotic intertrochanteric fractures.

Some complications in cement augmentation may include bone cement implantation syndrome and cement leakage [21-23]. Bone cement implantation syndrome is a deadly complication of orthopedic procedures involving bone cement, and it is characterized by hypoxia, hypotension, cardiac arrhythmias, and cardiac arrest [21].

No patients in our study had a 20% reduction in blood pressure perioperatively, and none had SpO<sub>2</sub> <88. Anesthesia teams are cautioned to apply anesthetics slowly and with low pressure, to prevent bone cement implantation syndrome before cement injection. A cement leak occurred in 1 patient in the study; however, no complications were observed in this patient in the follow-up period. Care should be taken not to perforate the femoral head of the guide wire of the lag screw in order to prevent cement leakage. During cement injection, it should be ensured that sufficient cement has reached the femoral head using anterior, posterior, and lateral fluoroscopy images.

### Limitations

This study has some limitations. Firstly, the sample size of the experimental group was relatively small. Secondly, the follow-up period was relatively brief. Thirdly, a comparison group was absent. Thus, future studies are encouraged to use larger sample sizes and longer follow-ups.

### Conclusion

This study demonstrated that this PFN design, which offers cement augmentation, is likely to provide mechanical advantages and reduce implant failure. It can be a valuable option for treating osteoporotic intertrochanteric fractures with a low complication rate.

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# The effects of sound-and-light toy as a distraction method on pain and physiological parameters in infants regarding circumcision procedure

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**Ethics Committee Approval**

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All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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**Abstract**

**Background/Aim:** Circumcision is a common surgical procedure and a cause of pain and stress for infants. Nurses are in a key role for providing pain relief through implementation of non-pharmacological practices for pain management. This study aimed to assess the impact of distraction using a sound- and light-producing toy on pain and physiological parameters in infants regarding circumcision procedure.

**Methods:** This randomized controlled study was conducted with infants between six months and two years of age who presented to a private circumcision clinic. The sample consisted of 60 infants randomly allocated into intervention (n = 30) and control (n = 30) groups. During the procedure, the mothers of the infants in the intervention distracted the infants with the toy for 15 min. Infants in the control group were accompanied by their mothers during the procedure and did not receive any additional intervention other than the standard care. Data were collected using a questionnaire and the face, legs, activity, cry, consolability (FLACC) pain scale. Data were assessed using descriptive statistical analyses and parametric tests.

**Results:** Infants in the intervention and control groups were similar in terms of current and gestational ages, lengths, weights, and maternal and paternal ages and showed no differences in terms of physiological parameters before and after the procedure ( $P > 0.05$ ). Post-operative pain scores were lower in infants exposed to the toy with light- and sound than that in the infants in the control group; however, no significant difference between groups was found ( $P > 0.05$ ).

**Conclusion:** Considering the effect of sound- and light-producing toys on causing a reduction in pain severity, it may be recommended to use distracting practices by nurses to reduce/relieve pain associated with circumcision.

**Keywords:** Infant, Circumcision, Pain, Toy

## Introduction

Circumcision, the most common surgical procedure known worldwide, is estimated to have a global prevalence of 37% to 39% [1]. Owing to the high rates of circumcision among Muslim and Jewish men, the prevalence of this procedure in the Middle East and North Africa exceeds 95%. Circumcision prevalence in the United States (USA) is 91% among Caucasians, 76% among African-Americans, and 44% among Hispanics [1, 2]. The majority of the population in Turkey is Muslim, and circumcision is traditionally performed on male children at an early age. Although the most appropriate age for circumcision is between less than one year and one year of age, circumcision is reported to be performed usually between one and seven years of age in Turkey [3, 4].

Circumcision is a surgical procedure that typically heals within a week and has a low rate of adverse effects when performed by specialized physicians in a hospital setting. However, circumcision, which is a relatively frightening experience for children, is a cause of physiological stress and pain [5, 6]. Intra- and post-operative pain management is of particular importance in children during the circumcision procedure [6]. Pain relief in children is reported to minimize the need for medications during the post-operative period, shorten the length of hospital stay, improve patient satisfaction, and play an active role in reducing morbidity and mortality [7]. Pain management is best performed using a multimodal approach that combines pharmacological and non-pharmacological methods [8, 9]. Nurses are in a pivotal role to provide pain relief and improve the quality of life in children through implementation of non-pharmacological practices for pain management [10, 11].

Although a variety of methods are available for use in pain management for children, the American Pain Society, and studies in this area recommend using cognitive behavioral methods, particularly distraction in infants and young children [10–13]. Distraction can be used to strengthen coping mechanisms before and after an intervention, to minimize anxiety associated with an intervention, and to help calm the child after an intervention [14]. Guidelines and experts recommend using toy-mediated distraction during invasive procedures in children younger than three years as this technique is more effective in children in that age group [14–17]. However, to the best of our knowledge, no study has yet investigated these practices in the context of post-operative pain associated with circumcision. Thus, the aim of this study was to examine the effect of distraction using a sound- and light-producing toy on pain levels and physiological parameters in infants undergoing circumcision.

## Materials and methods

### Study design

This randomized controlled study was conducted between November 2021 and February 2022. Reporting of the study results is according to the latest version of the Consolidated Standards of Reporting Trials (CONSORT) guidelines. The hypotheses of the study are listed below.

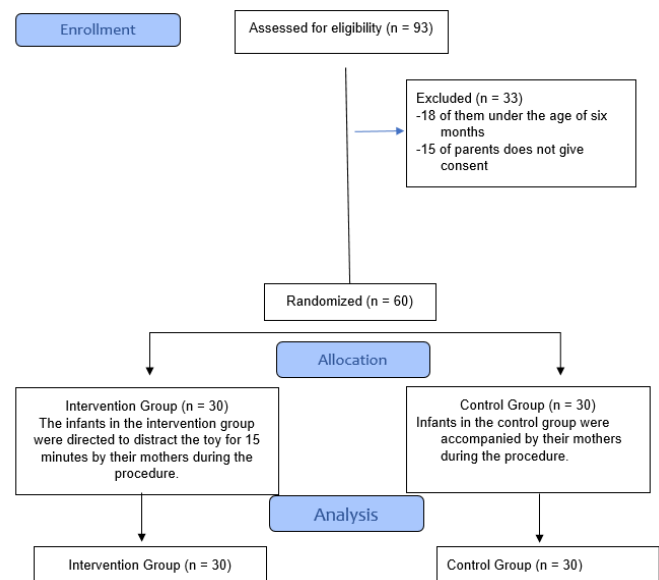
H<sub>1</sub>: Distraction using a sound- and light-producing toy affects pain associated with circumcision in infants.

H<sub>2</sub>: Using a sound- and light-producing toy affects post-operative physiological parameters associated with circumcision in infants

### Recruitment, randomization, and sample size

The sample consisted of infants ranging in age from six months to two years of age who presented to a private circumcision clinic between the specified dates, who did not show any chronic diseases, and whose parents provided written consent to participate in the study. Between specified dates and while researchers were in the clinic, 93 infants were circumcised at the clinic, and 33 of them were excluded because they did not meet the criteria (Figure 1). The sample size consisted of 60 infants. Infants were randomly categorized into the intervention and control groups using Urn randomization. This method features two parameters represented by  $\alpha$  and  $\beta$ , and the parameters represent balls of two different colors, namely black and white. A ball was drawn randomly from a black bag by a nurse other than nurse researchers with her eyes closed, and the infant was assigned to one of the study groups depending on the ball's color. This assignment process was repeated for each infant. The white ball represented the intervention group, and the black ball represented the control group [18, 19]. Based on this method, 60 infants were allocated into one of the study groups, 30 and 30 in the intervention and control groups, respectively. Power analysis was performed by researchers to determine the adequacy of the sample size. According to the power analysis in G\*Power 3.1.9.2,  $1-\beta$  was found as 0.85 ( $\alpha = 0.05$ , Df = 58, effect size  $|p| = 0.72$ ).

Figure 1: Consolidated Standards of Reporting Trials (CONSORT) flow diagram of the study



### Intervention

At the time of initial presentation for circumcision, infants were evaluated by the surgeon in terms of overall medical history and any disease(s) that would prevent circumcision. Subsequently, the date and time were selected for circumcision in agreement with the family, and an appointment was scheduled. Prior to circumcision, families were sent videos to inform them about the circumcision process and steps that need to be taken before and after the procedure. Circumcision was performed by the same surgeon (researcher-MD). All infants

were administered local anesthetics that had been prepared before circumcision (Bupivacaine 0.5%, 1 mg/kg; Lidocaine, 1 mg/kg) via dorsal penile nerve block and infiltration anesthesia (ring block). Circumcision was performed using the sleeve technique. This technique consists of marking the skin and mucosal line to delimitate the circumcision limits followed by a circumferential incision of the skin and mucosa over the marked areas using a scalpel. The part of the skin and mucosa between the two incisions is excised circumferentially. The procedure is terminated by approximating the proximal skin to the distal mucosa using 5/0 Vicryl Rapide sutures. The first 5 min was spent taking the infant to the operating table, stabilizing him, and information was provided to parents by the pediatric surgeon. Circumcision required a median duration of 15 min in both groups. During the procedure, mothers remained with their infants. After the procedure, the infant was moved to another room with her parents to monitor his general condition and physiological parameters.

**Intervention group (Group distracted using a toy with a light and sound):** Before the surgery, mothers were introduced to the toy and received instruction on how to use toy. During the procedure, toy distraction was directed by their mothers for 15 min. Distraction consisted of concurrent visual and auditory stimuli with three different sets of soothing music and projection entertainment. The toy was sterilized after each use.

**Control group:** Infants in the control group were accompanied by their mothers during the procedure and did not receive any additional intervention other than standard care.

Physiological parameters and pain assessments were performed 15 min before and 30 min after the procedure for infants in both groups. Physiological parameters were measured by the same researcher. Pain assessments were implemented separately by two researchers (Ph.D., RN). Inter-rater agreement between the two researchers was evaluated according to the intra-class correlation coefficient (ICC), and the ICC was found to be higher than 0.90. The patients were routinely discharged with a home follow-up form 30 min after the circumcision procedure.

#### Data Collection Tools

**Introductory Questionnaire:** This questionnaire was prepared by the researchers. It contained items related to the sociodemographic characteristics of the infant and their parents in addition to physiological parameters (heart rate, respiratory rate, oxygen saturation, body temperatures) of the infant.

**The Face, Legs, Activity, Cry and Consolability (FLACC) pain scale:** The FLACC pain scale was developed by Merkel et al. [20] in 1997 and is used to assess behavioral reactions to pain in children between the ages of two months and seven years who are unable to verbalize or communicate their pain. FLACC pain scale assesses five behavioral domains (facial expression, leg movement, activity, crying, and consolability), and each item is assigned a score of 0–2. The scale yields a minimum of 0 and a maximum of 10 points. Higher scores denote a higher level of pain, whereas lower ones denote less pain. The Turkish validity and reliability study for the FLACC pain scale was conducted by Şenaylı et al. [21] with toddlers and children one month to nine years of age who presented to a

pediatric surgery clinic. This scale is observational scale and can be applied by healthcare professionals.

#### Pulse Oximeter

Infants in the intervention/control group had their pre- and postoperative oxygen saturation levels and heart rate measured by “plusMED plus-50DL Finger Type” Pulse Oximeter. The device has Conformité Européenne (CE) certification. The pulse oximeter was deemed suitable for use in children. The screen of the device displays oxygen saturation percentage (SpO<sub>2</sub>) and the heart rate both numerically and as a bar graph. In case of non-contact, the device emits a visual signal.

#### Light- and Sound-Producing Toy

The toy has a plastic and soft structure for comfortable manipulation, and in accordance with the regulation of the Ministry of Health, does not involve any risk for children, namely, no small parts that can be swallowed. The toy projects green, blue, and red lights and stars. The light pulse lasts approximately 10 s. The toy is shaped like a ladybug (in dimensions, 10 x 22.50 x 22.50 cm), and when the wings unfold, it emits light and projects stars. The music consists of three different soothing tones.

#### Ethical aspects

Before starting the study, necessary permissions were obtained from the relevant institution and the Yozgat Bozok University clinical research ethics committee (Decision number: 2021.09.27\_05). The parents provided written informed consent after being informed about the purpose of the study and the confidentiality of the data.

#### Statistical analysis

Data were analyzed using the IBM SPSS Statistics V 25.0 (IBM Corp., Armonk, NY, USA) software suite. Descriptive data were expressed in minimum (min), maximum (max), mean (mean), standard deviation (SD), and median (M) values. Data were checked for normality of distribution using the Shapiro–Wilk test. The homogeneity of variance was evaluated using Levene’s test. For group comparisons, the independent and paired t-tests were used. Inter-rater agreement was analyzed using the intra-class correlation coefficient (ICC). Statistical significance was set at  $P < 0.05$ .

## Results

Table 1 presents the demographic characteristics of the infants in the intervention and control groups. Infants included in the study had a mean current age of 10.87 (6.90) and 11.18 (6.58) months, mean length of 74.43 (11.06) and 73.97 (11.16) centimeters (cm), and weight of 9.48 (3.11), and 9.74 (3.06) kilograms (kg), respectively. The groups were similar in terms of gestational age, current age, height, weight, and maternal and paternal age ( $P > 0.05$ ) as shown in Table 1.

Table 1: Similarity criteria of groups

Features	Intervention group (n = 30)		Control group (n = 30)		Test/P-value
	Mean (SD)	M(min-max)	Mean (SD)	M(min-max)	
Gestational age (week)	38.93 (0.76)	39(38-40)	39.16 (0.88)	39(38-41)	t = -1.058 P = 0.294
Current age (months)	10.87 (6.90)	6.50(6-24)	11.18 (6.58)	8(6-24)	t = -0.179 P = 0.858
Length (cm)	74.43 (11.06)	70.50(60-97)	73.97 (11.16)	71(60-99)	t = 0.160 P = 0.874
Weight (kg)	9.48 (3.11)	8.25(6-18)	9.74 (3.06)	9(6-18)	t = -0.332 P = 0.741
Maternal age (year)	30.14 (5.23)	30.50(19-39)	30.75 (5.03)	30(22-42)	t = -0.457 P = 0.649
Paternal age (year)	34.82 (5.90)	35(25-49)	34.72 (6.89)	35(22-52)	t = 0.061 P = 0.951

SD: standard deviation

The distribution of physiological parameters for the infants in the intervention and control groups before and after the procedure is presented in Table 2. Pre- and post-operative heart rates (beats per minute) were 95.75 (8.94) and 94.93 (8.45) in infants in the intervention group and 99.31 (9.15) and 97.50 (8.08) in infants in the control group, respectively. Pre- and post-operative respiratory rates (breaths per minute) was 20.50 (2.53) and 21.07 (2.85) in infants in the intervention group and 21.50 (2.32) and 21.81 (1.63) in infants in the control group, respectively. Pre- and post-operative oxygen saturation levels (mm Hg) for the intervention group were 95.75 (2.10) and 95.43 (2.42) and for the control group were 95.38 (2.13) and 95.22 (2.39), respectively. Pre- and post-operative body temperatures (°C) for the intervention group were 36.62 (0.24) and 36.62 (0.19) and for control group were 36.68 (0.19) and 36.62 (0.17), respectively. No statistically significant differences between the groups in terms of physiological parameters ( $P > 0.05$ ) were noted (Table 2).

