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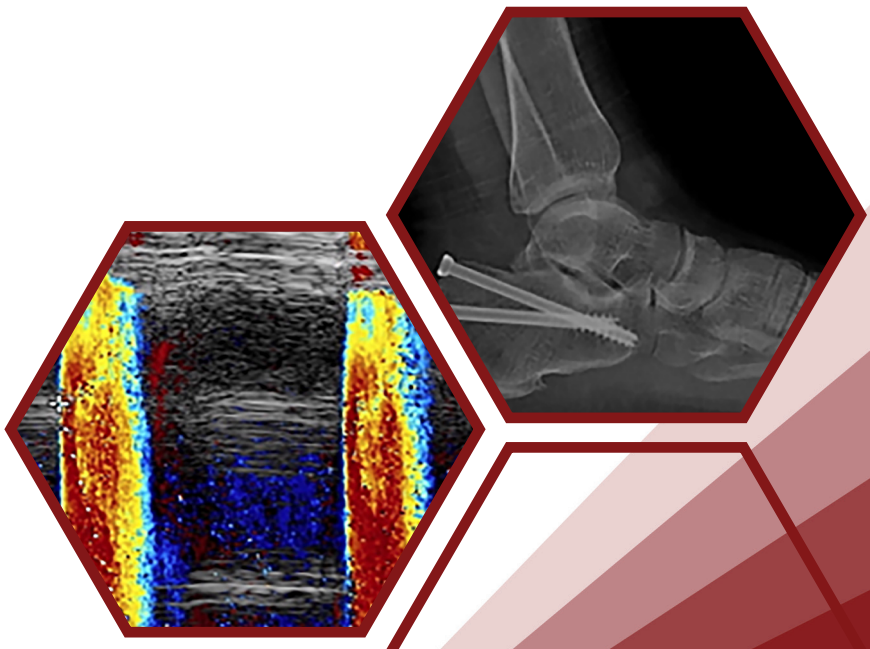

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Research Article

Comparison of Sinus Tarsi Versus Percutaneous Surgery in Displaced Intra-articular Calcaneal Fractures: Clinical, Radiological, and Pedobarographic Outcomes

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ABSTRACT

Objective: The objective is to compare the clinical, radiological, and pedobarographic outcomes of patients with intra-articular calcaneal fractures treated with sinus tarsi approach (STA) or percutaneous screw fixation postoperatively.

Methods: A consecutive cohort of 66 patients who underwent STA or percutaneous screw fixation for calcaneal fractures between January 2020 and June 2023 was documented. Patients who were at least 18 years of age and had more than 12 months post-operative follow-up were included in the study. Patients with orthopedic injuries to the ipsilateral or contralateral lower extremity, a prior history of lower extremity surgery, congenital deformities, neurological disorders, the utilization of drugs that may influence walking patterns and stability, open foot wounds, or any mental condition that could impair walking were excluded from the study.

Results: Of the patients, 24 underwent percutaneous screw fixation, while 42 underwent mini-open STA. No significant statistical differences were identified between the two groups in terms of demographic data, except for fracture classification. More advanced fracture patterns were observed in the sinus tarsi group. While statistically significant differences were found in the Talo-first metatarsal angle (P = .001), Talonavicular coverage angle (P = .001), Meary's angle (P = .001), and the angle between the medial cuneiform and fifth metatarsal (P = .022), no differences were observed in other radiological measurements. Clinically, significant differences in American Orthopaedic Foot and Ankle Society (AOFAS) (P = .005) and visual analog scale (VAS) (P = .049) scores were observed between the two groups. In dynamic pedobarographic analysis, when comparing the injured and uninjured extremities, significant differences were observed in the injured extremity of the sinus tarsi group in terms of forefoot maximum force (N) (P = .001) and hindfoot maximum pressure (N/cm^2) (P = .001).

Conclusion: While the STA group showed better functional and radiological outcomes, pedobarographic analyses revealed deficiencies in pressure and force distribution in the injured extremity within the STA group. These findings suggest that discrepancies in load and pressure distributions may not always be associated with functional and radiological outcomes, and despite consisting of patients with more severe fractures, ensuring the opening of the posterior facet and achieving joint reduction would increase patient satisfaction rates.

Keywords: Calcaneal fractures, sinus tarsi approach, percutaneous screw fixation, pedobarographic analysis, radiological evaluation

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INTRODUCTION

Calcaneal fractures comprise more than half of tarsal bone fractures and account for 1% to 2% of all bone fractures.[1] Approximately 75% of calcaneal fractures are classified as displaced intra-articular calcaneal fractures (DIACF).[2] Despite extensive research on the treatment of DIACFs, debates continue regarding the optimal approach.[3, 4] A review of the literature indicates that independent meta-analyses have shown that surgically treated DIACFs have faster return-to-work times and more satisfactory clinical and radiological outcomes.[3,4] In contrast, conservative treatment is often associated with subtalar arthritis, malunion, and poor functional outcomes.[5,6] The main topic of today's discussion is determining which surgical approach provides the most effective outcomes for DIACFs.[7]

The extensile lateral approach (ELA) has been used as the standard treatment in open surgery for DIACFs for many years.[7,8] This technique facilitates fracture reduction due to its ability to provide extensive visualization. In soft tissue mobilization, the bone is exposed with full-thickness flaps, and the application of the 'no touch technique' is included.[9] Despite the meticulous techniques employed, the ELA is still associated with significant wound healing complications, with reported rates varying between 5.8% and 43%. The fragile skin over the lateral calcaneal wall often leads to wound complications.[8,9] These complications include necrosis of the wound edges, dehiscence, hematoma, infection, and sural nerve injury.[10-12] Incidences of wound edge necrosis have been reported to range from 2% to 11%, soft tissue infections from 1.3% to 7%, and overall wound complication rates can reach up to 25%.[5,13,14]

Wound-related complications have guided orthopedic surgeons in the development of less invasive methods in this process. Recently, several minimally invasive techniques have been introduced, such as percutaneous fixation, external fixation, and arthroscopy-assisted methods using medial, lateral, or posterior approaches.[6,9,10,15,16] Among these techniques, the sinus tarsi approach (STA) has become popularized due to its advantages, such as limited skin incision, a lower rate of wound complications, and direct access to the posterior facet.[9,17,18] According to some authors, the limited access of minimally invasive approaches (MIA) to the joint line and their inability to provide adequate soft tissue looseness have been claimed to lead to deficiencies in fracture manipulation and reduction, complicating the procedures further.[9,19] However, research has shown that, despite limited access, STA allows for acceptable reduction of the posterior facet using plates and/or screws.[6,9,18] Percutaneous approaches were originally applied mainly to tongue-type fractures due to concerns about achieving proper joint reduction.

MAIN POINTS

- The sinus tarsi approach provided better clinical (AOFAS) and radiological outcomes with less postoperative pain.
- Reduced weight and pressure distribution were observed in the STA group due to more complex fractures, though this did not fully align with functional outcomes.
- The percutaneous group included simpler fractures, while the STA group dealt with more complex ones, which influenced the study's overall results.

Radiological imaging of the foot and ankle is frequently used to detect pathologies in this area. However, they are not dynamic images and do not provide clear information about the functionality of the patient's foot. Pedobarography, which has been used as a diagnostic and evaluation method for a long time, is of great importance for this functional analysis. This gait analysis technique offers highly accurate measurements of ground reaction forces during both walking and standing. It facilitates a static assessment of foot function and balance in a standing position, as well as a dynamic evaluation of pressure distribution on the plantar surface throughout all phases of the gait cycle. These devices deliver numerical values for pressure and visually represent the pressures on the plantar surface using a specific color scheme. Sequential images illustrate the pressure and contact areas from initial ground contact to the lift-off phase. Due to these benefits, pedobarography is increasingly used in some centers for foot and ankle disorders.[20,21]

This study aims to compare the clinical, radiological, and pedobarographic outcomes of patients with DIACF treated with STA or percutaneous screw fixation postoperatively.

METHODS

Patient Selection

It is a retrospective study that has been approved by the Ankara Bilkent City Hospital 2nd Clinical Research Ethics Committee Presidency (Approval number: E2-23-3577 Date: 27.03.2023). A consecutive cohort of 66 patients who underwent fixation for DIACF using either plate fixation with STA or percutaneous screw fixation between December 2020 and June 2023 at a hospital with a Level 1 trauma center was recorded and analyzed. The surgeries were performed through a mini open incision over the sinus tarsi or using the Modified Essex-Lopresti/Westheus closed reduction technique by two senior surgeons.[22-24] In the sinus tarsi group, the surgery was performed with a single L- or T-shaped plate (Figure 1) as described by Kikuchi and his collegeus.[25]

In the percutaneous group, the joint was indirectly reduced and the surgery was performed using 2 or 3 cannulated screws (Figure 2), as described by Ebrahimpour and his colleagues.[26]

Radiological images included anteroposterior, lateral, and calcaneal projections of the ankle. Preoperative computed tomography (CT) scans were also utilized for all patients. Twenty four patients were excluded due to concomitant injuries in the same extremity, neurological problems, and previous lower extremity surgeries. There were 90 patients who met the inclusion criteria, but 24 did not attend regular follow-ups. Therefore, 66 patients were included in the study. The treatment complications were classified into major and minor categories. Conditions requiring revision surgery, such as osteomyelitis, nonunion, and loss of reduction, are considered

major complications, while superficial wound-related issues (such as suture dehiscence, drainage, etc.) and symptomatic implants are classified as minor complications.

Clinical and Radiological Evaluation

Pain was evaluated using a 10 cm visual analog scale (VAS), with 0 indicating no pain and 10 signifying the most severe pain possible.[27] The active range of motion (ROM) of both ankles was assessed using a universal goniometer, following the guidelines established by the AOFAS. The ankle movements in the coronal and sagittal planes were assessed twice with the patient seated, and the average value was documented.[28]

Radiographs were obtained while the patient was standing, capturing dorsoplantar and lateral views of both feet. Fracture patterns were classified based on the Sanders classification.[5] Digital measurements included Kite's angle (talocalcaneal angle), talo-first metatarsal angle, and talonavicular coverage angle in the dorsoplantar view. In the lateral view, Meary's angle (talo-first metatarsal angle), lateral talocalcaneal angle, calcaneal pitch angle, Böhler's angle (the angle formed by two tangent lines to the calcaneus), Gissane angle (the intersection of the posterior facet and anterior process slopes), and the distance between the medial cuneiform and fifth metatarsal were recorded.[29,30]

Pedobarographic Evaluation

Pedobarographic measurements were performed using the Zebris FDM type 3 gait platform (Zebris Medical GmbH, Germany). Patients walked on the 10-meter-long platform for two minutes, during which data were collected from the sensor-equipped section of the platform, recorded on a computer, and analyzed using manufacturer-developed software. Both extremities were evaluated in the patients. Gait measurements, plantar force, and pressure distributions were recorded.

Statistical Analysis

The study data were analyzed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, released in 2013). The normality of the data was examined using the Shapiro-Wilk test, and Levene's test was applied to assess variance homogeneity. For group comparisons, independent t-tests, Welch tests, or Mann-Whitney U tests were used.

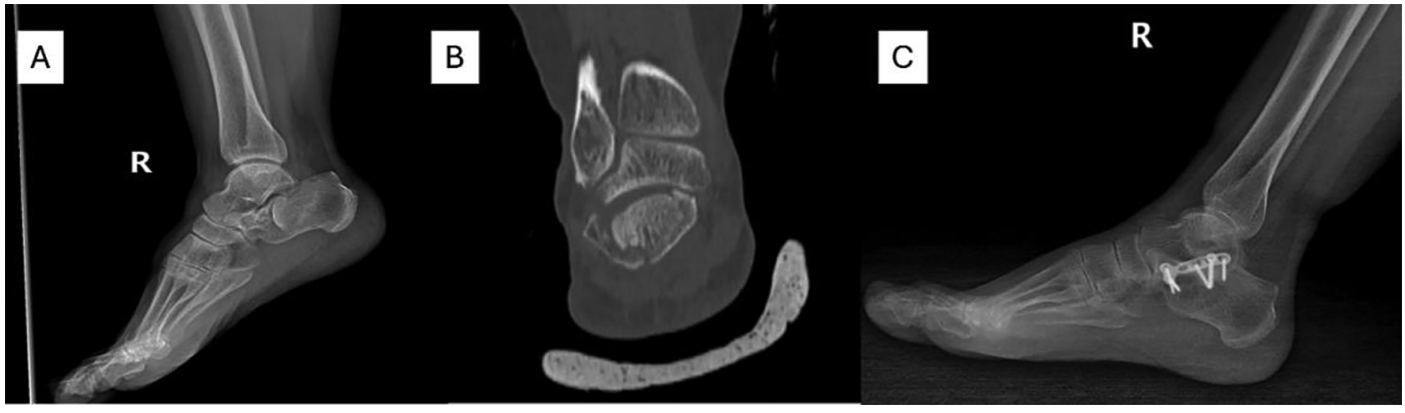

Figure 1. A patient operated on using the sinus tarsi approach. (A) Preoperative lateral X-ray image of the patient with a calcaneal fracture. (B) Coronal CT scan showing intra-articular comminution of the calcaneal fracture. (C) Postoperative lateral X-ray image showing fixation of the calcaneal fracture with a T-plate.

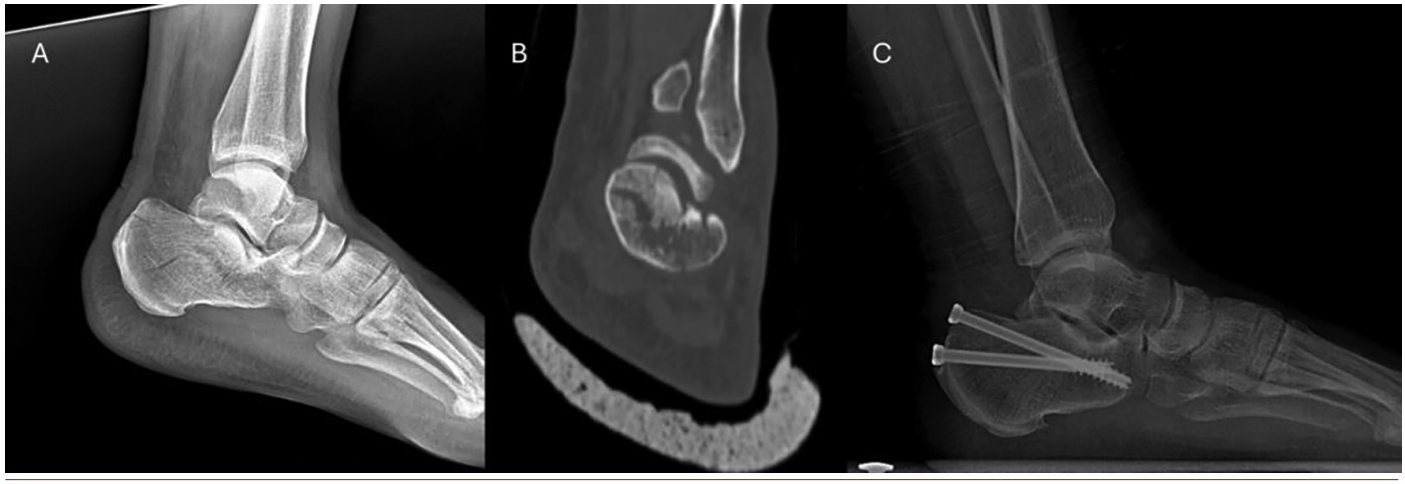

Figure 2. A patient operated on using percutaneous screws. (A) Preoperative lateral X-ray image of the patient with a calcaneal fracture. (B) Coronal CT scan showing intra-articular comminution of the calcaneal fracture. (C) Postoperative lateral X-ray image showing fixation of the calcaneal fracture with with 2 cannulated screws.

Fisher's exact test was employed for categorical variables. A 2-way analysis of variance (ANOVA) was performed to investigate the effect of injured versus uninjured limbs and stable versus unstable fractures on the outcome measures. The association between numerical variables was assessed using Pearson correlation or Spearman's rho. Continuous variables were presented as means with standard deviations or as medians with range values, depending on the context. Categorical data were presented as frequencies and percentages. In statistical analyses, a significance level of .05 and above was considered significant.