Table 2: Comparison of physiological parameters before and after the procedure

Parameters	Intervention group (n = 30)		Control group (n = 30)		Test/P-value
	Mean (SD)	M(min-max)	Mean (SD)	M(min-max)	
Heart rate					
Pre-procedure	95.75 (8.94)	97(80-116)	99.31 (9.15)	98(82-118)	t = -1.520 P = 0.134
Post-procedure	94.93 (8.45)	92(82-118)	97.50 (8.08)	97(82-116)	t = -1.203 P = 0.234
Test/P-value	t = 0.713; P = 0.482		t = 1.574; P = 0.126		
Respiratory rate					
Pre-procedure	20.50 (2.53)	20(18-28)	21.50 (2.32)	22(18-28)	t = -1.594 P = 0.116
Post-procedure	21.07 (2.85)	20(18-28)	21.81 (1.63)	22(20-24)	t = -1.253 P = 0.215
Test/P-value	t = -0.955; P = 0.348		t = -0.668; P = 0.509		
Oxygen saturation					
Pre-procedure	95.75 (2.10)	96(90-99)	95.38 (2.13)	95.5(92-99)	t = 0.683 P = 0.497
Post-procedure	95.43 (2.42)	96(88-98)	95.22 (2.39)	95.5(88-99)	t = 0.336 P = 0.738
Test/P-value	t = 0.000; P = 1.000		t = -0.671; P = 0.507		
Body temperature					
Pre-procedure	36.62 (0.24)	36.6(36.0-37.2)	36.68 (0.19)	36.7(36.2-37.2)	t = -1.049 P = 0.298
Post-procedure	36.62 (0.19)	36.6(36.2-37.0)	36.62 (0.17)	36.6(36.3-37.2)	t = 0.000 P = 1.000
Test/P-value	t = -0.091; P = 0.928		t = 1.579; P = 0.124		

SD: standard deviation, M: median

Pre- and post-operative pain scores for the infants are shown in Table 3. Pre-operative pain scores of the infants in the intervention and control groups were 0.71 (1.50) and 0.93 (1.07), and no significant intergroup difference was observed ( $P = 0.441$ ). However, post-operative pain scores were 5.03 (3.01) in the intervention group and 6.15 (2.81) in the control group. Although mean pain scores were lower in infants in the intervention group, no significant intergroup difference was observed ( $P = 0.142$ ). According to intra-group comparisons, post-operative pain scores were significantly higher in both

groups than pre-operative scores ( $P < 0.001$ ) as shown in Table 3.

Table 3: Comparison of Face, Legs, Arms, Cry, Consolability (FLACC) pain scores before and after the procedure

FLACC Pain Scores (0-10)	Intervention group (n = 30)		Control group (n = 30)		Test/P-value
	Mean (SD)	M(min-max)	Mean (SD)	M(min-max)	
Pre-operative	0.71 (1.50)	0.0(0.00-5.00)	0.93 (1.07)	1.00(0.00-5.00)	t = -.776 P = 0.441
Post-operative	5.03 (3.01)	5.0(1.00-10.00)	6.15 (2.81)	5.0(1.00-10.00)	t = -1.488 P = 0.142
Test/P-value	t = 6.791; P < 0.001		t = 11.580; P < 0.001		

SD: standard deviation

## Discussion

Toys are readily available, can easily be used as a source of distraction, and are thought to have a clinically important effect in reducing pain in children in cooperation with parents. Studies have reported that using toys of different types as a means of distraction is effective in reducing/relieving pain in children [14, 15, 22]. In the current study, the aim was to evaluate the impact of toy-mediated distraction on circumcision pain in infants aged six months to two years. No significant difference was observed in terms of the pre-operative FLACC scale scores and physiological parameters between the intervention and control groups; thus, it is evident that measurements were similar in both groups.

In this study, mean post-operative pain scores were 5.03 (3.01) in the intervention group and 6.15 (2.81) in the control group. Mean pain scores were lower for infants exposed to distraction mediated by the light- and sound-producing toy; however, the difference was not statistically significant. No differences between the groups in terms of physiological parameters were found. Since no previous study on the use of toys in infants during the circumcision process is available, the data were discussed with the findings of other studies using toys as a method of distraction in pain management. According to this concept, Ateş Beşirik and Gözen [23] investigated the impact of breastfeeding and toy-mediated distraction as a means to reduce/relieve pain in 120 infants between 1 and 12 months of age, and assessed pre- and post-immunization pain levels using the FLACC scale. Post-immunization pain scores in infants in the toy group (4.39 [2.18]) were significantly lower than those in the breastfeeding group (7.05 [1.55]). The post-vaccination SpO<sub>2</sub> value was higher in infants in the toy distraction group, whereas heart rate was lower in this group compared to the breastfeeding group. Dabas [24] conducted a study to investigate the effect of distraction techniques on pain severity in 100 infants who were 10-14 weeks of age and received a pentavalent vaccine. Infants were allocated to one of four groups: (1) electronic toy group, (2) key toy group, (3) simple toy group, or (4) control group. Analysis using the FLACC pain scale revealed that the mean pain score was higher in the control group (7.16 [0.16]) as compared to that of the electronic toy group (2.60 [0.16]), key toy group (4.80 [0.22]), and simple toy group (5.44 [0.18]). These results are in line with our results. Ristia et al. [15] conducted a study with 34 children aged 1-5 years and asked the parents of infants in the intervention group to try to distract their children using a teddy bear during intravenous access on the children (n = 17), while the control group received no intervention (n = 17). Pain severity was evaluated using the



FLACC scale with a single measurement after the procedure. They reported that the mean pain score in the intervention group was lower than that of the control group, which is consistent with our results. Gedam et al. [25] investigated the effectiveness of audio-visual distraction techniques in 350 children during and after vaccination. In addition, children in the first group were encouraged to play with light- and sound-producing toys, children in the second group were encouraged to watch cartoons, and children in the third group did not receive any distraction while receiving their immunizations. Pain levels were assessed using the FLACC pain scale. Pain scores were lower in children in the intervention groups during and after the procedure than those in the control group. The study results demonstrated that light- and sound-producing toys and cartoons were effective in producing a reduction in pain during routine medical interventions in children. Logan et al. [22] conducted a study with 54 children aged 3–10 years who were randomly allocated to one of three interventions: (1) interactive teddy bear, (2) digital avatar version of the teddy bear, and (3) normal plush teddy bear. They assessed distress and pain levels before and after the procedure. Children exposed to interactive teddy bears were reported to have more positive results characterized by higher levels of joy and compliance compared to those exposed to plush toys. These results are similar to the results of the current study.

### Strengths and limitation

The present study has some important strengths. First, this study is the first to evaluate the effects of a sound-light toy on pain during circumcision in children aged six months to two years. Second, the strength of the study is that the method of this study is based on the CONSORT guidelines. On the other hand, our study has several limitations. Because of the nature of the intervention, study subjects and outcome assessors could not be blinded to the intervention. In addition, in this study, post-operative pain assessment of children was obtained at 30 min to evaluate the real pain that the children will feel after the surgery, to have intensive patient circulation in the clinic, and to prevent bias. Our study was conducted in a private clinic, which may limit the generalizability of our results.

### Practice implications

Circumcision is one of the most common procedural painful interventions experienced by the majority of boys in Turkey. In this process, the comfort of infants deteriorates, and their physiological parameters are affected. Pain intervention with non-pharmacological methods can prevent harmful pain-related effects. In this study, an evidence-based randomized controlled study approach was used to determine the effect of distraction with a sound-light toy on pain during circumcision in infants aged six months to two years. It has been determined that a non-pharmacological practice, such as the use of toys with sound and light during circumcision, leads to a reduction in post-operative pain in infants. Based on this result, nurses should include non-pharmacological methods in pain management.

### Conclusion

In this study, post-operative pain scores were lower in infants exposed to toy with light- and sound than that in the infants in the control group; however, no significant difference between groups was found. Considering distraction using a light-

and sound-producing toy had an effect on reducing the severity of post-operative pain associated with circumcision in infants, further studies using different distraction practices or non-pharmacological methods are warranted in infants.

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# Does a relationship between type of hip fracture and osteoarthritis exist?

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**Ethics Committee Approval**

This study was approved by the Ethics Committee  
of Hatay Mustafa Kemal University (Decision  
no/date: 10/ May 12, 2022).

All procedures in this study involving human  
participants were performed in accordance with  
the 1964 Helsinki Declaration and its later  
amendments.

**Conflict of Interest**

No conflict of interest was declared by the  
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**Abstract**

**Background/Aim:** Many factors have been associated with the etiology of falls and hip fractures in the elderly. However, only a few studies have examined the relationship between osteoarthritis and hip fractures, which are common in this age group. The aim of this study was to determine the relationship between the knee and hip osteoarthritis (OA) and the type of hip fracture.

**Methods:** Patients who underwent surgery in the Orthopedics and Traumatology Department between January 2017 and December 2021 were eligible to participate in this retrospective cohort study. Patients who were 60 years and older with a hip fracture and adequate medical records and radiographs of bilateral hip and knee joints met the inclusion criteria. Data concerning patient co-morbidities, type of hip fracture, whether they had OA in their hip and knee joints, and the severity of their OA were assessed. The severity of the osteoarthritis presence was categorized with using the Kellgren–Lawrence (KL) classification. To categorize the patients, three groups were identified: (1) femoral neck, (2) trochanteric, and (3) subtrochanteric fracture groups. The presence and severity status of OA in the hip and knee joints and co-morbidity data were compared between the groups.

**Results:** Three-hundred forty-one patients with a M/F ratio of 148/193 are included in this study. Femoral neck fractures occurred in 142 (41.6%), trochanteric fractures in 147 (43.1%), and subtrochanteric fractures in 52 (15.2%) patients. The mean age of the cohort was 76.72 (10.165); The mean age of the patients in the trochanteric group was higher than in the subtrochanteric group ( $P = 0.001$ ). No effect of any existing co-morbidities on fracture type was observed. The overall prevalence of OA in the cohort that was observed in the hip joint was 34.3% with 33.7% in males and 35.3% in females. These rates were 66.6%, 53.4%, and 76.7% in the knee joint, respectively. No difference could be observed between hip OA presence and any type of hip fracture group ( $P = 0.833$  for right hip,  $P = 0.865$  for left hip). Similar rates of moderate and severe hip OA were found in the femoral neck and trochanteric fracture groups. However, the frequency of moderate hip OA was lower and the frequency of severe hip OA was higher in subtrochanteric fracture group compared to other groups ( $P = 0.164$  for right hip,  $P = 0.241$  for left hip). Knee OA was observed to be more common in the trochanteric fracture group ( $P = 0.003$  for the right knee,  $P = 0.002$  for left knee) and also, the rate of severe OA was higher in the trochanteric fracture group compared to other groups ( $P = 0.013$  for right knee,  $P = 0.006$  for the left knee).

**Conclusion:** In contrast to OA presence in the hip, knee OA presence and severity can be significant risk factors for occurrence of trochanteric type fractures in the elderly.

**Keywords:** Hip fractures, Osteoarthritis, Hip, Osteoarthritis, Knee

## Introduction

Although osteoporosis and falling are thought to be the two main risk factors for hip fractures, other factors have been recognized as contributing to fractures, including physical characteristics of the patient, bone morphology, the fall that results in the fracture, joint diseases that can affect gait and balance, neurological diseases, muscle weakness, proprioception disorders, chronic diseases, drugs, and visual issues and etc. [1-7]. It has also been reported that the nature and severity of the fall event have no impact on the type of fracture [1, 2]. A significant health issue that restricts daily living activities for elderly people is osteoarthritis (OA), particularly in the hips and knees [8, 9]. Some researchers have previously assessed the relationship between any fracture caused by an OA-related fall event. In a cohort of 258,696 patients, Jacob and Kostev [10] reported a 1.4-fold increased risk of fracture in patients with OA. While several studies demonstrating how hip and knee OA affect the etiology of falls are available [11, 12], relatively few reports demonstrating how fracture, its morphology, or fracture type are affected have been published. While the presence of OA was confirmed radiographically, in some of these cases, analyses between OA and hip fracture geometry were made in others by assuming the presence of OA based on pain or symptoms as assessed using questionnaires [13–15]. These analyses have frequently questioned whether OA contributes to the type of fracture that occurs and whether it leads to hip fractures. However, these outcomes are inconsistent with each other. The relationship between the type of fracture and the presence of OA in knee joints is also unclear [3, 16–19].

The primary objective of this study was to investigate the impact of hip and knee joint OA on various hip fracture types. Additionally, assessing whether a relationship between chronic diseases and the type of fracture exists was also intended.

## Materials and methods

This retrospective cohort study was approved by the Ethics Committee of Hatay Mustafa Kemal University (Decision no/date:10/ May 12, 2022) and performed in accordance with the Declaration of Helsinki. Patients who had surgery in the Orthopedics and Traumatology Department between January 2017 and December 2021 were enrolled. The inclusion criteria were: patients who were 60 years and older with diagnosis of hip fracture and who had adequate medical records and radiographs of bilateral hip and knee joints. Patients younger than 60 years old, patients with insufficient medical records, pathological hip fractures, hip fractures caused by high energy trauma, history of inflammatory arthritis, developmental and/or congenital pathologies of the lower extremity, muscular dystrophy, lower extremity trauma, and prior surgery (such as hip/knee arthroplasty) that could cause changes in kinematics were excluded.

Three-hundred forty-one patients (193 women, 148 men) were enrolled in the study. The type of hip fracture, the presence and severity of OA in the hip and knee joints, and the patients' pre-operative co-morbid conditions were noted. The Picture Archiving and Communication System (PACS) system

was used to perform radiographic evaluations and the presence of joint space narrowing, osteophyte formation, subchondral sclerosis and cysts in bilateral hip and knee joints were all noted. Data concerning the patients' co-morbidities, the type of hip fracture, whether they had OA in their hip and knee joints, and severity of their OA were assessed. The severity of the osteoarthritis presence was categorized using the Kellgren–Lawrence (KL) classification [20]. We partitioned the patients into two groups: (1) those with OA (+) and (2) those without OA (non-OA) order to assess the relationship between OA and the type of hip fracture. To avoid any confusion, KL stage 1 patients with possible osteoarthritic changes were placed in the non-OA group, while all other patients identified as KL stage 2, 3, or 4 were placed in the OA (+) group. In further analyses, patients were classified according to the severity of OA: patients diagnosed as stages 0 and 1 were classified as non-OA, (2) stage 2 as moderate, and (3) stages 3 and 4 as severe OA. The hip fracture type was determined, and patients were classified into three groups: (1) femoral neck, (2) trochanteric, or (3) subtrochanteric fracture groups. Additionally, thorough analyses were conducted by classifying the patients into intracapsular femoral fractures (ICFs) and extracapsular trochanteric fractures (ECFs) and when necessary, the subtrochanteric ones were included as were the fracture groups [21].

### Statistical analysis

Statistical analyses were conducted using the Windows-based SPSS 22 program (IBM Corp. Armonk, New York, USA). To determine means, standard deviations, and ranges, a descriptive analysis was performed. To determine whether the variables adhered to the normal distribution, the Kolmogorov–Smirnov tests were used. Mean and standard deviation values were given for variables with normally distributed distributions. Counts (n) and percentages (%) were presented for the nominal variables. To investigate the relationships between hip and knee OA status, KL stages, OA severity, gender, comorbidities, and fracture types, the chi-squared and Fisher's exact tests were used. Analysis of variance (ANOVA) and post hoc test (LSD test) was used to analyze the age differences between the groups. A *P*-value of 0.05 or lower was considered statistically significant.