RESULTS

Of the patients, 24 underwent percutaneous fixation, and 42 underwent STA fixation (Figure 3).There were no significant statistical differences between the groups in terms of patient age (P = .810), side of injury (P = .575), gender (P = .768), and follow-up duration (P = .763) (Table 1). According to the Sanders classification, most patients in the percutaneous group were type 2A, whereas the STA group primarily consisted of type 3AB patients. A statistically significant difference in classification between the two groups was observed (P = .001). While no major complications were observed in either group, minor complications included superficial wound infections in 5 patients in the STA group and in 3 patients in the percutaneous group, with no statistically significant difference detected between the two groups.

In the radiological evaluation using weight-bearing X-ray images, no significant differences were found between the groups for kite angle (P = .810), lateral talo-calcaneal angle (P = .186), Bohler's angle (P = .207), Gissane angle (P = .508), and calcaneal pitch angle (P = .400). However, significant differences were found in the talus-first metatarsalangle (P = .001), talonavicular coverage angle (P = .001), Meary's angle (P = .001), and medial cuneiform-fifth metatarsal angle (P = .022) (Table 2).

Clinically, significant differences were observed between the two groups in AOFAS (P = .005) and VAS (P = .049) scores (Table 3).

In dynamic pedobarographic analysis, when comparing the injured sides, significant differences were found in the midfoot (P = .007) and hindfoot (P = .031) maximum pressure (N/cm^2) values. In the percutaneous group, comparing the injured and uninjured sides revealed a significant difference in the forefoot time to maximum force (% of stance time) (P = .032), while no significant differences were observed in other measurements. In the STA group, significant differences were found in the forefoot maximum force (N) (P = .001), heel maximum pressure (N/cm^2) (P = .001), and heel time to maximum force (% of stance time) (P = .024) between the injured and uninjured sides, while no significant differences were found in other measurements (Table 4).

In butterfly and foot progression gait analyses, no significant differences were found between the injured and uninjured sides within each group or between the two groups (Table 5).

DISCUSSION

The most important findings of this study are that the STA group demonstrated significantly better clinical outcomes, as evidenced by a higher AOFAS score and less postoperative

Table 1. Demographics of the Study Groups

Characteristic	Percutaneous Group (n = 24)	Sinus Tarsi Group (n = 42)	P
Age (months)			
Mean ± SD	42.8 ± 11.2	43.4 ± 13.0	.810*
Median (min-max)	48 (22-54)	43 (18-64)	
Side			
Left	12 (50%)	18 (42.9%)	.575⁺
Right	12 (50%)	24 (57.1%)	
Sex			
Male	20 (83.3%)	31 (73.8%)	.768
Female	4 (16.7%)	11 (26.2%)	
Sanders Classification			
2A	15 (62.5%)	0 (0.0%)	**.001⁺**
2B	0 (0.0%)	3 (7.1%)	
2C	0 (0.0%)	3 (7.1%)	
3AB	6 (25.0%)	18 (42.9%)	
3AC	0 (0.0%)	0 (0.0%)	
3BC	0 (0.0%)	9 (21.4%)	
4	3 (12.5%)	9 (21.4%)	
Follow-up (months)			
Mean ± SD	30.1 ± 12.1	29.5 ± 12.5	.763*
Median (min – max)	34.0 (14.0-43.0)	36.0 (12.0-47)	

*Mann-Whitney U test, ⁺Pearson Chi Square test.

pain compared to the percutaneous group. Radiological findings indicated that both groups exhibited hindfoot varus, and there was a significant reduction in forefoot adduction in the percutaneous group compared to the STA group. Joint reduction has been achieved better in the STA group despite a more severe fracture morphology, due to direct visualization of the joint. Therefore, it seems reasonable that there is less pain in the STA group. Pain is likely to result from post-traumatic subtalar arthritis as a consequence of inadequate joint reduction.

Dynamic pedobarographic analyses revealed a significant reduction in the average maximum force (N) in the forefoot and the average maximum pressure (N/cm^2) in the hindfoot of the injured extremity in the sinus tarsi group compared to the healthy extremity. When comparing the injured extremities between the groups, the percutaneous group showed significantly lower average maximum pressure (N/cm^2) in the midfoot, while the STA group showed significantly lower average maximum pressure (N/cm^2) in the hindfoot.

Table 2. Radiological Measurements of the Study Groups

Measurement (degree)	Percutaneous Group (n = 24)	Sinus Tarsi Group (n = 42)	*P**
Kite's anlgle			
Mean ± SD	14.3 ± 7.1	13.0 ± 9.6	.810
Median (min-max)	11.9 (6.1-25.0)	14.1 (-10.2-28.3)	
Talus – first metatarsal angle			
Mean ± SD	-6.3 ± 8.8	4.8 ± 7.3	**.001**
Median (min-max)	-8.5 (-25.6-11.3)	2.7 (-3.1-20.5)	
Talonavicular coverage angle			
Mean ± SD	12.2 ± 7.2	0.6 ± 9.2	**.001**
Median (min-max)	13.8 (0.6-24.9)	3.8 (-20.4-10.7)	
Meary's angle			
Mean ± SD	12.4 ± 6.3	4.7 ± 6.8	**.001**
Median (min-max)	12.6 (2.3-22.0)	5.1 (-10.0-16.5)	
Lateral talo-calcaneal angle			
Mean ± SD	33.9 ± 14.7	32.0 ± 11.6	.186
Median (min-max)	41.2 (6.3-47.7)	31.0 (8.9-62.2)	
Bohler's angle			
Mean ± SD	22.0 ± 8.0	24.0 ± 15.0	.207
Median (min-max)	25.0 (8.0-31.4)	26.0 (-14.2-46.4)	
Gissane angle			
Mean ± SD	130.2 ± 13.4	132.1 ± 10.1	.508
Median (min-max)	129.0 (104.0-150.0)	131.5 (115.0-153.0)	
Medial cuneiform – fifth metatarsal angle			
Mean ± SD	5.5 ± 1.9	6.5 ± 3.0	**.022**
Median (min-max)	5.0 (3.6-10.0)	5.6 (0.1-12.0)	
Calcaneal pitch angle			
Mean ± SD	13.9 ± 4.4	14.2 ± 5.7	.400
Median (min-max)	13.5 (8.2-22.0)	15.0 (0.0-22.2)	

*Mann-Whitney U test.

Table 3. Clinical Scores Comparison Between the Study Groups

Score	Percutaneous Group (n = 24)	Sinus Tarsi Group (n = 42)	*P**
AOFAS Score			
Mean ± SD	63.2 ± 21.9	79.7 ± 13.5	**.005**
Median (min – max)	56.0 (37.0-100.0)	76.5 (54.0-100.0)	
VAS Score			
Mean ± SD	3.7 ± 2.1	3.0 ± 1.6	**.049**
Median (min – max)	4.0 (0.0-6.0)	3.0 (0.0-5.0)	

*Mann-Whitney U test.

Chronic pain after foot and ankle fractures is a prevalent and important issue that requires attention, as patients commonly report enduring pain following these injuries. This pain adversely influences functionality and quality of life. In this study, postoperative pain severity was assessed using the VAS score. The average VAS score was 3.7 ± 2.1 in the percutaneous group and 3.0 ± 1.6 in the STA group, with a statistically significant difference between the groups (*P* = .049). While there are studies in the literature comparing VAS scores following percutaneous or open reduction and internal fixation (ORIF) treatment of DIACF, comparisons specifically involving the STA are limited.[20,31] This study observed that patients treated in the STA group experienced less postoperative pain compared to those in the percutaneous group, which contradicts the existing literature.[32] These findings highlight the critical importance of the quality of posterior facet reduction in reducing chronic postoperative pain.

In our study, the mean postoperative AOFAS score was 63.2 ± 21.9 in the percutaneous group and 79.7 ± 13.5 in the STA group, demonstrating a statistically significant difference (*P* = .005). In line with authors who consider this procedure the gold standard for calcaneal fractures, we observed

Table 4. Pedobarographic Assessments For The Forefoot, Midfoot and Heel.