## Results

Descriptive information and comorbidity data of the patients are given in table 1. The overall prevalence rate of OA in the hip joints in the cohort was 34.3%; 33.7% in males and 35.3% in females. These rates were 66.6%, 53.4%, and 76.7% in the knee joints, respectively. The rates of OA presence in the patients in the different fracture type groups are given in table 2. When evaluated using the KL classification, no statistically significant differences in hip joint OA severity status distribution between the groups of fracture types ( $P = 0.132$ ) were found (Figure 1). Similar to this result, when comparing the fracture type groups, no difference in the distribution of the knee joint OA severity status ( $P = 0.065$ ) was found (Figure 2). The comprehensive analysis revealed that the fracture type groups' gender distributions were comparable ( $P = 0.392$ ). The rates for KL OA stages 0, 1, 2, 3, and 4 in the hip joint were 5.4%, 60.8%, 20.9%, 10.1%, and 2.7% in male patients, and 5.2%, 60.6%, 22.3%, 10.9%, and 1% in females ( $P = 0.837$ ), respectively. In

the knee, these rates were 2.7%, 43.9%, 23%, 18.9%, and 11.5% for male patients and 3.1%, 20.2%, 21.8%, 24.9%, and 30.1% for females, respectively ( $P < 0.001$ ). The rates of OA severity status of the patients in the fracture type groups are given in table 3.

Figure 1: Hip osteoarthritis (OA) severity scale according to Kellegren–Lawrence (KL) classification.

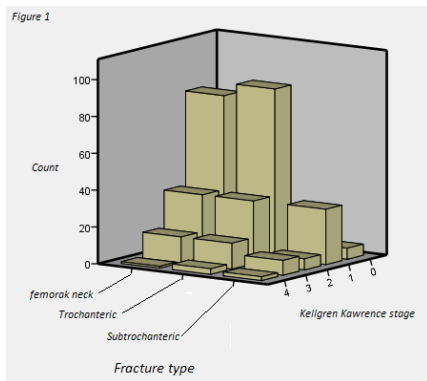
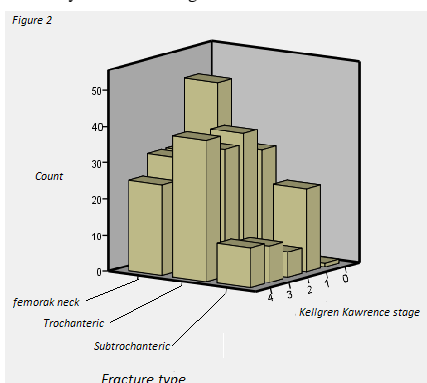


Figure 2: Knee OA severity scale according to KL classification



## Discussion

Our findings show that no relationship between hip OA and any type of hip fracture could be found. However, a statistically significant relationship between the occurrence of trochanteric hip fractures and knee OA was shown.

In epidemiological studies, varying prevalence rates of hip OA of up to 45% were reported [22, 23]. However, studies that examined patients with hip fractures reported that this rate could reach 67.5% [3, 13, 14, 18]. To our knowledge, four local and no countrywide population-based studies in Turkey have been conducted that investigate the hip OA prevalence. In a comparable age group, the hip OA prevalence was reported to be 21.5% by Göker [24] and approximately 30% by Dequeker and Johnell [16] in the MEDOS study. Despite being in the range reported before, we discovered a higher prevalence of hip OA in our study (34.3%) compared to the two previous local studies. Relatively few studies in the literature concerning the relationship between OA and hip fractures or the different types of fractures are available. Conflicting evidence exists, but it has been suggested that the type of hip fracture is affected by the presence of hip OA. While some research studies suggest that hip OA is a significant factor influencing the frequency of hip fractures and the type of fracture [16, 17, 25, 26], others report that OA and the odds of hip fractures are inversely related [13, 19, 27–29]. Some researchers declared that hip OA may act as a preventative factor against intracapsular hip fractures in addition to previous studies [3, 16–18].

Table 1: Definitive information and comorbidity data of the patients

	Fracture type			Total n- / Mean(SD)	P-value
	Femoral neck n-%/Mean(SD)	Trochanteric n- / Mean(SD)	Subtrochanteric n- % / Mean(SD)		
Sex					
Female	85(44%)	77 (39.9%)	31 (16.1 %)	193(56.6%)	
Male	57(38.5%)	70 (47.3%)	21 (14.2 %)	148 (43.4%)	0.392
Age	76.17(10.942)	78.71(9.462)	72.62 (8.483)	76.72(10.165)	0.001
Fracture laterality					
Right hip	63(36.8%)	83(48.5%)	25(14.6%)	171 (50.1%)	
Left hip	79 (46.5%)	64(37.6%)	27(15.9%)	170 (49.9%)	0.115
Comorbidity					
Hypertension	49 (14.4%)	60 (17.6%)	16(4.7%)	125(36.7%)	0.341
Diabetes	35(10.3%)	34 (10.0%)	10 (2.9%)	79 (23.2%)	0.731
CHF	18 (5.3%)	13 (3.8%)	5(1.5%)	36 (10.6 %)	0.554
Dementia dis.	19 (5.6 %)	10 (2.9%)	5(1.5%)	34 (10%)	0.175
Parkinson d.	14 (4.1%)	5 (1.5%)	5(1.5%)	24 (7%)	0.073
CVD	6 (1.8%)	9 (2.6%)	3(0.9%)	18 (5.3%)	0.760
CAD	4 (1.2%)	12 (3.5%)	2(0.6%)	18 (5.3%)	0.112
COPD	4 (1.2%)	6 (1.8%)	4(1.2%)	14 (4.1%)	0.317
CKD	7 (2.1%)	6 (1.8%)	0 (0.0%)	13 (3.8%)	0.276
BA	6 (1.8%)	6 (1.8%)	0 (0.0%)	12 (3.5%)	0.326

CHF: Chronic heart failure, CVD: Cerebrovascular disease, CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, CKD: Chronic kidney disease, BA: Bronchial asthma

Table 2: The rates of osteoarthritis presence of the patients' in the fracture type groups

Joint	Fracture type			Total n:341 n (100%)	P-value
	Neck n=142 (41.6%)	Trochanteric n=147(43.1%)	Subtrochanteric n=52(15.2%)		
Left hip	49 (34.5%)	51 (34.7%)	16 (30.8%)	116 (34%)	0.865
Right hip	49 (41.9%)	52 (35.4%)	16 (30.6%)	117 (34.3%)	0.833
Left knee	87(61.3%)	112 (76.2%)	27 (51.9%)	226 (66.3%)	0.002
Right knee	87(61.3%)	112 (76.2%)	28 (53.8%)	227 (66.6%)	0.003

Table 3: The rates of osteoarthritis severity status of the fracture type groups

Joint	Grade	Fracture type			Total n=341 n (100%)	P-value
		Neck n=142(41.6%)	Trochanteric n=147 (43.1%)	Subtrochanteric n=52(15.2%)		
Right hip	Absent	93 (65.5 %)	95 (64.6%)	36 (69.2%)	224(65.7 %)	0.164
	Moderate	32 (22.5 %)	34 (23.1%)	5 (9.6 %)	71 (20.8 %)	
	Severe	17 (12 %)	18 (12.2 %)	11 (21.2 %)	46 (13.5 %)	
Left hip	Absent	93 (65.5%)	96 (65.3%)	36 (69.2%)	225 (66 %)	0.241
	Moderate	34 (23.9%)	34 (23.1%)	6 (11.5%)	74 (21.7 %)	
	Severe	15 (10.6%)	17 (11.6%)	10 (19.2%)	42 (12.3 %)	
Right knee	Absent	55(38.7%)	35 (23.8%)	24 (46.2%)	114(33.4%)	0.013
	Moderate	31 (21.8%)	38 (25.9%)	7 (13.5%)	76 (22.3%)	
	Severe	56 (39.4%)	74 (50.3%)	21(40.4%)	151(44.3%)	
Left knee	Absent	55(38.7%)	35(23.8%)	25(48.1%)	115(33.7%)	

According to Maluta et al. [18], a diagnosis of hip OA was made in 53.01% of patients with ICFs, while the proportion was 83.12% in the group with ECFs. fractures. Contrary to those studies, Cumming and Klineberg [13] reported the risk of fracture as one-third with the presence of hip OA compared to those patients without OA. Interestingly, Dretakis et al. [17] reported that unlike other studies, no hip OA in any patient with femoral neck fractures could be found. Robstad et al. [3] declared that the presence of hip OA does not protect from hip fracture; however, hip OA incidence was more in the trochanteric fracture group compared to the femoral neck fracture group (22% to 15%). In our study, we could not demonstrate a protective or causal relationship between OA as observed in both the fractured and intact hip joints and the risk of developing any type of fracture.

The severity of OA was felt to be another factor affecting the type of hip fracture [6, 15, 18]. Maestro-Aguda et al. [15] declared that patients with severe hip OA had a higher rate of extracapsular hip fractures, and patients with moderate OA had a higher rate of ICFs. Partially in contrast, Maluta et al [18] found a 2-fold increase in the risk of ECF compared to ICF in patients with moderate OA (stage 2), and a 3-fold increased risk of ECF in patients with advanced OA (stage 3 and 4). Although Calderazzi et al. [25] reported that the fracture is not related to the severity of OA, they reported a 3-fold increase in the risk of trochanteric fractures in the presence of OA compared to femoral neck fractures, consistent with the findings of Maluta et al. [18]. In our study, the rates of moderate and severe OA in the femoral neck and trochanteric fracture groups were comparable. Remarkably, moderate hip OA was less frequent in subtrochanteric fractures than in the other two fracture groups, whereas severe OA was more frequent. We could not identify any study examining subtrochanteric fractures, except one by Franklin et al. [29]. However, due to the small number of patients with this type of fracture (about 5% of the cohort), they also examined these patients within the extracapsular fracture group. So, we could not be able to compare the subtrochanteric fracture group separately. We did not notice an inverse relationship with hip OA when we combined the subtrochanteric fractures with the trochanteric ones in the ECF group and compared them to intracapsular fractures, such as those of Franklin et al. [29].

Similar to the wide range of reported rates for the prevalence of hip OA in the general population, the prevalence of knee OA was reported to reach 70.8% [22, 30]. Research conducted on patients with hip fractures reported this rate as high to be as high 30.78% [13, 14, 17, 31]. Although some evidence of knee OA-related falls and associated hip fractures has been published, the relationship between hip fracture type and knee OA is unclear. According to Arden et al. [31], patients with knee OA and knee pain present an increased risk of hip fractures. Regardless of bone mineral density and postural stability parameters, Bergink et al. [32] declared that knee OA is linked to an increased fracture incidence that could not be explained by an increase in the risk of falling. According to Cai et al. [33], patients with bilateral moderate knee OA had a lower risk of fractures and falls than those with early-stage OA unlike Dretakis et al. [17] who reported that 45% of patients with trochanteric fractures and 14% of patients with femoral neck

fractures had ipsilateral knee OA. Despite the lack of a nationwide prevalence study, Kaçar et al. [34] reported this rate to be as high as 14.8% in a local study. However, our prevalence rate for knee OA (66.6%) was quite high and close to the upper bound of the range noted in the literature. This rate, which was found to be quite high, prompted us to think that knee OA may be a facilitating factor rather than a protective factor in the occurrence of hip fracture as Bergink et al. [32] stated. We hypothesized that additional evidence of the influence of knee OA on the type of hip fracture exists because of the statistically significant correlation between the trochanteric hip fracture and the presence of knee OA that we found in our analysis.

According to Pereira et al. [35], it was determined that the radiological stage and clinical variables, functional status, and quality of life parameters deteriorated and the group that showed the most significant difference was the group of patients with knee OA Stage 4, while no similar relationship was found between the functional status and radiological stage of hip OA. Considering the view that OA creates a serious increase in the risk of falling, we thought that the correlation found between the presence of fracture and the stage in patients with knee OA, but not found in hip OA patients, could be explained by this hypothesis. Although Franklin et al. [29] stated that no difference in males could be found, they stated that ECF was more common in females with KL stage  $\geq 2$ . However, when we examined the hip joint, we could not find a difference in either sex. We also observed that no difference in the evaluation of OA severity by gender existed. In addition, when we analyzed the effect of OA severity on fracture types according to gender, we did not observe any relationship with hip OA severity. The severity of OA was found to have no effect on the type of fracture in the knee joint in males, but it was found to be significantly associated with trochanteric fractures in females with knee OA status KL stage  $\geq 2$ . Additionally, similar to hip OA, the subtrochanteric fracture group had a lower rate of moderate OA than the other two groups. These two conditions suggest that the development of trochanteric and subtrochanteric fractures may be influenced by the presence of OA in the joint.

According to data from previous studies [10, 36–39], a number of chronic diseases, primarily causing osteoporosis and changes in bone architecture, can lead to an increase in the risk of hip fracture. However, no information that specifically examines the impact of fracture type in addition to OA is available. In our study, no relationship between each of the comorbidities and the fracture type was observed when examined using a detailed analysis.

#### Limitations

We did not examine the patients' walking ability and posture balance status. Therefore, the effects of deterioration on the existing balance and gait biomechanics on fracture formation were not evaluated. Bone mineral density and bone microarchitecture of the patients were not evaluated by any method. Therefore, the effect of the possible presence of osteoporosis was not evaluated. Although the design of our study was different since the incidence of OA and the distribution of etiological data were found to be correlated with increases in the risk of falls and hip fractures in the population were not fully known, analyses could not be performed in detail on this issue.

The frequency of co-morbidities of our patients may be similar to those in the literature, which may be because our institution is a tertiary hospital that operates on patients who have multiple co-morbidities.

### Conclusion

To the best of our knowledge, our study is the first to demonstrate the effect of hip and knee OA on subtrochanteric fractures. No relationship could be found between hip OA and any type of hip fracture. However, a significant relationship between the occurrence of trochanteric fractures and knee OA was found. In patients with knee OA, but not those with hip OA, a clear relationship between the type of fracture and the severity of OA was shown. Although the results of our study on subtrochanteric fractures are remarkable, larger series of data are required for confirmation. The hip fracture type is associated with knee OA, and the multifactorial etiology of fall and hip fracture development reveals the necessity of comprehensive studies in which all possible factors are evaluated together.

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# A cross-sectional study determining the prevalence of musculoskeletal diseases in automotive factory workers

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**Ethics Committee Approval**

Ethics committee approval was obtained from Health Sciences University Kocaeli Derince Training and Research Hospital (2019-110). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

**Conflict of Interest**

No conflict of interest was declared by the authors.

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## Abstract

**Background/Aim:** Work-related musculoskeletal disorders (WMSDs) develop due to exposure to physical and psycho-social factors in the work environment. The diagnostic criteria and prevalence of WMSDs are not well established. In this study, we aimed to determine which WMSDs occur in automotive industry workers and what the underlying risk factors may be.

**Methods:** A cross-sectional study was designed that included 200 automotive industry workers who were diagnosed with a WMSD by physical and radiological examination in the physical therapy and rehabilitation outpatient clinic in the past year. We recorded demographic data, risk factors and WMSD diagnosis names for the patients.