	Pedobarographic Parameter		**Percutaneous Group Mean ± SD Median (min-max)**	**Sinus Tarsi Group Mean ± SD Median (min-max)**	***P****
Forefoot	Maximum Force (N)	Injured extremity	555.6 ± 229.9 577.7 (223.4-818.6)	506.6 ± 223.3 564.8 (223.2-838.3)	*.548*
		Uninjured extremity	576.3 ± 222.7 605.2 (162.7-836.3)	654.1 ± 195.6 708.7 (260.7-851.9)	
		P*	.853	**.001**	
	Maximum pressure (N/cm²)	Injured extremity	29.7 ± 15.6 30.3 (7.6-51.5)	27.2 ± 13.4 23.5 (9.8-50.4)	*.471*
		Uninjured extremity	28.6 ± 12.8 29.0 (6.9-50.2)	31.2 ± 9.8 30.8 (16.2-51.1)	
		*P**	.853	.083	
Midfoot	Maximum Force (N)	Injured extremity	208.9 ± 60.8 194.7 (123.8-292.0)	200.8 ± 78.0 218.4 (35.2-313.5)	.819
		Uninjured extremity	223.0 ± 48.3 222.1 (160.9-290.4)	174.8 ± 79.1 155.3 (31.3-313.2)	
		*P**	.577	.159	
	Maximum pressure (N/cm²)	Injured extremity	14.6 ± 3.5 14.3 (9.8-22.3)	15.7 ± 3.9 16.1 (8.0-24.3)	**.007**
		Uninjured extremity	15.9 ± 5.6 14.4 (9.8-26.4)	14.4 ± 3.9 14.2 (8.5-22.8)	
		*P**	.780	.058	
Heel	Maximum Force (N)	Injured extremity	520.1 ± 129.1 564.2 (255.2-677.8)	509.7 ± 151.2 527.2 (179.5-714.4)	.719
		Uninjured extremity	506.1 ± 116.7 540.1 (300.8-690.1)	532.2 ± 148.9 556.3 (202.3-692.8)	
		*P**	.265	.091	
	Maximum pressure (N/cm²)	Injured extremity	28.8 ± 6.1 26.5 (22.1-41.6)	26.2 ± 5.8 24.2 (17.5-36.6)	**.031**
		Uninjured extremity	29.5 ± 9.3 25.1 (20.0-48.5)	30.0 ± 5.2 29.2 (22.7-39.6)	
		*P**	.457	**.001**	

*Mann-Whitney U test.

superior clinical outcomes in patients who underwent open reduction compared to those who received percutaneous reduction.[31,33]

Previous studies have shown that varus heel, loss of height, and decreased forefoot adduction are common issues following DIACF and can be detected through radiological measurements.[34-36] Çolak and colleagues compared the injured side with the uninjured side after surgical treatment of DIACF and reported an increase in hindfoot varus, a decrease in medial arch height, and an increase in forefoot adduction on the injured extremity using radiological and pedobarographic measurements.[34] Varus deformity of the hindfoot is commonly seen after trauma, and this deformity can lead to undesirable conditions such as osteoarthritis in the posterior facet, stress fractures, compression of the peroneal tendons, stiffness in the subtalar joint, and anterior ankle impingement.

In our current study, we found no statistically significant difference in kite and lateral talocalcaneal angles, which assess hindfoot varus, and calcaneal pitch angle, which evaluates medial arch height, between the injured extremities in both groups. The lack of comparison between injured and uninjured extremities might have contributed to these results. However, significant differences were observed in talus-first metatarsal and talonavicular coverage angles, which assess forefoot adduction, between the 2 groups. Our findings indicate that patients treated with percutaneous screws exhibited a greater tendency toward forefoot adduction.

Weight is transferred to the upper articular surface of the calcaneus through the axial loading of the talus's 3 articular facets. The primary load transfer happens at the posterior facet surfaces. A collapse of the posterior facet is indicated by a reduction in Böhler's angle and an increase in Gissane's angle, both of which are directly associated with functional outcomes and the severity of the injury. In our study, no significant differences were found in Böhler's and Gissane's angles between the injured limbs in both groups. While the average values of Gissane's angle were within the normal range in both groups, the average values of Böhler's angle were slightly lower than the normal range in both groups. Previous studies have demonstrated a statistically greater improvement in Böhler's angle in patients treated with the classic open technique compared to those treated with percutaneous screws. The absence of a significant difference in our study may be attributed to the higher number of Sanders type 3 patients in the STA group.

Since 2000, studies using dynamic pedobarographic measurements have shown a variety of results concerning patient numbers, treatments, follow-up periods, outcome scores, and pressure measurement parameters. However, many have reported similar results in regional foot pressure measurements after intra-articular fractures. Studies by Jansen et al.[37] and Colak et al.[34] have reported elevated midfoot pressure on the injured side compared to the healthy side following calcaneal fracture surgery. Another study found a reduction in hindfoot pressure, along with increased pressure in the lateral and midfoot regions of the forefoot.[38]

In our study, pedobarographic analysis showed that patients in the sinus tarsi group bore significantly less weight and pressure in both the forefoot and hindfoot of the injured extremity compared to the uninjured extremity during walking. We believe this condition may be due to the higher number of patients with more fragmented fractures, as classified by Sanders, in the STA group.

Table 5. Comparison of Butterfly Parameters and Foot Rotation Angle of the Study Cohorts

	Pedobarographic Parameter		Percutaneous Group Mean ± SD Median (min-max)	Sinus Tarsi Group Mean ± SD Median (min-max)	P*
Butterfly parameters	Length of gait line (mm)	Injured extremity	230.0 ± 18.8 239.2 (203.0-249.0)	218.5 ± 33.6 230.9 (134.9-250.5)	*.254*
		Uninjured extremity	225.5 ± 26.5 235.4 (171.7-250.2)	222.6 ± 25.0 231.7 (161.3-249.0)	
		P*	.353	.840	
	Single limb support line (mm)	Injured extremity	90.1 ± 45.1 110.9 (13.3-133.1)	79.7 ± 43.3 96.1 (11.1-143.5)	*.119*
		Uninjured extremity	95.0 ± 40.4 110.6 (22.9-18.9)	98.4 ± 29.8 105.6 (38.4-134.0)	
		*P**	0.642	0.053	
Geometry parameters	Foot rotation angle (degree)	Injured extremity	9.0 ± 5.8 8.5 (0.0-16.7)	8.4 ± 8.3 6.2 (-1.2-32.6)	*.254*
		Uninjured extremity	10.0 ± 5.1 8.6 (4.4-18.9)	7.3 ± 6.8 6.1 (-3.9-16.9)	
		P*	.457	.747	

*Mann-Whitney U test.

Our study is valuable for comparing 2 surgical approaches pedobarographically, radiologically, and clinically. However, it has certain limitations. Our study is retrospective, and the effects of the pre-injury characteristics of the injured foot were not considered. In the percutaneous group, there was a higher representation of type 2 patients according to the Sanders classification, which led to a significant difference in classification between the groups and negatively affected the results of the STA group.

CONCLUSION

While the STA group showed better functional and radiological outcomes, pedobarographic analyses revealed deficiencies in pressure and force distribution in the injured extremity within the STA group. These findings suggest that discrepancies in load and pressure distributions may not always be associated with functional and radiological outcomes, and despite consisting of patients with more severe fractures, ensuring the opening of the posterior facet and achieving joint reduction would increase patient satisfaction rates.

Ethics

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Ankara Bilkent City Hospital 2nd Clinical Research Ethics Committee Presidency (Approval number: E2-23-3577; Date: 27.03.2023)

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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Footnotes

Author Contributions

Concept – H.A.; Design – H.A., E.V.; Supervision – A.F.; Funding- Y.K.; Materials – Y.E.; Data collection &/ or processing – Y.E., Ş.G.; Analysis and/or interpretation –V.B.; Literature search – Ş.G.; Writing – H.A.; Critical review – A.F.