**Results:** In our study, the most common diagnosis was low back disorder (66.5%), followed by neck and shoulder (58%) and upper extremity (23%) disorders. There was a statistically significant increase in the occurrences of shoulder-neck diseases, upper extremity, and low back-lower extremity diseases in workers with inappropriate posture ( $P < 0.001$ ). Workers who exerted heavy effort or performed repetitive motions were statistically more likely to experience upper extremity disorders ( $P < 0.001$ ) as well as low back-lower extremity disorders ( $P = 0.020$  and  $P < 0.001$ , respectively); there was no statistically significant change in the incidence of shoulder and neck diseases with heavy effort ( $P = 0.538$ ).

**Conclusion:** WMSD is a serious health and economic problem. In our study, we found that low back and lower extremities and neck and shoulder problems are the most common types of WMSDs in individuals working in the automotive sector. Not using proper posture while working causes health problems in the shoulders, neck, upper extremities and low back and lower extremities. Employees in this sector should be encouraged to use good work ergonomics.

**Keywords:** Occupational musculoskeletal diseases, Work-related musculoskeletal diseases, Repetitive strain injury, Pain, Back pain, Knee pain

## Introduction

Work-related musculoskeletal disorders (WMSDs) are associated with exposure to physical and psycho-social risks during work activities and can develop from pain, movement restrictions and injuries. WMSDs usually don't have a single cause; rather, various factors play a role. Among physical causes and organizational risk factors, bending, movements requiring repetitive force, awkward (wrong) and static postures, vibrations, poor lighting, cold working environments, fast-paced work, prolonged sitting or standing in the same position, and carrying loads are especially problematic [1, 2]. These diseases often affect the low back, lower extremities and especially the upper extremities and neck [3]. In recent years, these disorders have garnered the attention of employees, employers, governments, health care systems and insurance companies in industrialized countries due to their increased frequency and associated cost. An increasing number of studies on WMSDs have focused on ergonomic programs and rehabilitation approaches, including risk factors, ergonomic training and ergonomic initiatives. These studies frequently conclude that there are great uncertainties about the diagnosis, follow-up and rehabilitation of WMSDs [3-5]. One of the most striking issues when we take a look at the research performed so far is that the majority of the studies performed by non-physicians group WMSDs by painful body parts [6, 7]. Another important issue is that most of the studies done by physicians include only disorders of the neck and upper extremities [8-10] and not the low back and lower extremities because they focused on office workers. However, WMSDs need to be considered in a wide range of workers, especially heavy industrial workers, who are more likely to develop WMSDs [11].

Since our hospital is in a busy industrial area with many factories and most of our patients are heavy industry workers, especially automotive industry workers, in our study, we aimed to determine which regions of the body are most commonly affected in these types of workers diagnosed with WMSD and what are the associated risk factors.

## Materials and methods

Ethics committee approval was obtained from Health Sciences University Kocaeli Derince Training and Research Hospital (2019-110) before the study was initiated. A total of 200 automotive factory workers who came to the physical medicine and rehabilitation outpatient clinic in the past year and were diagnosed with WMSD based on physical and radiological examinations such as x-ray, magnetic resonance imaging, ultrasonography, electrodiagnostic method (electromyography) were included in the study. The workers worked in four main areas: assembly line, paint shop, welding shop and press shop. Considering the work done by the workers, the risk factors were divided into the following areas: inappropriate posture, heavy effort, static posture, repetitive movements and vibration. A form was created that included these main titles with additional risk factors from other studies in the automotive sector.

We included those workers who had complained of pain for at least 6 months. In addition to their demographic data, the patients were called by phone to determine how many years they had been working at the factory, their department, alcohol-

cigarette habits, exercise habits and the treatment methods (physical therapy, exercise program, injection, medical therapy). This information was recorded in the same form.

We grouped WMSDs as neck-shoulder, upper extremity (elbow, hand-wrist) or low back-lower extremity (hip-knee-foot-ankle). Patients with chronic disease (such as diabetes mellitus, polyneuropathy, fibromyalgia, other rheumatological diseases, etc.), with a complaint period of less than 6 months or who worked in the factory for less than 2 years were not included in the study.

### Statistical analysis

The IBM SPSS Statistics 17.0 software package (IB Corporation, Armonk, NY, USA) was used for the statistical analysis. Descriptive statistics were reported. Categorical variables were expressed as the number of cases and (%), while averages were expressed as the mean (standard deviation) or median (minimum - maximum) for numerical variables.

To determine whether there is a statistically significant correlation between working time and complaint time, Spearman's rank numbers were investigated with the correlation test. If the expected frequency is below 5 in at least 1/4 of the cells in the 2x2 cross tables, the categorical data is evaluated by Fisher's exact probability test; when the expected frequency is between 5 and 25, the continuity correction chi-square test is used; otherwise it is evaluated by Pearson's chi-square test. If RxC (if at least one of the categorical variables in the row or column has more than two results), the expected frequency is below 5 in at least 1/4 of the cells in the cross tables, the categorical data in question are analyzed with the likelihood ratio test; otherwise it's evaluated by the square test. Results for  $P < 0.05$  were considered statistically significant.

## Results

The descriptive statistics regarding the demographic and clinical characteristics of the participants are given in Table 1.

Table 1: Demographic and clinical features of the cases

	n = 200
Age(year) (mean [SD])	31.1 (6.8)
Age range (years)	20-51
Gender (n [%])	
Female	35 (17.5%)
Male	165 (82.5%)
Education status (n [%])	
Primary education	25 (12.5%)
High school	139 (69.5%)
College	36 (18.0%)
Marital status (n [%])	
Married	127 (63.5%)
Single	67 (33.5%)
Divorced	6 (3.0%)
Number of children (n [range])	1 (0-3)
Body mass index (kg / m2) (mean [SD])	25.5 (3.75)
Working time (years) (n [range])	5 (1-25)
Complaint duration (months) (n [range])	12 (2-120)
Smoking history (n [%])	112 (56.0%)
Alcohol history (n [%])	22 (11.0%)
Exercising (n [%])	21 (10.5%)
Drug use (n [%])	160 (80.0%)
Use of orthoses (n [%])	39 (19.5%)
Physical Therapy (n [%])	156 (78.0%)
Injection (n [%])	29 (14.5%)

Table 2 shows the frequency of cases with respect to work area, inappropriate posture, heavy effort, static posture, and repetitive movements. It is noteworthy that 65% of the patients were assembly line workers. The most common inappropriate posture was binding-rising. Weight pulling and pushing was more common than lifting heavy weights. Among the static postures, standing all day was the most common posture.



Table 3 shows the frequency distributions of the cases in terms of the incidence of the different types of occupational musculoskeletal diseases (shoulder and neck, upper extremity, and low back/lower extremities).

Table 2: Frequency distribution of the cases with respect to work area, inappropriate posture, heavy effort, static posture, and repetitive movements

	n (%)
Working area	
Assembly line	130 (65.0)
Welding shop	38 (19.0)
Paint shop	29 (14.5)
Press shop	3 (1.5)
Inappropriate posture	
No	1 (0.5)
Working by bending the neck	35 (17.5)
Nonergonomic hand tool use	18 (9.0)
Bending rising	66 (33.0)
Arms up	21 (10.5)
Combined motions	59 (29.5)
Heavy effort	
No	64 (32.0)
0-5 kg transport	52 (26.0)
5-10 kg transport	10 (5.0)
10-25 kg transport	5 (2.5)
>20 kg transport	7 (3.5)
Weight push pull	62 (31.0)
Static posture	
No	2 (1.0)
Standing all day long	165 (82.5)
Sitting down all day long	21 (10.5)
Kneeling	12 (6.0)
Repetitive motion	
No	14 (7.0)
Working on the assembly line	91 (45.5)
Getting in and out of the vehicle	15 (7.5)
Vehicle wiping and sanding	13 (6.5)
Using a gun	11 (5.5)
Percussion or suppression work	7 (3.5)
Manual material handling	27 (13.5)
Frequently twisting-rotating	17 (8.5)
Step up and down	5 (2.5)

Table 3: Frequency distributions of the cases in terms of incidence of occupational musculoskeletal diseases

	n (%)
Shoulder and neck	
No	84 (42.0)
There is	116 (58.0)
CDH	61 (30.5)
Forward head posture	30 (15.0)
RCT/IMP	8 (4.0)
Biceps tendonitis	3 (1.5)
RCT/IMP + CDH	14 (7.0)
Upper limb	
No	154 (77.0)
There is	46 (23.0)
LE	15 (7.5)
DQT	15 (7.5)
CTS	4 (2.0)
Trigger Finger	4 (2.0)
Cubital Tunnel Syndrome	2 (1.0)
LE+CTS	4 (2.0)
LE+DQT	1 (0.5)
CTS, DQT	1 (0.5)
Low back and lower extremities	
No	67 (33.5)
There is	133 (66.5)
LDH	63 (31.5)
Lomber strain	31 (15.5)
Knee disorders	11 (5.5)
LDH + knee disorders	10 (5.0)
Thoracal Disc Hernia	5 (2.5)
LDH + Thoracal Disc Hernia	4 (2.0)
Ankle disorders	3 (1.5)
Lomber strain + knee disorders	3 (1.5)
Lomber strain + hip disorders	1 (0.5)
LDH + ankle disorders	1 (0.5)
LDH + knee + ankle disorders	1 (0.5)

CDH: Cervical Disc Hernia, RCT: Rotator Cuff Tendonitis, IMP: Impingement syndrome DQT: De Quervain Tenosinovitis, CTS: Carpal Tunnel Syndrome, LE: Lateral Epicondylitis LDH: Lumber Disc Hernia

Table 4 shows the comparisons made with regards to the frequency of musculoskeletal diseases in terms of inappropriate postures. There were statistically significant increases in the incidence of shoulder-neck, upper extremity, and low back and lower extremity diseases in response to inappropriate postures ( $P < 0.001$ ). Shoulder and neck diseases were more common in the neck bending, arms up and combined

motion groups ( $P < 0.001$ ). Compared to all other inappropriate posture groups, upper extremity diseases were seen at a higher rate in the group using non-ergonomic hand tools ( $P < 0.001$ ). Low back and lower extremity diseases were seen at a higher rate in the bent-up group compared to all other inappropriate posture groups ( $P < 0.001$ ). In Figure 1, the incidence of musculoskeletal diseases in terms of inappropriate posture is shown in the bar graph.

Table 4: Comparisons of the frequency of musculoskeletal diseases in terms of inappropriate posture

	No disorder n (%)	There is disorder n (%)	P-value†
Shoulder neck			<0.001
Working by bending the neck	2 (5.7)	33 (94.3)	
Nonergonomic hand tool use	15 (83.3) <sup>a</sup>	3 (16.7) <sup>a</sup>	
Bending-rising	49 (74.2) <sup>a</sup>	17 (25.8) <sup>a</sup>	
Arms up	4 (19.0) <sup>b,c</sup>	17 (81.0) <sup>b,c</sup>	
Combined motion	14 (23.7) <sup>b,c</sup>	45 (76.3) <sup>b,c</sup>	
Upper extremity			<0.001
Working by bending the neck	32 (91.4)	3 (8.6)	
Nonergonomic hand tool use	2 (11.1) <sup>a</sup>	16 (88.9) <sup>a</sup>	
Bending-rising	64 (97.0) <sup>b</sup>	2 (3.0) <sup>b</sup>	
Arms up	15 (71.4) <sup>b,c</sup>	6 (28.6) <sup>b,c</sup>	
Combined motion	40 (67.8) <sup>a,b,c</sup>	19 (32.2) <sup>a,b,c</sup>	
Low back and lower extremities			<0.001
Working by bending the neck	19 (54.3)	16 (45.7)	
Nonergonomic hand tool use	15 (83.3)	3 (16.7)	
Bending-rising	0 (0.0) <sup>a,b</sup>	66 (100.0) <sup>a,b</sup>	
Arms up	12 (57.1) <sup>c</sup>	9 (42.9) <sup>c</sup>	
Combined motion	20 (33.9) <sup>b,c</sup>	39 (66.1) <sup>b,c</sup>	

† Pearson's Chi-Square test; the differences between which groups are indicated with letters; a: The difference between the groups with the posture that bends the neck is statistically significant ( $P < 0.05$ ), b: The difference between the groups using the nonergonomic hand tool is statistically significant ( $P < 0.001$ ), c: The difference between the bending and rising posture group was statistically significant ( $P < 0.01$ ).

Table 5 shows the comparisons made with regards to the frequency of the occurrence of musculoskeletal diseases in terms of heavy effort. While there was no statistically significant increase in the incidence of shoulder and neck diseases in response to heavy effort ( $P = 0.538$ ), a statistically significant increase was found in the incidence of upper extremity diseases ( $P < 0.001$ ). This effect was due to the group carrying 0-5 kg rather than the group not expending heavy effort or pushing/pulling weight ( $P < 0.001$ ). There was a statistically significant increase in the incidence of low back and lower extremity diseases in response to heavy effort ( $P = 0.020$ ); this was due to the higher incidence of low back and lower extremity diseases in the group pushing and pulling weight compared to the group carrying 0-5 kg ( $P = 0.004$ ).

Table 6 shows the comparisons made with regards to the frequency of the occurrence of musculoskeletal diseases in terms of static posture. Static posture was found to be a statistically significant risk factor for the incidence of shoulder-neck ( $P = 0.014$ ) and low back-lower extremity ( $P = 0.002$ ) diseases. Compared to the kneeling group, it was the more common occurrence of shoulder and neck diseases in the group working sitting all day long ( $P = 0.013$ ), whereas low back and lower extremity diseases were seen more common in the kneeling group compared to the groups without static posture, standing all day and sitting all day ( $P = 0.032$ ).

Table 5: Comparisons of the frequency of musculoskeletal diseases in terms of heavy effort

	No disorder n (%)	There is disorder n (%)	P-value†
Shoulder neck			0.538
No	23 (35.9)	41 (64.1)	
0-5 kg transport	21 (40.4)	31 (59.6)	
>5 kg transport	10 (45.5)	12 (54.5)	
Weight push-pull	30 (48.4)	32 (51.6)	
Upper extremity			<0.001
No	57 (89.1)	7 (10.9)	
0-5 kg transport	26 (50.0) <sup>a</sup>	26 (50.0) <sup>a</sup>	
>5 kg transport	17 (77.3)	5 (22.7)	
Weight push-pull	54 (87.1) <sup>b</sup>	8 (12.9) <sup>b</sup>	
Low back and lower extremities			0.020
No	22 (34.4)	42 (65.6)	
0-5 kg transport	24 (46.2)	28 (53.8)	
>5 kg transport	9 (40.9)	13 (59.1)	
Weight push-pull	12 (19.4) <sup>b</sup>	50 (80.6) <sup>b</sup>	

Pearson's Chi-Square test, the differences between which groups are indicated with letters: a: The difference between the group without heavy effort is statistically significant ( $P < 0.001$ ), b: The difference between 0-5 kg transporting group is statistically significant ( $P < 0.01$ ).