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REFERENCES

1. Zwipp H, Rammelt S, Barthel S. Calcaneal fractures—open reduction and internal fixation (ORIF). *Injury*. 2004;35 (Suppl 2):SB46-SB54. [CrossRef]
2. Luo X, Li Q, He S, He S. Operative versus nonoperative treatment for displaced intra-articular calcaneal fractures: a meta-analysis of randomized controlled trials. *J Foot Ankle Surg*. 2016;55(4):821-828. [CrossRef]
3. Zhang W, Lin F, Chen E, Xue D, Pan Z. Operative versus nonoperative treatment of displaced intra-articular calcaneal fractures: a meta-analysis of randomized controlled trials. *J Orthop Trauma*. 2016;30(3):e75-e81. [CrossRef]
4. Rammelt S. An update on the treatment of calcaneal fractures. *J Orthop Trauma*. 2014;28(10):549-550. [CrossRef]
5. Sanders R. Review-displaced intra-articular fractures of the calcaneus. *JBJS*. 2000;82(2):225-250. [CrossRef]
6. Sampath Kumar V, Marimuthu K, Subramani S, Sharma V, Bera J, Kotwal P. Prospective randomized trial comparing open reduction and internal fixation with minimally invasive reduction and percutaneous fixation in managing displaced intra-articular calcaneal fractures. *Int Orthop*. 2014;38(12):2505-2512. [CrossRef]
7. Seat A, Seat C. Lateral extensile approach versus minimal incision approach for open reduction and internal fixation of displaced intra-articular calcaneal fractures: a metaanalysis. *J Foot Ankle Surg*. 2020;59(2):356-366. [CrossRef]
8. Benirschke SK, Kramer PA. Wound healing complications in closed and open calcaneal fractures. *J Orthop Trauma*. 2004;18(1):1-6. [CrossRef]
9. Kline AJ, Anderson RB, Davis WH, Jones CP, Cohen BE. Minimally invasive technique versus an extensile lateral approach for intra-articular calcaneal fractures. *Foot Ankle Int*. 2013;34(6):773-780. [CrossRef]
10. Zhou HC, Yu T, Ren HY, et al. Clinical Comparison of Extensile Lateral Approach and Sinus Tarsi Approach Combined with Medial Distraction Technique for Intra-Articular Calcaneal Fractures. *Orthop Surg*. 2017;9(1):77-85. [CrossRef]
11. Buckley R, Tough S, McCormack R, et al. Operative compared with nonoperative treatment of displaced intra-articular calcaneal fractures: a prospective, randomized, controlled multicenter trial. *JBJS Am*. 2002;84(10):1733- 1744. [CrossRef]
12. Erinc S, Cam N, Kanar M, Mustafa Ozdemir HM. Comparison of two surgical techniques for periprosthetic supracondylar femoral fractures: minimally invasive locking plate versus retrograde femoral nails. *Sisli Etfal Hastan Tip Bul*. 2021;55(4):477-485. [CrossRef]
13. Rammelt S, Amlang M, Barthel S, Gavlik J-M, Zwipp H. Percutaneous treatment of less severe intraarticular calcaneal fractures. *Clin Orthop Relat Res*. 2010;468(4):983-990. [CrossRef]
14. Subaşı İÖ, Çepni Ş, Tanoğlu O, et al. A clinical comparison of two different surgical techniques in the treatment of acute Achilles tendon ruptures: limited-open approach vs. percutaneous approach. *Ulus Travma Acil Cerrahi Derg*. 2023;29(8):935-943. [CrossRef]
15. Weber M, Lehmann O, Sägesser D, Krause F. F. Limited open reduction and internal fixation of displaced intra-articular fractures of the calcaneum. *J Bone Joint Surg Br*. 2008;90(12):1608-1616. [CrossRef]
16. De Boer AS, Van Lieshout EM, Den Hartog D, Weerts B, Verhofstad MHJ, Schepers T. Functional outcome and patient satisfaction after displaced intra-articular calcaneal fractures: a comparison among open, percutaneous, and nonoperative treatment. *J Foot Ankle Surg*. 2015;54(3):298-305. [CrossRef]

17. Li L-H, Guo Y-Z, Wang H, et al. Less wound complications of a sinus tarsi approach compared to an extended lateral approach for the treatment of displaced intraarticular calcaneal fracture: a randomized clinical trial in 64 patients. *Medicine*. 2016;95(36):e4628. [CrossRef]

18. Schepers T. The sinus tarsi approach in displaced intraarticular calcaneal fractures: a systematic review. *Int Orthop*. 2011;35(5):697-703. [CrossRef]

19. Yeo J-H, Cho H-J, Lee K-B. Comparison of two surgical approaches for displaced intra-articular calcaneal fractures: sinus tarsi versus extensile lateral approach. *BMC Musculoskelet Disord*. 2015;16:63. [CrossRef]

20. Schepers T, Van der Stoep A, Van der Avert H, Van Lieshout EM, Patka P. Plantar pressure analysis after percutaneous repair of displaced intra-articular calcaneal fractures. *Foot Ankle Int*. 2008;29(2):128-135. [CrossRef]

21. Genc Y, Gultekin A, Duymus TM, Mutlu S, Mutlu H, Komur B. Pedobarography in the assessment of postoperative calcaneal fracture pressure with gait. *J Foot Ankle Surg*. 2016;55(1):99-105. [CrossRef]

22. Gould N. Lateral approach to sinus tarsi. *Foot Ankle*. 1983;3(4):244-246. [CrossRef]

23. Tornetta III P. The Essex-Lopresti reduction for calcaneal fractures revisited. *J Orthop Trauma*. 1998;12(7):469-473. [CrossRef]

24. Pillai A, Basappa P, Ehrendorfer S. Modified Essex-Lopresti/Westheus reduction for displaced intra-articular fractures of the calcaneus. Description of surgical technique and early outcomes. Acta Orthop Belg. 2007;73(1):83-87.

25. Kikuchi C, Charlton TP, Thordarson DB. Limited sinus tarsi approach for intra-articular calcaneus fractures. *Foot Ankle Int*. 2013;34(12):1689-1694. [CrossRef]

26. Ebrahimpour A, Kord MHC, Sadighi M, Chehrassan M, Najafi A, Sajjadi MM. Percutaneous reduction and screw fixation for all types of intra-articular calcaneal fractures. *Musculoskelet Surg*. 2021;105(1):97-103. [CrossRef]

27. Bijur PE, Silver W, Gallagher EJ. Reliability of the visual analog scale for measurement of acute pain. *Acad Emerg Med*. 2001;8(12):1153-1157. [CrossRef]

28. Dingenen B, Blandford L, Comerford M, Staes F, Mottram S. The assessment of movement health in clinical practice: a multidimensional perspective. *Phys Ther Sport*. 2018;32:282- 292. [CrossRef]

29. Schepers T, Ginai AZ, Mulder PG, Patka P. Radiographic evaluation of calcaneal fractures: to measure or not to measure. *Skelet Rad*. 2007;36(9):847-852. [CrossRef]

30. Qiang M, Chen Y, Jia X, et al. Post-operative radiological predictors of satisfying outcomes occurring after intra-articular calcaneal fractures: a three dimensional CT quantitative evaluation. *Int Orthop*. 2017;41(9):1945-1951. [CrossRef]

31. Biz C, Barison E, Ruggieri P, Iacobellis C. Radiographic and functional outcomes after displaced intra-articular calcaneal fractures: a comparative cohort study among the traditional open technique (ORIF) and percutaneous surgical procedures (PS). *J Orthop Surg Res*. 2016;11(1):92. [CrossRef]

32. Weng Q-H, Dai GL, Tu Q-M, et al. Comparison between percutaneous screw fixation and plate fixation via sinus tarsi approach for calcaneal fractures: an 8-10-year follow-up study. *Orthop Surg*. 2020;12(1):124-132. [CrossRef]

33. Yu X, Pang Q-J, Chen L, Yang C-C, Chen X-J. Postoperative complications after closed calcaneus fracture treated by open reduction and internal fixation: a review. *J Int Med Res*. 2014;42(1):17-25. [CrossRef]

34. Çolak İ, Çolak T, Polat MG, Timurtaş E, Bulut G, Gülabi D. The results of physical, radiologic, pedabarographic, and qualityof-life assessments in patients with surgically treated intraarticular calcaneus fractures. *J Foot Ankle Surg*. 2018;57(6):1172-1180. [CrossRef]

35. Stapleton JJ, Belczyk R, Zgonis T. Surgical treatment of calcaneal fracture malunions and posttraumatic deformities. *Clin Podiatr Med Surg*. 2009;26(1):79-90. [CrossRef]

36. Lim EV, Leung JP. Complications of intraarticular calcaneal fractures. *Clin Orthop Relat Res*. 2001;(391):7-16. [CrossRef]

37. Jansen H, Frey SP, Ziegler C, Meffert RH, Doht S. Results of dynamic pedobarography following surgically treated intra-articular calcaneal fractures. *Archives of orthopaedic and trauma surgery*. 2013;133:259-265.

38. Hirschmüller A, Konstantinidis L, Baur H, et al. Do changes in dynamic plantar pressure distribution, strength capacity and postural control after intra-articular calcaneal fracture correlate with clinical and radiological outcome? *Injury*. 2011;42(10):1135-1143. [CrossRef]

ABCResearch

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Research Article

The Radiographic and Clinical Outcomes of Proximal Humerus Fractures in Patients Over 60 Years of Age

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ABSTRACT

Objective: To present and compare the results of surgical methods used in the treatment of osteoporotic proximal humerus fractures (PHFs).

Methods: A retrospective examination of patients who underwent surgery for osteoporotic PHF between 2009 and 2013 was conducted. The demographic data of the patients, surgical methodology, concomitant injuries, time intervals before surgery, hospitalization time, and follow-up time were recorded. Constant-Murley score and American Shoulder and Elbow Surgeons score were utilized for functional evaluation. Shoulder abduction and flexion ranges of motion were measured as objective evaluation.

Results: Sixteen patients (64%) were operated with plate-screw osteosynthesis, two patients (8%) with percutaneous Kirschner wire fixation and seven patients (28%) with partial shoulder arthroplasty. A significant correlation was identified between treatment and Neer classification (P = 0.011). No significant correlation was observed between functional scores and surgical method (P > 0.05 for each). Objective evaluations revealed a significant difference in shoulder abduction range of motion between patients and surgical method (P = 0.030). Post-hoc analyses showed a significant difference between plate-screw osteosynthesis and hemi-arthroplasty groups (P = 0.010).

Conclusion: Percutaneous techniques, plate-screw osteosynthesis, or arthroplasty methods may be preferred in osteoporotic PHFs, with no superiority over each other. The decision regarding the surgical method for geriatric PHFs should be based on patient -and fracture- related factors.

Keywords: Osteoporosis, geriatric proximal humerus fracture, Neer classification, surgery

INTRODUCTION

Proximal humerus fractures (PHFs) can occur even in low-energy trauma, such as simple falls, due to declining bone quality (osteoporosis), especially in older age. PHFs are the most common fracture site after hip and distal radius fractures in the elderly.[1,2] Most geriatric PHFs are treated conservatively, given the decreased functional expectation and increased comorbidities. However, for fractures with significant displacement and multiple comminution, surgical treatment come to the fore. As a result of the increasing incidence of fractures in this region and technological developments in orthopedic implants, various surgical methods have been used to PHFs. Despite the numerous studies conducted on the subject, a consensus on the optimal surgical method remains elusive and the relative merits of each method continue to be debated.[3] The primary goal of surgery for geriatric PHFs is to allow patients to resume their daily activities as soon as possible. Age, bone quality, fracture pattern, and surgical timing all significantly affect the patient's functional result. Each PHF is patient-specific, and there is no single universal surgical method that can be used for every patient when conservative treatment is not possible. Therefore, a patient-specific, evidence-based treatment approach should be selected.[4]

This study aims to present and compare the results of surgical methods used to treat osteoporotic PHFs.

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MATERIAL AND METHODS

Study Population and Data Collection

Following approval by the Gülhane Military Medical Academy Haydarpaşa Training and Research Hospital Ethics Committee (approval no.: 2013-114, date: 26.12.2013), all patients who underwent surgery for a PHF at the study clinic between October 2009 and December 2013, aged over 60 years, were retrospectively reviewed. Within the specified period, 38 patients were identified who underwent surgery with a diagnosis of osteoporotic PHF. Inclusion criteria were defined as being over 60, having undergone surgical treatment for a PHF in our clinic, and having regular follow-up visits. Seven individuals passed away for a variety of causes, thus they were not included in the study. Three patients were unreachable due to alterations in their contact information. Three patients did not want to take part in the study. Consequently, 13 patients were excluded from the study, whereas 25 patients were included.

Surgical Technique and Rehabilitation

The percutaneous method was used for Kirschner wire (K-wire) fixation.[5] For plate osteosynthesis (Proximal Humerus Locking Plates, TST Orthopedics®, TST Medical Tools®, İstanbul, Türkiye) and arthroplasty (Partial Shoulder Prosthesis, Hipokrat Incorporated Company, İzmir, Türkiye), A deltopectoral technique was used to reach the proximal humerus.[6] Passive shoulder exercises were initiated on the first postoperative day. Patients who did not have any problems at the wound site were discharged and asked to have dressings every day. All patients were contacted for a follow-up two weeks after the operation, at which point sutures were removed. In the third postoperative week, active assisted shoulder exercises were described in addition to passive shoulder exercises. Postoperative rehabilitation recommendations were obtained for all patients, and home rehabilitation plans were arranged and encouraged.

Demographic Data and Functional Evaluation

Anteroposterior and lateral radiographs or computed tomography (CT) scans of the shoulder taken on admission were used to classify PHFs according to the Neer classification.[2] CT scans were used to diagnose and classify cases of multiple comminuted fractures and fracture-dislocations and to determine the surgical method. None of the patients underwent magnetic resonance imaging. Concomitant injuries and the procedures performed for these injuries were recorded. Waiting times for surgery after fracture, reasons, and comorbidities were recorded. The methods used for surgery (K-wire fixation, plate and screw fixation, and arthroplasty) were listed.

Patients were contacted using the contact details in the hospitalization file and the hospital information system. Included patients were invited to our hospital by telephone, provided that a minimum follow-up of at least one year had been achieved. Constant-Murley scoring and American Shoulder and Elbow Surgeons (ASES) scoring were used for functional assessment.[7,8] Constant-Murley scoring was used for clinician-based assessment and ASES scoring was used for patient-based assessment. Radiological assessment was performed with direct anterior-posterior and lateral radiographs of the shoulder. Fixation failure and union were assessed on direct radiographs. In terms of objective evaluation, shoulder abduction and flexion ranges of motion were measured on all patients at the last follow-up. Using a standard universal goniometer and the triangulation sites, the same physician assessed the patient's range of motion.

Statistical Analysis

The International Business Machines (IBM®) Statistical Package for the Social Sciences (SPSS®) software, version 26.0 (IBM SPSS Corp.; Armonk, NY, USA), was used to conduct the statistical analysis. Descriptive statistics such as mean, standard deviation, and minimum-maximum values were utilized. Frequency (percentage) were used as descriptive statistics for categorical data. When evaluating the scale data in three-group comparisons the groups were compared using the Kruskal-Wallis test, and post-hoc analyses were carried out using the Mann-Whitney U test. The categorical data were compared using the chi-square test. When the *P* value was less than 0.05, statistical significance was deemed to exist.

RESULTS

Sixteen patients (64%) were operated with plate-screw osteosynthesis, 2 patients (8%) with percutaneous K-wire fixation and 7 patients (28%) with partial shoulder arthroplasty. The mean age of the patients was 75.08 ± 8.505 years (range: 60-92). According to Neer Classification, 10 patients (40%) had two-part fractures, 13 patients (52%) had three-part fractures and 2 patients (8%) had four-part fractures (Figure 1). Detailed demographic data of the patients are shown in Table 1.

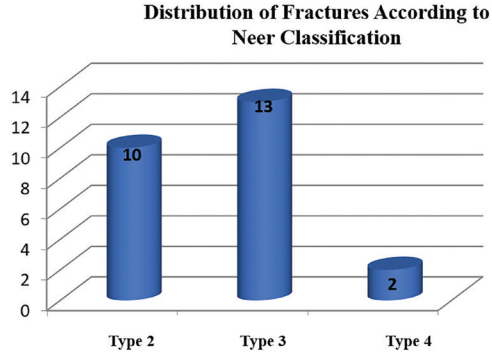

Figure 1. Distribution of fractures according to Neer classification.