Table 6: Incidence of musculoskeletal diseases in terms of static posture

	No disease	Diseased	P-value †
Shoulder-neck			0.014
None	0 (0.0%)	2 (100.0%)	
Standing all day	70 (42.4%)	95 (57.6%)	
Sitting all day	5 (23.8%)	16 (76.2%)	
Kneeling	9 (75.0%) <sup>a</sup>	3 (25.0%) <sup>a</sup>	
Upper extremity			0.057
None	2 (100.0%)	0 (0.0%)	
Standing all day	122 (73.9%)	43 (26.1%)	
Sitting all day	20 (95.2%)	1 (4.8%)	
Kneeling	10 (83.3%)	2 (16.7%)	
Low back-lower extremity			0.002
None	2 (100.0%)	0 (0.0%)	
Standing all day	58 (35.2%)	107 (64.8%)	
Sitting all day	7 (33.3%)	14 (66.7%)	
Kneeling	0 (0.0%) <sup>a,b,c</sup>	12 (100.0%) <sup>a,b,c</sup>	

† Likelihood Ratio test, the differences between which groups are indicated with letters: a: The difference between the group that sits all day long is statistically significant ( $P < 0.05$ ), b: The difference between the group that does not have static posture is statistically significant ( $P = 0.011$ ), c: The difference between the group that works all day standing up is statistically significant ( $P < 0.05$ ) the difference is statistically significant ( $P = 0.009$ ).

Table 7: Comparisons of the frequency of musculoskeletal diseases in terms of repetitive motion

	No disorder n (%)	There is disorder n (%)	P-value†
Shoulder neck			0.084
No	8 (57.1)	6 (42.9)	
Working on the assembly line	36 (39.6)	55 (60.4)	
Getting in and out of the vehicle	5 (33.3)	10 (66.7)	
Vehicle wiping and sanding	3 (23.1)	10 (76.9)	
Using a gun	7 (63.6)	4 (36.4)	
Percussion or suppression work	1 (14.3)	6 (85.7)	
Manual material handling	10 (37.0)	17 (63.0)	
Frequently twisting-rotating	10 (58.8)	7 (41.2)	
Step up and down	4 (80.0)	1 (20.0)	
Upper extremity			<0.001
No	12 (85.7)	2 (14.3)	
Working on the assembly line	88 (96.7)	3 (3.3)	
Getting in and out of the vehicle	15 (100.0)	0 (0.0)	
Vehicle wiping and sanding	5 (38.5) <sup>a,b,c</sup>	8 (61.5) <sup>a,b,c</sup>	
Using a gun	2 (18.2) <sup>a,b,c</sup>	9 (81.8) <sup>a,b,c</sup>	
Percussion or suppression work	1 (14.3) <sup>a,b,c</sup>	6 (85.7) <sup>a,b,c</sup>	
Manual material handling	25 (92.6) <sup>d,e,f</sup>	2 (7.4) <sup>d,e,f</sup>	
Frequently twisting-rotating	1 (5.9) <sup>a,b,c,g</sup>	16 (94.1) <sup>a,b,c,g</sup>	
Step up and down	5 (100.0) <sup>d,e,f,h</sup>	0 (0.0) <sup>d,e,f,h</sup>	
Low back and lower extremities			< 0.001
No	5 (35.7)	9 (64.3)	
Working on the assembly line	26 (28.6)	65 (71.4)	
Getting in and out of the vehicle	4 (26.7)	11 (73.3)	
Vehicle wiping and sanding	6 (46.2)	7 (53.8)	
Using a gun	10 (90.9) <sup>a,b,c,d</sup>	1 (9.1) <sup>a,b,c,d</sup>	
Percussion or suppression work	3 (42.9) <sup>e</sup>	4 (57.1) <sup>e</sup>	
Manual material handling	3 (11.1) <sup>d,e</sup>	24 (88.9) <sup>d,e</sup>	
Frequently twisting-rotating	10 (58.8) <sup>b,g</sup>	7 (41.2) <sup>b,g</sup>	
Step up and down	0 (0.0) <sup>e,h</sup>	5 (100.0) <sup>e,h</sup>	

† Likelihood ratio test, the differences between which groups are indicated with letters: a: The difference between the group with no repetitive movement is statistically significant ( $P < 0.05$ ), b: The difference between the group working on the assembly line is statistically significant ( $P < 0.05$ ), c: Difference between getting in and out of the vehicle is statistically significant ( $P < 0.01$ ), d: The difference between vehicle wiping and sanding group is statistically significant ( $P < 0.05$ ), e: The difference between gun using group is statistically significant ( $P < 0.05$ ), f: The difference between the percussion or suppression working group is statistically significant ( $P < 0.05$ ), g: The difference between the group handling the manual material is statistically significant ( $P < 0.001$ ), h: The difference between the group doing frequently twisting and rotating is statistically significant ( $P < 0.05$ ).

Although there was no statistically significant change in the incidence of shoulder and neck diseases associated with repetitive motion ( $P = 0.084$ ), there was a statistically significant increase in the incidence of upper extremity diseases ( $P < 0.001$ ) (Table 7). The effect on the upper extremities was due to the

vehicle wiping and sanding, using a gun, percussion or suppression work and frequently twisting-rotating groups ( $P < 0.05$ ) rather than the groups that do not have repetitive movement (working on the assembly line, getting in and out of the vehicle, manual material handling and step up and down). There was also a statistically significant increase in the incidence of low back and lower extremity diseases ( $P < 0.001$ ) associated with repetitive motion. Low back and lower extremity diseases were rarely encountered in the group using a gun compared to all other subgroups except for the frequent twisting-rotating group ( $P < 0.05$ ). In addition, lower back and lower extremity diseases were seen statistically less often in the working on the assembly line and frequently twisting-rotating groups compared to the manual material handling group ( $P = 0.032$  and  $P = 0.002$ , respectively).

## Discussion

In our study, WMSDs were seen most frequently in assembly line workers, which is due to the repetitive movements performed by such workers. Previous studies have shown that repetitive movements are among the most important risk factors for the occurrence of WMSDs [12]. Clinicians should keep in mind that a WMSD may be the cause of the complaints in a patient exposed to repetitive, compelling, prolonged uneven postures or vibration [13].

In our study of automotive workers with WMSDs, low back-lower extremity disorders were most common, followed by neck-shoulder and then upper extremity disorders. In the study conducted by Deros et al. [7] at an automotive factory in Malaysia, the most common WMSDs in order of frequency were low back, foot and ankle and upper back diseases. The fact that WMSDs are seen more frequently in these regions of the body supports the conclusion that exposure to trauma with repetitive movements and inappropriate posture cause this type of disease.

In our study, shoulder-neck diseases were found more frequently in individuals who sat all day, and low back-lower extremity disorders were more frequent in individuals who kneel a lot. The forklift operator of the sitting group, who performs continuous neck rotation, explains the first observation, and biomechanical overload in the kneeling group is felt to be responsible for the second conclusion. The common reasons for neck and back pain in forklift users include static stationary position while driving (hands and feet are held fixed on handles and pedals), repeated exposure to awkward body postures for short and long periods (trunk twisting and rotation) especially during reverse maneuvers, and exposure of the whole body to vibration while driving [14].

Performing repetitive bending and standing movements while working increases the incidence of low back-lower extremity diseases. This may be due to biomechanical damage to the tissues around the joints that results from overuse load on the joints [15].

Upper extremity diseases were found to be higher in the groups that wiped vehicles, sandblasted, used guns, hit-squeezed, and twisted frequently compared to the groups working on the assembly line, handling manual materials, and step and down by pressing. Because these patients apply continuous long-term hammer use, repetitive supination and pronation of the forearm,

strong wrist extension/or arm extended grip, excessive use of the thumb and ulnar or radial deviation of the wrist, prolonged use of hammer, repetitive supination and pronation of the forearm, strong wrist extension / or arm extension grip.

In 2018, in a systematic review of studies of office workers with WMSDs, Hoe et al. [16] found that ergonomic measures alone were not sufficient to resolve patients' complaints; additional breaks from work were needed. Since repetitive motion and poor ergonomics are the most important factors in the etiopathogenesis of WMSDs, even if the ergonomics are optimal, increasing the number of breaks can decrease the total number of repetitive movements, providing additional relief. The workers in our study worked 8 hours a day and rested for 50 minutes, including 30 minutes for a meal break and 20 minutes of additional break time. The workers could be scheduled to work in 2-hour shifts with 20-minute breaks in between.

The limitation of our study is that the risk assessment was performed only in individuals who were seen at our outpatient clinic and were diagnosed with WMSD. There is a need for WMSD risk assessment studies to be carried out on all factory employees to determine what measures would best protect the health of employees in such environments.

### Conclusion

WMSD still has no clear diagnostic criteria, which causes serious diagnostic and prevalence differences among countries and sectors. In automotive factories, which are a branch of heavy industries, WMSDs are frequently observed due to the inconvenient postures and repetitive movements required. Therefore, an occupational health and safety culture should be adopted in these lines of work. Ergonomic measures should be increased in the sections where WMSDs are frequently seen, and the number and duration of breaks should be increased if necessary. Inter-department rotations can prevent a worker from constantly doing the same movement. In this way, the incidence of WMSDs can be reduced.

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# Laparoscopic clips can be a safe buttressing method for the sleeve gastrectomy operations: An experimental study on resected sleeve gastrectomy specimens

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## Ethics Committee Approval

Ethics Committee approval was taken from the Ethics Committee of Keçiören Training and Research Hospital (B.10.4.ISM.4.06.68.49/2015, date: 11.03.2015).

All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

## Conflict of Interest

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## Abstract

**Background/Aim:** Laparoscopic sleeve gastrectomy has been accepted in obesity surgery, as it provides rapid weight loss and has low mortality rates. However, because of the long staple line, leakage is a significant problem for these patients. Buttressing methods can be used to reduce the leakage. The aim of this study was to evaluate the efficacy of clips for buttressing the staple line on resected sleeve gastrectomy patients.

**Methods:** The study included 20 patients aged 18–60 years who underwent laparoscopic sleeve gastrectomy surgery in our clinic. Any patients with connective tissue disease or with the removed stomach tissue not intact were excluded from the study. The age, gender, height, weight, and additional disease data were recorded. A manual manometer and inflation mechanism was created, and when the pressure suddenly dropped and a bubble was observed from the staple line, this value was recorded as the leakage pressure. By measuring the leakage pressure in the staple line by inflating the resected and removed stomach, leakage pressure and leakage location were recorded as no-clip leakage pressure. Then, the observed area of leakage was buttressed with laparoscopic clips, and the leakage pressure was measured once more by inflating the stomach; this value was recorded as the clipped leakage pressure.

**Results:** The first pressure value observed had a mean of 43.8mmHg (range, 35–55 mmHg); after application of the clips, the mean was 43.8 mmHg (range (40–50 mmHg) ( $P = 0.20$ ). The leakage was located in the upper section in 14 (70%) cases, in the mid-section in 5 (25%) cases, and in the lower section in 1 (5%) case. Micro-leakage was observed in 15 (75%) cases, 1-mm leakage in 1 (5%) case, 2-mm leakage in 2 (10%) cases, and 3-mm leakage in 2 (10%) cases.

**Conclusion:** Leakage is the most significant complication following sleeve gastrectomy surgery. The use of laparoscopic clips was described as a buttressing method, but no positive effect of metal clips on leakage pressure was observed in our study. Clarification of the effect of the buttressing with metallic clips is required using *in vivo* and *ex vivo* experiments.

**Keywords:** Obesity, Sleeve gastrectomy, Leakage

## Introduction

Laparoscopic sleeve gastrectomy was first applied as a part of biliopancreatic diversion operations [1]. Over time, it came into use in obesity surgery due to its low mortality rates and the provision of rapid weight loss [2]. However, because of the long staple line, leakage is a significant problem in these operations. To prevent this problem, tissue adhesives, sutures, and laparoscopic clips are used to buttress the staple line; however, their efficacies have not been proven [3–5]. This study examined the maximum pressure that the gastric resection staples could withstand. Then, we evaluated whether reinforcing clips applied to leakages in the staple line were useful in preventing leakage.

## Materials and methods

The study was conducted at Keçiören Training and Research Hospital. Approval for the study was granted by the Ethics Committee of Keçiören Training and Research Hospital (B.10.4.ISM.4.06.68.49/2015), and informed consent was obtained from all of the voluntary participants. Power analysis was calculated using G\*Power 3 (Faul, Erdfelder, Lang, & Buchner, 2007) to test the difference between two independent group means using a two-tailed test, with a medium effect size ( $d = 0.50$ ) and an alpha of 0.05. The results revealed that a total sample size of 20 participants was required to achieve a power of 80 [6]. The study included selected patients aged 18–60 years who presented at the General Surgery Obesity Clinic and for whom sleeve gastrectomy surgery was planned. Any patients with connective tissue disease or with the removed stomach tissue not intact were excluded from the study. The age, gender, height, weight, and additional disease data were recorded. After removal of stomach tissue, the stomach dimensions were measured as length and upper 1/3 width, mid-1/3 width, and lower 1/3 width, and recorded. The width measurements were made in the mid-section of the area being measured. The stomach corpus level was opened with a 0.5-cm incision from the staple line. By applying purse sutures around this area, a Foley probe was advanced from here and inflated. A manual manometer and inflation mechanism was created over the Foley probe. By inflating the stomach, the leakage pressure in the staple line was measured, and this value and the leakage location were recorded (Figure 1). The stomach was inflated and the maximum pressure the stapler line could withstand was recorded. Then the leak point was reinforced with the clip and the pressure was measured again (Figure 2).

### Statistical analysis

Statistical analyses were performed using SPSS software version 18. The variables were investigated using analytical methods to determine whether the variables are normally distributed. The paired Student's *t*-test was used to compare the measurements at two time points (first leakage/without clips, after clips). A *P*-value of less than 0.05 was considered to show statistical significance.

Figure 1: Micro-leakage in mid-1/3 width.

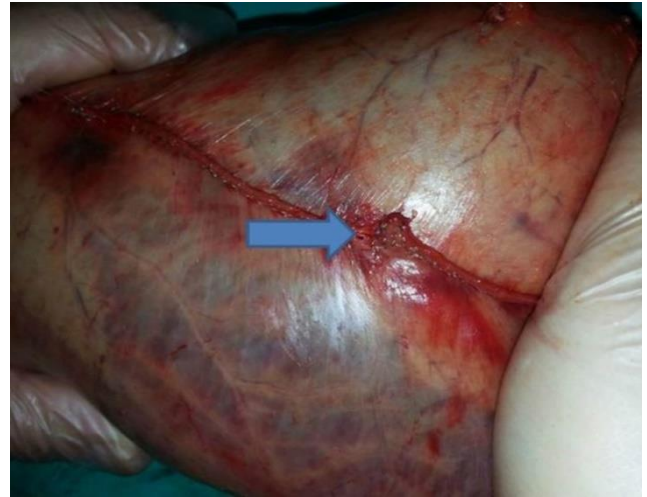
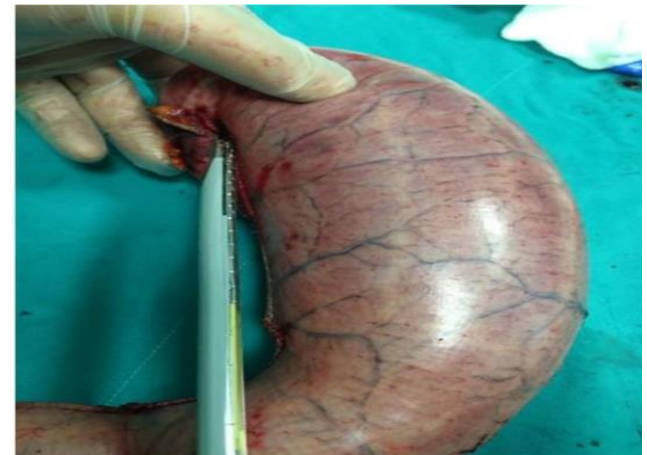


Figure 2: Buttressing the staple line with laparoscopic clip.