MAIN POINTS

- Different surgical alternatives are not superior to each other in terms of functional scores in geriatric proximal humerus fractures (PHFs).
- Satisfactory clinical results can be obtained with plate-screw osteosynthesis in geriatric PHFs.
- Patient-based and fracture-based factors should be considered when deciding on the surgical method in geriatric PHFs.

It was determined that 62.5% of the patients treated with plate-screw osteosynthesis had Neer type 2 fractures and 85.7% of the patients treated with arthroplasty had Neer type 3 fractures. There was a significant correlation between the treatment and Neer classification (P = 0.011). There was no significant correlation between the treatment and other fracture and patient characteristics (Table 2).

There was no significant correlation between the functional scores and the surgical method applied in the last follow-up of the patients (P > 0.05 for each). In the objective evaluations, there was a significant difference between the shoulder abduction range of motion of the patients and the surgical method applied (P = 0.030). Post-hoc analyses revealed no significant difference between osteosynthesis with plate-screw and fixation with K-wire (P = 0.941) and between fixation with K-wire and hemi-arthroplasty (P = 0.111), whereas a significant difference was found between osteosynthesis with plate-screw and hemi-arthroplasty groups (P = 0.010). The relationship between the applied surgical method and functional and objective measurements is shown in detail in Table 3.

In one patient treated with plate osteosynthesis, revision plate osteosynthesis was performed in the sixth postoperative week due to loss of reduction. In the follow-up of the same patient, parenteral antibiotherapy was applied for superficial infection due to serous discharge at the wound site and the complaint regressed. In another patient treated with plate osteosynthesis, the fixation materials were removed 1.5 years postoperatively due to pain and abduction limitation despite physiotherapy and the complaints disappeared afterwards.

DISCUSSION

Surgical techniques for PHFs include many options such as minimally invasive techniques, plate and screw applications, hemiarthroplasty, and total shoulder arthroplasty. Our study investigated the superiority of three different surgical techniques described in the literature for osteoporotic PHFs. The most striking finding of this study was that none of the surgical methods investigated was superior to the other in terms of functional scores. Another point that should be emphasized is that the shoulder abduction range was greater in the plate-screw osteosynthesis group.

In epidemiological studies, osteoporotic PHFs are more common in women, and fractures usually occur in low-energy trauma, such as falls from the same level. In our study, PHFs were more common in women (92% vs. 8%). Our results are consistent with the literature. In epidemiological studies with larger patient series, fractures are more common in women and the incidence of fractures increases with the aging of the population.[9]

In our study, the mean interval between initial presentation and surgery was calculated to be 18.48 (3-153) days. The large discrepancy between the waiting times was because several patients were initially indicated for conservative management, while surgery was later decided due to loss of reduction and one patient underwent surgery at a late stage due to non-union. The mean length of hospital stay in our study was 14.6 (3-66) days. Prolonged preoperative preparation and increased need for postoperative care due to comorbidities and concomitant fractures were the reasons for the increased length of hospital stay. Eighteen patients had comorbidities.

Table 1. Demographic profile of the patients

		Number of patients (%) (n=25)
Gender	**Female**	23 (92%)
	Male	2 (8%)
Age* (years)		75.08 ± 8.505 (60-92)
Side	**Right**	10 (40%)
	Left	15 (60%)
Mechanism of injury	**Simple Fall**	23 (92%)
	Traffic Accident	2 (8%)
Neer classification	**Type 2**	10 (40%)
	Type 3	13 (52%)
	Type 4	2 (8%)
Time interval between injury and initial hospital admission* (days)		14.12 ± 30.783 (0-151)
Time interval between initial hospital admission and operation* (days)		18.48 ± (3-153)
Postoperative hospitalization* (days)		14.6 ± 12.049 (3-66)
Surgery	**Plate-screw osteosynthesis**	16 (64%)
	Kirschner wire fixation	2 (8%)
	Arthroplasty	7 (28%)
Follow-up* (months)		32.36 ± 15.545 (12-54)

n, number of patients; *, mean, standard deviation and minimum-maximum values were used as descriptive statistics.

Table 2. Comparison of demographic characteristics of patients according to surgical groups

		Plate-screw osteosynthesis (n=16)	Kirschner wire fixation (n=2)	Arthroplasty (n=7)	*P*
Gender	**Female**	15 (%93.8)	2 (%100)	6 (%85.7)	0.594
	Male	1 (%6.2)	0	1 (%14.3)	
Age* (years)		74.06 ± 8.903 (60-92)	73 ± 9.899 (66-80)	78 ± 7.789 (67-87)	0.427
Side	**Right**	7 (%43.7)	1 (%50)	2 (%28.6)	0.827
	Left	9 (%56.3)	1 (%50)	5 (%71.4)	
Mechanism of injury	**Simple Fall**	15 (%93.7)	2 (%100)	6 (%85.7)	0.594
	Traffic Accident	1 (%6.3)	0	1 (%14.3)	
Neer classification	**Type 2**	10 (%62.5)	0	0	0.011
	Type 3	5 (%31.3)	2 (%100)	6 (%85.7)	
	Type 4	1 (%6.3)	0	1 (%14.3)	
Time interval between injury and initial hospital admission* (days)		15.06 ± 37.049 (0-151)	12.5 ± 17.678 (0-25)	12.43 ± 17.329 (0-47)	0.897
Time interval between initial hospital admission and operation* (days)		18.88 ± 36.527 (4-153)	17.50 ± 16.236 (6-29)	17.86 ± 17.883 (3-53)	0.529
Postoperative hospitalization* (days)		12.06 (5.961 (3-23)	7.5 ± 3.536 (5-10)	22.43 ± 19.603 (10-66)	0.091

n, number of patients; *P*, statistical significance value; *, mean, standard deviation and minimum-maximum values were used as descriptive statistics.

Table 3. Functional scores and range of motion of the patients

	Plate-screw osteosynthesis (n=16)	Kirschner wire fixation (n=2)	Arthroplasty (n=7)	*P*
ASES score	64 (35-95)	82.5 (75-90)	53 (18-88)	0.165
Constant Murley score	76 (31-95)	82.5 (77-88)	42 (17-90)	0.050
Shoulder flexion Range of motion	100 (50-155)	127.5 (125-130)	55 (25-170)	0.053
Shoulder flexion Range of motion	90 (40-145)	95 (80-110)	65 (20-110)	0.030

n, number of patients; *P*, statistical significance value mean; standard deviation and minimum-maximum values were used as descriptive statistics; ASES, American Shoulder and Elbow Surgeon

These included hypertension, diabetes mellitus, heart disease, hyperlipidemia, lung disease, Alzheimer's disease, hypothyroidism, and chronic renal failure. In addition, six patients in our cohort had concomitant fractures; the first patient had a lateral plateau fracture and osteosynthesis was achieved with two cannulated screws. In addition, a symphysis pubis arm fracture and a fibular shaft fracture were conservatively managed. In the second patient, the concomitant patella fracture was fixed with a traction device. In the third patient, intramedullary nailing was performed for the diaphyseal fracture of the femur. In the fourth patient, the distal radius fracture was treated with closed reduction and a short arm cast. In the fifth patient, partial hip arthroplasty was performed for the collum femoris fracture. The sixth patient underwent proximal femoral nailing for the intertrochanteric femoral fracture and closed reduction with percutaneous pinning for the distal radius fracture.