## Results

The study included evaluations of stomach tissue removed from 20 patients following laparoscopic sleeve gastrectomy. The sample comprised 7 (35%) males and 13 (65%) females, with a mean age of 39.3 years (range, 21–54 years) and a mean BMI of 46.4 (range: 38.5–58.4). In 9 (45%) patients, there was a history of chronic disease (Table 1). The mean operative time was 52 minutes, and 5 out of the 20 patients were smokers.

Table 1: Demographic characteristics and leakage information

	n = 20
Age*	39.3 (21–54)
Gender – female, n(%)	13 (65)
BMI*	46.4 (38.5–58.4)
Comorbid disease	9 (45)
Smoking	5 (25)
Leakage, n(%)	
Upper section	14 (70)
Mid-section	5 (25)
Lower section	1 (5)
Leakage pressure value	
First observed*	45.3 (35–60) mmHg
After the application of the clips*	42.3 (30–55) mmHg

\* median (IQR: interquartile range)

The measurements of the removed stomach tissue were as follows: mean length 24.2 cm (range, 15–32 cm), upper third width 4.8 cm (4–7 cm), mid-third width 4.6 cm (3–6 cm), and lower third width 3.8 cm (3–5 cm). The mean first pressure value of the observed leakage was 45.3 mmHg (range, 35–60 mmHg); after application of the clips, the mean was 42.3 mmHg (range, 30–55 mmHg) ( $P = 0.20$ ).

After the application of the clips, 20 (100%) of the leakages occurred under the clips. The mean maximum pressure

applied to the stomach tissue was 187 mmHg (range, 150–200 mmHg). The leakage was in the upper section in 14 (70%) cases, in the mid-section in 5 (25%), and in the lower section in 1 (5%) case. Micro-leakage was observed in 15 (75%) cases, 1-mm leakage in 1 (5%) case, 2-mm leakage in 2 (10%) cases, and 3-mm leakage in 2 (10%) cases.

## Discussion

One of the most important problems following sleeve gastrectomy operations is leakage. The long staple line makes locating the leakage difficult. Previous studies have touched on the challenges of determining the leakage size and location [7, 8]. In this study, there were difficulties in locating the leak since the leaks caused by the application of pressure were generally at the micro level. Therefore, liquid soap was used to locate the leak. As it is difficult to determine the leakage location in an experimental environment, it is even more difficult in clinical environments. Clinicians have opted for using low-pressure contrast or dye to minimize contamination at the leakage site, as such contamination increases the difficulty of clinical diagnosis.

Leakages occurring after sleeve gastrectomy surgery are as serious a problem in diagnosis as in treatment. Although there is not a complete algorithm for treatment, the priority must be stabilization of the patient, followed by percutaneous drainage. Furthermore, endoscopic procedures should be applied prior to surgery [7]. In the current study, the defects occurring after pressure were millimetric. If there is no tissue bleeding or distal obstruction, a fistula of this size can be expected to be closed with non-operative techniques.

In clinical observations, staple line leakages following gastrectomy are generally near the gastro esophageal junction. This can be due to surgical technical difficulties, anatomical, physiological, or physical reasons [2]. In the current study, the leakages were determined to be in the mid-section in 14 (70%) cases and in the upper section in 5 (25%) cases. No leakage was observed in the end sections. Leakages occurred associated with millimetric tears of the tissue from the staples, due to the tension of the staple line. The reasons for more leakages in these areas can be explained by Pascal's Law. In areas where the radius is greater, areas of greater surface tension are formed, and leakages occur due to the staple cut.

Leakage pressures in stomach tissue removed after sleeve gastrectomy have been previously researched. López-Monclova et al. [9] determined a mean leakage pressure of 35 mmHg in the staple line, using a special mechanism. In the current study, the mean value of the leakage pressure was 45.3 mmHg (range, 35–60 mmHg). The differences in these pressures could be due to the differences in methodologies used.

There are many methods to buttress the staple line during sleeve gastrectomy operations, such as oversewing, or using biomaterials or metallic clips; however, the utility of such methods in sleeve gastrectomy operations has been a matter of debate. Specifically, clinical research showed that there is no difference between the buttressed and non-buttressed groups. On the other hand, experimental studies revealed that the buttressed group had better outcomes than the non-buttressed group [3, 5, 10–12]. Our study revealed that buttressing with metallic clips did not result in better outcomes.

In our previous study, we studied the same pressure model on resected sleeve gastrectomy specimens in three groups. It revealed that, in the sutureless group, the knotless suture group and the knotted suture group, the pressure levels causing leakage were 42.7 (1), 98.7 (3.9), and 97.7 (4.1) mmHg, respectively. Buttressing with sutures increased the bursting pressures significantly [11]. However, in our recent study, buttressing with metallic clips had the same bursting pressure as the nonbuttressed group (42.3 mmHg). It should be noted that we calculated our sample size with the pressure level of the other buttressing techniques. More samples are needed to make inferences with such similar pressure values.

In their prospective randomized clinical study, Yiğit et al. [12] concluded that buttressing the staple line with metallic clips was effective in terms of leakage. However, in our study, we could not observe any positive effect of metallic clips to support the staple line. This discrepancy indicates that leakage after sleeve gastrectomy operations depends not only on pressure, but also on other, complex factors. In the current study, the pressure level that the clip-supported regions can withstand was found to be 42.3 mmHg (range: 30–55 mmHg). All of the leaks occurred in areas where clips were placed. The leaks in areas where the clips were placed occurred through the sliding of the clip due to the tension created by the stomach inflation. This evidence suggests that buttressing the staple line with metallic clips may not be safe.

## Limitations

The most important limitation of this study was its reliance exclusively on mechanical factors. Physiological etiopathogenetic factors, which play important roles in leakage mechanisms, were not investigated. We calculated our sample size with the pressure level of the other buttressing techniques. More studies are needed to make inferences with such similar pressure values, which will enable us to better understand the complex etiopathogenesis of these leakages.

## Conclusion

Leakage is the most significant complication following sleeve gastrectomy surgery. Buttressing methods can be used to prevent this complication. Although there are few studies that argue that metal clips can be a reinforcement method, no positive effect of metal clips on leakage pressure was observed in our study. Clarification of the pathophysiology is required to be able to overcome difficulties in diagnosis and treatment.

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## Care of the organ transplant receiver: Review

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### **Abstract**

Organ transplantation is the process of replacing damaged/inoperative organs with healthy ones. Many parameters are considered in the decision-making process for this procedure. At first, compatibility parameters of the recipient individual and the donor should be evaluated. All laboratory values and tissue compatibility tests should be compared. The organ transplant coordinator shares the patient's compliance information with the team. The recipient patient is informed of the match, and the process begins. Preparing the recipient for transplantation is as difficult as finding the appropriate organ. During the first stages, the individual is evaluated and meets with the entire transplant team. Everyone on the transplant team explains their roles and responsibilities. The patient can ask questions. Information is given about complications and negative care processes encountered after transplantation. Patients most often experience differences of opinion in religious and cultural dimensions. On the one hand, he/she wants to live; on the other hand, he/she thinks transplantation is a "sin". These confusing thoughts can increase and be replaced by psychosocial issues. The transplant nurse initiates the patient's rehabilitation process. This process is based on an immunosuppressive treatment plan to strengthen the patient's immunity before transplantation. The transplantation plan provides guidance on transplant day, donor patient preparation, and organ safety. This review serves as a guide for recipient individual. This review study consists of specific sub-titles related to the subject.

**Keywords:** Organ transplant, Nursing care, Peri-operative care, Organ recipient

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## Introduction

Organ transplantation is a known treatment method for replacing a non-functioning organ and is used in both developed and developing countries. It is accepted as the removal of damaged organs from the body and replacement with healthy organs. The specialization in this is context handled in nursing care. Since the nursing profession requires a patient-oriented study, all patients receive nursing care. A holistic approach taken by organ transplant patients is important to patient care. All applications bind to a certain protocol. A professional transplant nurse observes the patient's physiological parameters before the patient undergoes organ transplantation. The nurse reports observations and takes precautions against complications and possible rejections that may occur after surgery. This study was carried out to address the lack of an adequate supply of resources for the care of organ recipient patients. The study acts as a guide. Organ transplantation is performed to cure a recipient patient. Thus, a holistic view of the patient is required. The aim such care is to improve the quality of life of the organ recipient in the pre-operative period. For this, a holistic approach is used to develop a specific care plan for activities [1, 2].

### Scientific questions

- Do surgical nurses of the transplant patient provide symptomatic treatment or traditional care?
- What is the order of priorities for surgical nurses while caring for patients who are undergoing immunosuppressive treatment?

### Type and purpose of the study

These study data were written as a traditional review by scanning the relevant literature. In the literature review, transplantation patients are mentioned as general surgery patients. Nursing services should always provide personal and holistic care. Transplant patients should be separated into donor and recipient care groups because the procedure for the two patients is not the same. Since an organ was removed from one and placed into another individual, the required care for the two individuals is not the same.

### Religious and intercultural ethical dimensions in organ transplantation

Organs taken from both living and deceased individuals have always been analyzed. Cultural differences in terms of transplantation process exist [4]. Whether organ transplantation is permissible and its effects on the hereafter are also debated [5]. This topic is confusing not only for those who belong to the religion of Islam but also for other religions. No matter how the clergy speaks on this issue, it is not easy to overthrow the old teachings [6, 7].

While our religion encourages us to donate, people can say "no" to organ donation [8–10]. Such a strict stance against organ donation is not a religious belief but rather represents conservatism. This attitude reveals the differences in belief between cultures. The ethical dimension also affects the way of perception and legal regulations [1].

The process of organ donation was performed in Christian communities living in America and Europe. "In eternity we will neither have nor need our bodies: old things will pass, all will be renewed" [11]. According to this belief, they know that

nothing can come between God and his servant even after death [6, 11]. The sect known as Jehovah's Witnesses is different from conventional Christianity. The problem with organ transplants is that Jehovah's Witnesses refuse to receive a blood transfusion although all dialysis infusions, plasma exchange, and administration of albumin, and coagulation factors are allowed [6, 11]. According to Jehovah's Witnesses, God forbids taking another person's organ. This view changed in the 1980s as "transplantation can do without blood transfusion" [6, 7]; however, organ transplantation is not possible without blood transfusions [6].

Since brain death is not accepted in Buddhism, organ transplantation is not accepted. Organs believed to have died with their previous owner are thought to be of no use to anyone else [6–11].

### Recipient immunology

Precautions should be taken to prevent organ rejection before organ transplantation. Thus, the chance of success increases. Some tests need to be performed between the donor and the recipient to ensure the acceptance of the organ by the recipient's body. Various tests are used to examine organ compatibility between the recipient and the donor. The first of these tests is performed to determine the blood group. Cross-matching, human leukocyte antigen (HLA) tissue type screening, and anti-HLA antibody tests are among the group of tests. Also, in the pre-transplant tests, the levels of Scd30 and C4d should be monitored before and after the operation. These values indicate organ acceptance/rejection and allows us to determine whether the body accepts the organ or if complications develop [7, 12].

Blood group incompatibility causes tissue rejection [13]. However, in critical cases, some measures can be taken at an antibody level between 1/8 and 1/16, and transplantation can then be done [12].

HLA tissue types are viewed in two ways. In the serology test, lymphocytes are placed on different types of antibody-coated tissue. Tissue type is determined according to lymphocyte death. The molecular method and the polymerase chain reaction (PCR) tests are used together. Tissue compatibility is checked when these tests are used together [14].

The anti-HLA antibody test is a four-stage review method. First, a complement-dependent cytotoxicity (CDC) test with serology is performed and indicates the danger of hyperacute excretion; however, it is not very reliable. The amount of antibodies that will pass from the donor to the recipient can be calculated by flow cytometry [15, 16]. The enzyme-linked immunosorbent assay (ELISA) test is sensitive enough to detect low levels of IgG antibodies. It is more reliable and faster. Also, with the cross-match test, the donor's lymphocytes are compared with the recipient's serum. The flow cytometer can also detect previously undetectable antibodies [14]. If both the serological method and ELISA tests are positive, transplantation is not performed. If T-lymphocyte positivity is found regardless of other parameters, transplantation should also not be performed [12, 14, 18].

Three main reasons why the recipient remains unresponsive exist, namely, antigen, cytokine, and transplantation tolerance. As a result of these factors, predetermined immunosuppressive treatment is planned, and post-transplant

organ rejection complications can be minimized. The immunotherapeutic approach is initiated earlier is to adapt to the steps of the process [7, 12].

Antigen, cytokine, and other complex mechanisms should readjust after precautions are taken before transplantation. The regeneration time and pathogen parameters of the allograft should improve as a result of these actions [14]. Immune responses show rapid recovery.

### Organ Conservation Protocol

The basic aim of organ protection is to prevent organ damage and loss of function. Organs can be stored for a long time using a simple hypothermic method, which is used as a precaution against adverse situations. Organs can be stored using this method according to their tissue and structure characteristics. Heart and lung can stay viable for 4 to 6 h, kidney 18 to 36 h, liver 12 to 18 h, and pancreas up to 12 h [14, 19].

Basic principles for proper preservation of the organ:

- **Hypothermia:** Hypothermia is used to reduce cell edema and slow down enzyme destruction. The simplest method is to wash the organ with a cold solution (4 °C) and transfer it to a sterile organ bag. A cold chain must ensure. In another method, the organ is placed in a device and perfused until it reaches the recipient. Thus, the function of the vessels is preserved. The ischemia time of the organ increases using these methods; thus, they allow the organ to remain viable for a longer time. It is a very safe method [20, 21].

- **Prevention of Intracellular Acidosis:** Using the right solution for perfusion prevents tissue damage. Ringer's lactate is one such solution. Various solutions were developed later [20, 21].

- **\*Eurocollins Solution;** forms crystalline precipitates above the solubility of magnesium phosphate. Magnesium is extracted from this solution and made compatible with the organ.

- **\*UW (University of Wisconsin) Solution.** This solution provides the best hepatic protection. Cold increases the ischemia time at least 2–3 times [20, 21].

- **\*HTK (Custodial, Bretschneider) Solution.** It is cardioplegia (Perfect tamponade). It can be used for kidneys, livers, and pancreases and is low-cost [14].

- **\*Celsior Solution;** It is the only extracellular solution with low potassium [20].

- **\*Low potassium dextran (LPD);** its use is increasing at present [22].

- **Transport:** The organ should be packed. It is placed in a 3-stage sterile organ bag. The organ is placed in the first bag with enough physiological cold (4 °C) solution. The amount of solution added to the bag is important and should be such that the organ does not come into contact with cooling elements or crushed ice. The first bag is placed in the second bag containing the cold solution. The second bag is then placed in the third organ bag, which is empty and is the outermost bag. These bags should be sterile and sealed [22].

Labeling and container placement after organ packaging is also very important. On the organ carrying bag/container, the "HANDLE WITH CARE. HUMAN ORGAN" label must be affixed. Date, time, hospital, organ type, organ side, donor information, institutions, and addresses should be reported. Waterproof filing should be supplied. This prepared file should be added to the recipient's file [14].

The transplant coordinator organizes everything for organ removal and transfer. More than one organ can be transferred at the same time. In this case, a delay in processing time should be considered [21].

### Precautions to be taken against complications and psychosocial statuses

Different psychosocial statuses are similar in all organs and systems as they represent a common background for all patients [23, 24]. However, although complications vary, infection, bleeding, thrombosis, and rejection are the most common ones [14].

- **Bleeding:** Bleeding is a complication resulting from different reasons specific to each organ. For example, it may be due to undetected trauma during nephrectomy for a kidney transplant for which early repair is possible. Necrotic leaks due to infection at the distal or proximal end of the anastomosis may occur, and bleeding may occur with the development of an aneurysm [28]. Liver-related hemorrhaging is generally seen on the entire surface. Fresh frozen plasma and platelets are administered to stop bleeding. However, it should be known that these agents can increase the coagulation factor. Gastrointestinal system organ transplant bleeding is generally related to rejection and infection. Necrosis can be seen in four anastomoses performed in whole heart transplantation. Cutting the recipient distal to the removed heart vessels entails grafting, which prolongs the procedure time for the heart, a process that needs to be performed within 4 h. A technical error in the procedure can cause prolonged bleeding [25].

- **Infection:** It is an important step to interrupt resistance to the transplant via the use of immunosuppressive therapy. This step is done to prevent the development of infection in the organ after transplantation. In the first month after transplantation, an infection may occur in the lung, surgical wound, and urinary system. Opportunistic microorganisms that can develop within 1–6 months, including cytomegalo virus (CMV), Epstein-Barr Virus (EBV), herpes virus (HSV), hepatitis, non-cardiac, toxoplasma, and Listeria fungi, and pneumonia types. To reduce the risk of hospital infections, prophylactic immunotherapy is started. Skin integrity must be preserved. Fluid-electrolyte balance is checked at least twice a day [26].

- **Thrombosis:** Arterial thrombosis is usually associated with hypercoagulation. Slowing of blood flow in arteries and veins develops due to shrinkage and fracture of blood vessels. Microsurgery is used in liver transplantation to reduce the incidence of hepatic artery thrombosis [25].

- **Rejection:** Rejection is defined as the body's rejection of an organ or tissue that it considers foreign to itself. Organ rejection is the most serious and irreversible complication. Through immunosuppressive therapy, immunity can be strengthened. With this treatment, recovery is maintained to prevent post-operative organ rejection [27, 28]. Rejection can be hyperacute, acute, or chronic. Hyperacute manifests itself in the first 48 hours. Acute occurs within 1–5 hours and is seen during the week after transplantation surgery. Chronic rejection is seen in the first six months. After transplantation, a decrease in the amount of urine occurs. Symptoms, such as fever, hypertension, weight gain, increased organ size, increased organ sensitivity, and decreased

platelet number, suggest the presence of infection, which subsequently suggests organ rejection [29].

Table 1 includes the important causes of rejection of the heart, kidney, and liver.

- **Psychosocial problems:** With the increasing need for transplantation, medical parameters are not the only criteria. Psychosocial assessment has also become an important criterion since pre-transplant psychosocial problems will continue after transplantation [30]. According to the Stanford Integrated Psychosocial Assessment for Transplantation (SIPAT) scale, physical status is not the only adequate parameter to choose a transplant person. The psychosocial status of the patient should also be considered because stress management in the recovery process is the most important part of pre- and post-transplant care [14, 30, 31].

Table 2 includes risk factors within the scope of Stanford Integrated Psychosocial Assessment for Transplantation.

### Role and Responsibility of the Transplant Nurse

A transplant nurse is a trained caregiver. He/she manages follow-up and treatment after the patient has been admitted. This nurse provides team organization to improve the quality of service and also has various roles [14]:

- Leadership
- Use and delegation of resources
- Leveraging evidence-based practice and research
- Compliance with ethical rules
- Ensuring cooperation among the whole team
- Education and training
- Evaluating the contribution of professional practices to the healing process
- Managing maintenance

Organ transplant nurses have served under the name of “coordinator” in recent years, namely, clinical care coordinator, care coordination, and advanced clinical care coordinator [3].

#### · *Clinical Care Coordinator*

The task of the coordinator involves pre- and post-transplant education of the patient and his family [14].

#### · *Maintenance Coordination Coordinator*

For direct or indirect maintenance, planning is made and team members are directed. By managing time, this coordinator ensures the synchronous progress of the transplantation. He/she is an educator, advocate, and consultant and has analytical skills. He/she makes quick decisions and is experienced in the transplant field [14].

#### · *Advanced Clinical Care Nurse Coordinator*

These coordinators are nurses who have completed their education at a master’s or doctoral level. This person takes precautions for acute and chronic problems that may develop. Nurses with the same training in the United States are known as nurse practitioners. These nurses are authorized to prescribe medication and diagnose medical issues. They work as organizers in Turkey. We have nurses in Turkey who receive such training and manage difficult cases. For this reason, these nurses should have the authority to diagnose and administer drugs, such as the nurses in developed countries do because it is a very special unit considering its working potential. Transplant surgery should no longer be considered a sub-branch but rather its own field [3].

### Transplant recipient education

Patient education for the transplant recipient should be patient-centered. A holistic approach, which is an important principle of nursing, is applied to the patient. This training begins before transplant process and continues with the post-transplant discharge and home care processes [32]. The purpose of this training is to manage the recipient’s stress throughout the transplant process. The recipient should know beforehand the risks he will face [33, 34].

#### *Pre-Transplantation*

✓ The patient is admitted to the transplant center. Necessary isolation stages are enacted. Visiting restrictions and their importance are explained. Information about the duration of the operation is given.

✓ Training materials and methods should be chosen (assessment, difficulties, support systems, and others).

✓ Information is given about organ rejection. The patient is alerted to such a possible situation.

✓ The patient is allowed to express his or her feelings.

✓ Post-operative deep breathing exercises, use of spirometer, in- and out-of-bed exercises are taught.

✓ The intensive care process is planned according to the type of transplant. This process describes the length of stay in the intensive care unit (ICU), pain management, intravenous arterial cannulas, drains, and the early Ambu procedure.

✓ Before the operation, the patient is reminded to bathe.

✓ On the morning of the operation, surgical gown, and bonnet are put on the patient, and he/she is transported to the operating room along with his/her medical file [3].

#### *Post-Transplantation*

✓ Confidentiality is respected.

✓ Necessary safety precautions are taken in the room to minimize the risk of falling.

✓ The intensive care period last 1 to 3 days, the clinical period for 7 to 12 days, and then the home care period begins. Thus, the patient is given the necessary education about the home care process.

✓ The importance of diet, exercise, medication, and appointment times is emphasized.

✓ Anxiety can occur in the first days of life at home. The patient may experience a mild episode of depression. In this case, they are referred to psychological support.

✓ Infections may develop in all parenteral routes and immunosuppressive therapy. Thus, appropriate care is given, and aseptic technique is used.

✓ Also, attention should be paid to personal care in terms of medication therapy.

✓ Harmful habits, such as smoking and alcohol, should be stopped.

✓ A salt-free or less salty diet is recommended [14].

#### *Drugs and Use*

✓ Immunity is supported to prevent organ rejection. Antibiotics are used to prevent infection, diabetes, and blood pressure fluctuations. If necessary, cholesterol-lowering drugs are used [11].

✓ A special treatment program is prepared for the patient. The name of the drug, dosage, mode of use, and daily intake times are documented. He/she should always carry the drug user guide with him after discharge.

- ✓ The patient understands the side effects of the drugs.
- ✓ The patient is always told to take their medication 10–15 days in advance. He/she should always have spare medicine with him.
- ✓ The chronic disease drugs used before the transplant are also continued.
- ✓ If the drug is not taken on time or the wrong dose is taken, the patient must inform the transplant doctor.
- ✓ In general, certain drug derivatives are used to prevent organ rejection. These include cyclosporine-A, tacrolimus, Cellcept, sirolimus, Imuran, and corticosteroid medication [33, 34].

### Conclusion

Beliefs, religions, broad cultural attitudes, and interactions about organ donation are quite complex. The clergy should be educated about brain death and organ donation for transplantation. The process starts with organ donation. To be successful, the recipient's parameters must be compatible with the donor's parameters. Psychosocial preparation and adequate communication with the team are required. Post-transplant care is very important for acceptance of the organ by the body. A special care plan is prepared for the needs of the patient. Communication with the transplant team is supported. The importance of possible complications is explained and actions to be taken are planned. A holistic approach is provided to the patient. A nursing duty is to optimize post-transplantation by using pre-transplant care and precautions.

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# Metastatic multiple gastric neuroendocrine tumors with a long history of proton pump inhibitor use: A case report

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The authors stated that the written consent was obtained from the patient presented with images in the study.

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No conflict of interest was declared by the authors.

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## Abstract

It is widely accepted that gastric neuroendocrine tumors (NETs) develop due to enterochromaffin-like (ECL) cell proliferation following exposure to hypergastrinemia, which causes hyperplastic-dysplastic-neoplastic changes. Here we describe the case of a 46-year-old female patient diagnosed with metastatic NETs by liver biopsy and evaluated at an external center. At our hospital, nodular structures extending from the cardia to the antrum were observed by gastroscopy, considered the primary tumor focus. Histopathological examination revealed a trabecular-insular pattern, with microNETs consisting of monotone cells with round-oval nuclei and surrounding neuroendocrine cell hyperplasia foci and fundic gland polyps. The patient had a history of regular proton pump inhibitor (PPI) use for 10 years and a serum gastrin of 9240 pg/mL. A 3-cm metastatic lesion in the left lobe of the liver was observed in whole-body imaging with octreotide. By gastrectomy, we observed a large number of nodular lesions in the corpus-antrum and a 3-cm diameter lesion in the hepatectomy material. Histopathological examination revealed NETs in multiple foci with submucosal invasion in the stomach. The Ki-67 proliferative index was 3%. Metastatic tumors of similar morphology were found in the liver and three of the greater curvature lymph nodes. We made a diagnosis of multiple gastric NETs (Grade 2). In Type I gastric NETs, the neuroendocrine cell proliferation spectrum up to NET is observed as a result of hypergastrinemia due to atrophic gastritis. Also, in experimental studies, prolonged hypergastrinemia has been reported to cause ECL cell neoplasms in animals treated with PPIs. Although our case could be accepted as Type 1 NET, the possibility of developing NET secondary to long-term PPI use should also be considered.

**Keywords:** Stomach, Neuroendocrine tumor, Proton pump inhibitor usage

## Introduction

Gastric neuroendocrine tumors (NETs) are observed at a rate of 8% among gastrointestinal NETs [1, 2]. Although it is rare, since endoscopic examinations are routinely used as a screening method, and awareness of these lesions has increased, NET diagnosis has been included in pathology reports in recent years [1-3].

The widely accepted opinion in the pathogenesis of gastric NETs that develops as a result of enterochromaffin-like (ECL) cell proliferation is exposure to hypergastrinemia, which causes hyperplastic-dysplastic-neoplastic changes [4, 5].

Gastric NETs are classified into three groups: Type 1 NET due to hypergastrinemia in the background of atrophic gastritis, Type 2 NET due to hypergastrinemia secondary to Zollinger-Ellison Syndrome (ZES)/Multiple Neuroendocrine Neoplasia-1 (MEN), and Type 3 NET with normal serum gastrin level which is sporadic [6]. Recently, ECL cell NET has been associated with an intrinsic defect in parietal cell acid secretion [6]. Proton pump inhibitors (PPI), widely used in the treatment of acid-related diseases, also inhibit gastric acid secretion, causing gastric hypoacidity and secondary hypergastrinemia due to chronic use [7].

In addition, PPI induces ECL cell hyperplasia. A few experimental studies have reported that long-term hypergastrinemia causes ECL cell neoplasms in animals (rats) treated with PPI [8]. However, it is controversial whether PPI affects humans in this direction [9-13].

We present a very rare case of metastatic gastric NET characterized by multiple foci, who had a history of long-term use of PPIs which was successfully treated with total gastrectomy.

### Case presentation

A 46-year-old female patient attended an external center with dyspeptic complaints, such as nausea, burning, and heartburn. The abdominal ultrasonographic examination revealed grade 1 steatohepatitis and a  $23 \times 17$  mm hyperechogenic solid lesion in the second segment of the liver. In the additional magnetic resonance (MR) examination, the lesion found in the lateral segment of the left lobe was  $40 \times 35 \times 30$  mm in size with a smooth contour. Histopathological examination of the needle biopsy performed on the lesion, which was interpreted in favor of adenoma in the imaging, resulted in NET.

Following admission to our hospital with these findings, additional examinations were performed primarily in terms of the possibility of a primary NET originating from the extrahepatic organ due to the rare NETs in the liver.

Laboratory findings [Hb: 11.8 g/dL (reference: 13.6–17.2), Hct: 37.6% (reference: 39.5–50.3), MCV: 72.2 fL (reference: 80.7–95.5), MCH: 22.7 pg (reference: 27.2–33.5)] results were evaluated as microcytic anemia. Tumor markers [CEA: 0.82 ng/mL (reference: 0–4.0), CA19-9: 21.35 IU/mL (reference: <27), CA125: 15.59 IU/mL (reference: <35) and AFP: 5.34 ng/mL (reference: <7)] was within normal limits. In the whole abdominal computed tomography (CT) examination, an anteromedial subcapsular lesion, approximately  $28 \times 27$  mm in size, at the liver segment 2 level, with a smooth border, accompanied by millimetric calcification in the central and mild heterogeneity in the upper contour, was observed. No feature was found in thorax CT.

In the patient's medical history, there was a history of operation for urolithiasis and parathyroid adenoma and a history of regular use of proton pump inhibitors at a dose of 30 mg/day for 10 years.

In the gastric endoscopic examination performed during systemic scans, hard, nodular structures raised from the mucosa, starting from the cardia and reaching the antrum, were observed. Biopsies with a diameter of 0.4–0.3 cm were taken with the preliminary diagnosis of gastric carcinoma and neuroendocrine tumor. In one of the samples, we noted tumoral infiltration in the trabecular pattern, which is 0.5 cm in size, and consists of round cells in the lamina propria, containing a nucleus with a uniform, salt-black pepper chromatin structure and small round nests of different sizes, consisting of similar cells in the surrounding mucosa. The immunohistochemical study observed positive staining in these cells with synaptophysin and chromogranin (MRQ-40 and LK2H10 Cell Marque, USA). Also, hyperplasia and cytoplasmic apical budding were observed in the parietal cells. There were fundic gland polyps in a few fragments. With these findings, it was diagnosed as a “microneuroendocrine

tumor and neuroendocrine cell hyperplasia in the surrounding mucosa”.

It was interpreted that the present pathological findings might be related to the long-term use of proton pump inhibitors in the clinical history, and it was recommended to evaluate the whole stomach in terms of NET spread. A liver biopsy, which was evaluated in an external center, was also re-examined in our department. The tumor observed in its cross-sections and having a morphology similar to that seen in stomach biopsies was verified as a “metastatic neuroendocrine tumor”.

The gastrin level was 9240 pg/mL (reference: 13.0–115.0). In addition, intense In-111 octreotide uptake, representing a solitary metastatic lesion in the left lobe of the liver, was observed on body imaging with octreotide. Radiopharmaceutical uptake in other areas of the body was within physiological limits. As a result of all examinations, the patient underwent total gastrectomy and left liver segmentectomy operation. The entire gastrectomy specimen was sampled. On gross examination, multiple nodular lesions, the largest of which were 0.8 cm in diameter, with a smoothly circumscribed cross-section, were gray-white and firm. Numerous nodular lesions were noted on the entire gastric mucosa (Figure 1). The lesions were more common in the fundus and corpus. Macroscopic examination of the liver revealed two gray-white colored nodular lesions,  $3 \times 3 \times 2.5$  cm in size and 0.1 cm in diameter, adjacent to the capsule.

Figure 1: a-b: Numerous tumor foci in sections of gastric resection material.



Histopathological examination revealed numerous nodular structures in the gastric tissue that invaded the submucosa and showed a trabecular-insular pattern containing a myxoid stroma in the focal areas (Figure 2, 3a). Mitosis was 1–2 at 10 high power fields in tumor foci with a morphological appearance similar to those observed in the endoscopic biopsy (Figure 3b), and the Ki-67 proliferative index (SP6 Cell Marque, USA) was 3% (Figure 4b). Widespread neuroendocrine cell hyperplasia foci of micronodular, adenomatoid, and dysplastic types (Figure 5a) and fundic gland polyps were observed in most areas (Figure 5b). Intestinal metaplasia was observed in focus in mostly atrophic mucosa. Neuroendocrine tumor metastasis was

detected in three large curvature lymph nodes (Figure 6a). Liver sections showed metastatic tumor foci (Figure 6b), anastomosing with each other, forming trabecular structures, and solid islands in a hyalinized stroma with a tumor-like morphology in the stomach. In the immunohistochemical study performed on tumor tissues in the stomach and liver, cells were stained positively with synaptophysin and chromogranin (Figure 4a). With these findings, a “Multifocal Neuroendocrine Tumor Grade II” diagnosis was made for gastric tissue and a “Metastatic Neuroendocrine Tumor” for tumor foci in the liver and three large curvature lymph nodes. During the follow-up of the patient, who had been followed up by the oncology clinic for 6 years and did not receive additional treatment, no pathological finding was detected. The patient has given written consent for this case report.

Figure 2: Tumor tissue with submucosal invasion (HE, ×40).

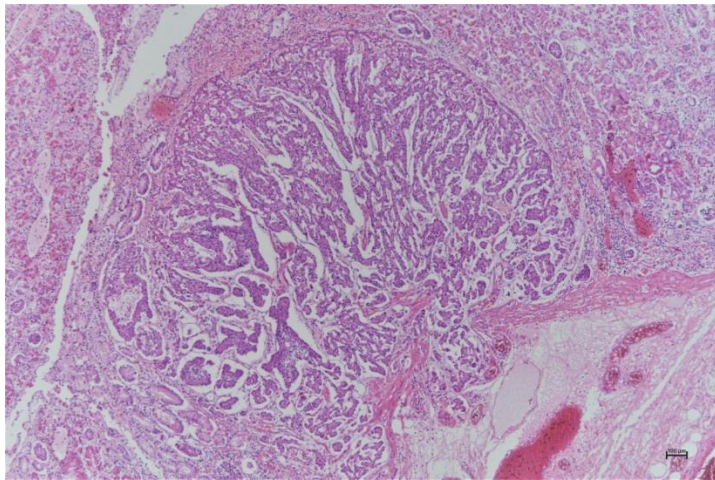


Figure 3: a: Cells with eosinophilic cytoplasm and round nuclei in tumor tissue consisting of solid islands (HE, ×200). b: Mitotic figure (HE, ×400).

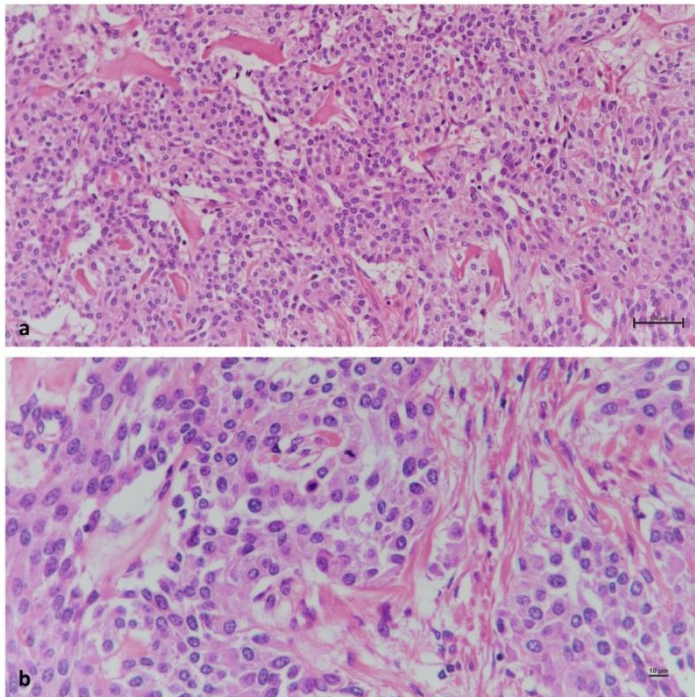


Figure 4: a: Chromogranin expression in tumor cells (×20). b: Ki-67 expression in tumor cells (×400).

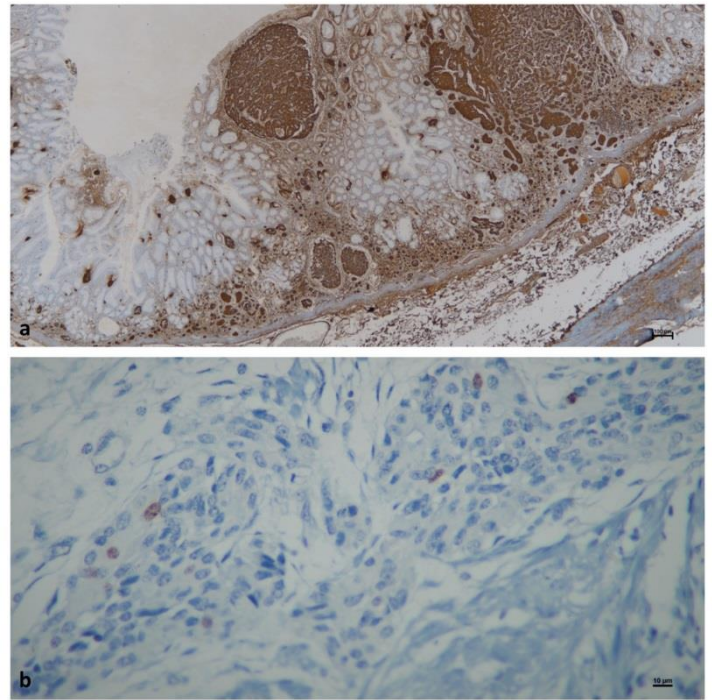


Figure 5: a: Fundic gland polyps in the surrounding stomach tissue (HE, ×40). b: Neuroendocrine cell hyperplasia foci in the surrounding gastric mucosa (HE, ×100).

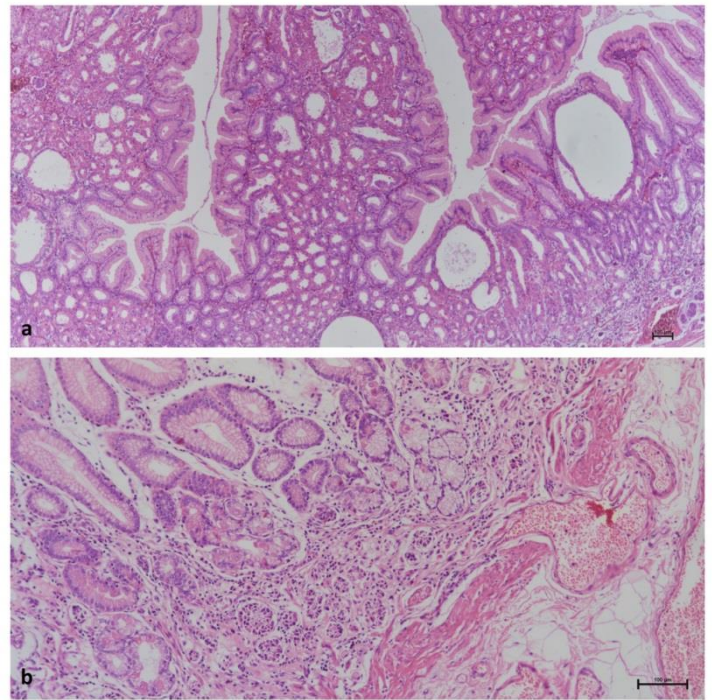
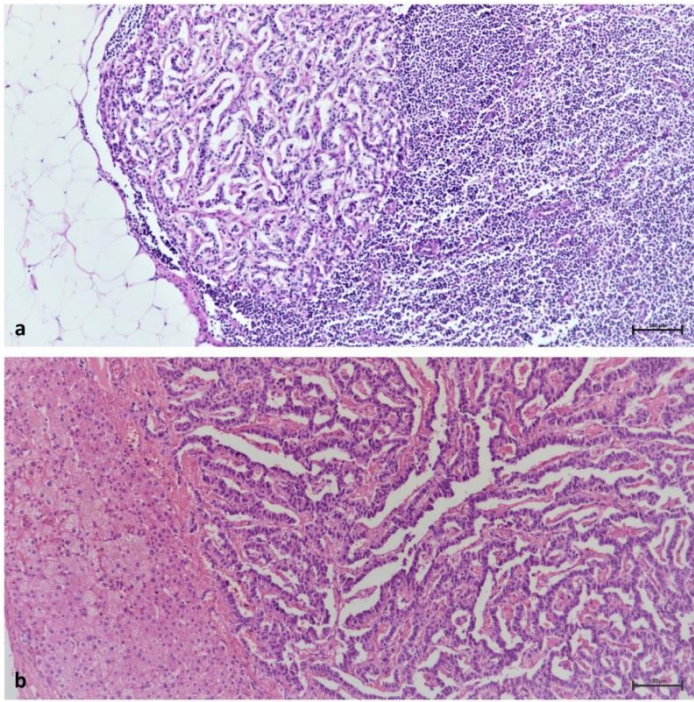


Figure 6: a: Metastasis focus in the lymph node in the greater curvature region (HE,  $\times 100$ ). b: Metastatic focus in liver (HE,  $\times 100$ ).



## Discussion

In the stomach, the neuroendocrine cell component is scattered throughout the gastric epithelium. This component, mostly composed of ECL cells (15–30%), also includes G cells, D cells, A cells, enterochromaffin cells, and X cells. ECL cells and G cells are prominent in gastric NET pathology. ECL cells are mostly localized in the fundus. G cells are located in the neck region of the mucous glands in the antrum and pylorus [5].

Gastrin, normally secreted by G cells, is regulated by the luminal hydrogen concentration secreted from parietal cells. Histamine secreted by ECL cells in response to gastrin stimulation stimulates the parietal cells. Endogenous parietal cell destruction due to autoimmune disease or with low acidity hypergastrinemia caused by exogenous drugs such as PPI, hypergastrinemia may also result in ECL cell hyperplasia [5, 8]. Linear, micronodular, and adenomatoid type ECL cell hyperplasia and dysplasia characterized by enlarged or fused micronodules consisting of atypical cells, microinvasion, or newly formed stroma are precursor lesions of NET and are precursor lesions that develop from ECL cells detected histopathologically [5]. In our case, there were precursor lesions consisting of diffuse ECL cells around microNET foci.

ECL cell hyperplasia in the surrounding mucosa is commonly observed in Type 1 and Type 2 gastric NETs. In addition, intestinal and pseudopyloric metaplasia is observed in the atrophic mucosa in Type 1 NET, while the mucosa is hyperplastic in Type 2 NETs. In type 3 NET, the surrounding gastric mucosa is normal. Recently defined ECL cell NET is associated with hypergastrinemia, and multiple lesions similar to Type 1 and Type 2 NETs are observed. In the surrounding mucosa, unlike other types, diffuse dilated oxyntic glands containing inspissated material in their lumen are observed [6]. In our case, hypergastrinemia and our morphological findings are more consistent with Type 1 gastric NET with the presence of atrophic mucosa, although intestinal metaplasia is not common.

PPI inhibits acid secretion by blocking the parietal cell's H<sup>+</sup>/K<sup>+</sup> ATPase enzyme system. With this effect, it is a preferred and widely used drug in treating acid-related diseases, such as gastroesophageal reflux and preventing aspirin/nonsteroidal anti-inflammatory drug-related ulcers and recurrences. Hypoacidity caused by PPI may cause an increase in plasma gastrin levels more than three times the normal (<100 ng/mL). Hypergastrinemia can also stimulate the proliferation of ECL cells, which is common in the fundic mucosa [14]. It has been reported that there may be undesirable consequences such as gastrointestinal infection, VitB 12 and iron deficiency, gastric fundic gland polyps, NET, and gastric and colon cancer associated with acid inhibition due to long-term use of the drug [8, 14]. In addition, studies show that it increases the frequency and severity of atrophic gastritis in patients with helicobacter pylorus [15, 16].

In experimental studies, it has been reported that long-term hypergastrinemia in animals (rats) treated with PPI leads to ECL cell proliferation and NET development by neoplastic transformation [8]. Although it causes ECL cell hyperplasia in humans, it is controversial whether it affects tumor development [8,17]. While there are more case reports in the literature, there are very few studies on this subject [2,9-13,18]. While no relationship was found between NET and PPI use in one of the existing studies, it was reported in another study that it was related and that NETs with less aggressive behavior emerged [13, 18].

In our case, many millimeter-sized tumor foci accompanying widespread ECL cell hyperplasia-dysplasia in the surrounding mucosa and the absence of a clinical picture associated with ZES/MEN-1 were absent more compatible with Type I NET among gastric NET types. However, in the case where we did not have information about serum antiintrinsic factor and antiparietal cell antibody levels, the presence of intestinal metaplasia in focus in the mucosa, which is generally atrophic, the presence of diffuse fundic gland polyps and high gastrin level, 10 years of PPI use in the history may be a possible factor in the development of gastric NETs.

In clinics, NETs diagnosed incidentally during routine endoscopic examination mostly progress with nonspecific findings [19, 20]. Therefore, they are typically diagnosed late, as in our case. Therefore, some cases have metastasis at diagnosis [20]. Our case was diagnosed with the detection of a metastatic tumor focused on the liver tissue.

High rates of local recurrences are defined in Type I NETs with low mortality risk. Therefore, surgical treatment may vary with tumor size and spread and approach differences [1, 21, 22]. Our patient, who was found to have liver metastasis, underwent total gastrectomy with lymph nodes due to his clinical condition. No pathology was found during the 6-year follow-up period.

## Conclusion

Although our patient's diagnosis is accepted as Type I NET based on current findings, because of the patient's history, the possibility of developing NETs secondary to long-term PPI use should also be considered. The recent increase in gastric NETs suggests a need for more frequent endoscopic controls, especially in cases with long-term PPI use and high serum



gastrin levels. Large-scale studies involving such cases can also contribute to understanding the pathogenesis of gastric NETs.

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