In our study, 10 patients (40%) had Neer type 2 fractures and 13 patients (52%) had Neer type 3 fractures. Although osteoporotic fractures are expected to be more comminuted due to the fragile bone structure, our results differ from this hypothesis. We believe that the most important reason for this is that almost all the injury mechanisms in our study (92%) were caused by low-energy injuries. Another important reason for the low number of multi-segment Neer type 4 fractures in our cohort may be that conservative treatment of these fractures, especially in the geriatric population, is more prominent both in the literature and in our study group.[10,11]

Although higher functional scores were obtained with K-wire fixation and plate-screw osteosynthesis compared to the arthroplasty group, the difference between them was not statistically significant in our study. Similar results have been reported in the literature. However, recent studies have reported that reverse shoulder arthroplasty is preferred to partial shoulder arthroplasty in geriatric multisegment PHFs, and the functional results are similar to those of plate osteosynthesis.[12,13]

Our study's most notable observation was the considerable variation in shoulder abduction range of motion during the

last follow-up (P = 0.03). In post-hoc analyses, no significant difference was found between plate-screw osteosynthesis and K-wire fixation (P = 0.941) and between K-wire fixation and hemiarthroplasty (P = 0.111), whereas a significant difference was found between the plate-screw osteosynthesis and hemiarthroplasty groups (P = 0.010). When analyzing the reasons for this situation, it is striking that the groups were not homogeneously distributed. The limited number of patients with percutaneous fixation (K-wire) may have influenced the statistical analyses. Another point to emphasize is that the rate of Neer type 2 fractures was higher in the plate-screw fixation group. Finally, all arthroplasties in our study were partial shoulder arthroplasties. As mentioned above, the number of publications in the literature reporting satisfactory results with reverse shoulder arthroplasty for PHFs is increasing daily.[13,14]

Study Limitations

Our study had some limitations. These are;

- The number of patients and surgical techniques used in our study were small and the groups were not homogeneous,

- Absence of reverse shoulder prosthesis cases among the surgical methods used, which are becoming more common today,

- Differences in the time interval between hospital admission and surgery,

- Postoperative bone mineral density (BMD) was not measured and the relationship between BMD age and BMD fracture incidence was not evaluated.

In conclusion, the number of osteoporotic fractures is increasing with the ageing of the population, and PHFs constitute a significant proportion of these. There are many surgical methods for treating geriatric PHFs, and our study showed that these surgical methods are not clearly superior to each other. Although arthroplasty options have become increasingly prevalent in this age group due to technological advancements, satisfactory clinical outcomes can be achieved with plate-screw osteosynthesis in geriatric PHFs.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Gülhane Military Medical Academy Haydarpaşa Training and Research Hospital Ethic Committee (approval no.: 2013-114, date: 26.12.2013).

Informed Consent: Written informed consent could not be obtained due to the retrospective nature of the study. Verbal consent was obtained from all patients and their relatives when called by telephone.

Footnotes

Author Contributions

Concept - S.S.O., K.K.; Design - S.S.O., K.K.; Supervision - K.K.; Resources - S.S.O., K.K.; Materials - K.K.; Data Collection and/or Processing - S.S.O., K.K.; Analysis and/or Interpretation - S.S.O., K.K.; Literature Search - S.S.O.; Writing Manuscript - S.S.O.; Critical Review - K.K.; Other - S.S.O., K.K.

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REFERENCES

1. Gencer B, Ender İbaç S, Teoman Yeni B, Sezer T, Doğan Ö. Surgical treatment of bilateral distal radius fractures: An analysis of epidemiological variables and outcome parameters. *Arch Basic Clin Res*. 2024;6(3):202-208. [CrossRef]
2. Rudran B, Little C, Duff A, Poon H, Tang Q. Proximal humerus fractures: anatomy, diagnosis and management. *Br J Hosp Med (Lond)*. 2022;83(7):1-10. [CrossRef]
3. Handoll HH, Brorson S. Interventions for treating proximal humeral fractures in adults. *Cochrane Database Syst Rev*. 2015;(11):CD000434. [CrossRef]
4. Namdari S, Voleti PB, Mehta S. Evaluation of the osteoporotic proximal humeral fracture and strategies for structural augmentation during surgical treatment. *J Shoulder Elbow Surg*. 2012;21(12):1787-1795. [CrossRef]
5. Yang L, Li B, Pan XY, et al. [Percutaneous reduction and fixation of osteoporotic fractures for the proximal humerus in a geriatric population]. Zhonghua Wai Ke Za Zhi. 2006;44(12):830-832. [CrossRef]
6. Thompson JH, Attum B, Rodriguez-Buitrago A, Yusi K, Cereijo C, Obremskey WT. Open reduction and internal fixation with a locking plate via deltopectoral approach for the treatment of three and four-part and proximal humeral fractures. *JBJS Essent Surg Tech*. 2018;8(4):e26. [CrossRef]
7. Constant CR, Gerber C, Emery RJ, Søjbjerg JO, Gohlke F, Boileau P. A review of the constant score: modifications and guidelines for its use. *J Shoulder Elbow Surg*. 2008;17(2):355-361. [CrossRef]
8. Richards RR, An KN, Bigliani LU, et al. A standardized method for the assessment of shoulder function. *J Shoulder Elbow Surg*. 1994;3(6):347-352. [CrossRef]
9. Court-Brown CM, Duckworth AD, Clement ND, McQueen MM. Fractures in older adults. A view of the future? *Injury*. 2018;49(12):2161-2166. [CrossRef]
10. Gavaskar AS, Pattabiraman K, Srinivasan P, Raj RV, Jayakumar B, Rangasamy NK. What factors are associated with poor shoulder function and serious complications after internal fixation of three-part and four-part proximal humerus fracture-dislocations? *Clin Orthop Relat Res*. 2022;480(8):1566-1573. [CrossRef]
11. Solberg BD, Moon CN, Franco DP, Paiement GD. Surgical treatment of three and four-part proximal humeral fractures. *J Bone Joint Surg Am*. 2009;91(7):1689-1697. [CrossRef]
12. Lanzetti RM, Gaj E, Berlinberg EJ, Patel HH, Spoliti M. Reverse total shoulder arthroplasty demonstrates better outcomes than angular stable plate in the treatment of three-part and four-part proximal humerus fractures in patients older than 70 years. Clin *Orthop Relat Res*. 2023;481(4):735-747. [CrossRef]
13. Jobin CM, Galdi B, Anakwenze OA, Ahmad CS, Levine WN. Reverse shoulder arthroplasty for the management of proximal humerus fractures. *J Am Acad Orthop Surg*. 2015;23(3):190-201. [CrossRef]
14. Garrigues GE, Johnston PS, Pepe MD, Tucker BS, Ramsey ML, Austin LS. Hemiarthroplasty versus reverse total shoulder arthroplasty for acute proximal humerus fractures in elderly patients. *Orthopedics*. 2012;35(5):703-708. [CrossRef]

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Research Article

Evaluation of Anxiety Levels in Relatives of Patients in the Intensive Care Unit

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ABSTRACT

Objective: Using the State-Trait Anxiety Inventory (STAI) scale, relatives of patients in intensive care (IC); the aim of this study was to evaluate the impact of age, gender, intimacy level, profession, education, and experience in IC, as well as the patients'age, education, and bedtime, on their anxiety levels using the STAI scale and relatives in patients with IC.

Methods: Age 18 and over 18 years old patients were included for the present study. Demographic data, education, and degree of closeness of the patient's relative were recorded. Relatives of patients on admission, 1, 2, 3, 4, 5, 7, 10. "STAI FORM TX-1" was filled in on these days. Relatives of the patient; age, gender, intimacy levels, educational status, professions, their own or their relatives' IC experiences, and anxiety levels were compared.

Results: When compared according to patient age, gender, IC scores, Glasgow Coma Scale, patient relative age, past IC experience, degree of closeness, frequency of meeting with the patient, education level and income level; group of the IC experience has statistically difference ($P < 0.05$). Also, it was staistically difference in the group whose bedtime was 20.00-08.00 hrs ($P < 0.05$). However, it was no statistically difference between the patient's relative's age, degree of closeness, frequency of meetings and income level ($P > 0.05$).

Conclusion: Our findings provide that there are multiple factors that can cause anxiety in the relatives of patients with IC. It has been observed that hospitalization experience of patient relatives in IC unite have high anxiety during hospitalization. Anxiety; although we think that it decreases with adequate information, we think that more detailed research should be done.

Keywords: Anxiety, State-Trait Anxiety Inventory (STAI) scale, patient relatives

INTRODUCTION

Instensive care unit (ICU) represents a crucial sector for healthcare system, wherein healthcare professionals, including physicians and nurses, utilize advanced technologies to sustain patients' survival and support physiological functions that may be compromised. This unit is equipped to maintain respiratory and other essential functions through the application of lifesaving equipment, such as ventilators. Consequently, patients' conditions are stabilized, allowing for the effective administration of treatments. Patients may be admitted to the ICU for a variety of serious conditions, including but not limited to respiratory failure, severe infections (such as pneumonia or meningitis), myocardial infarction, abrupt arrhythmias, loss of consciousness, shock, trauma, poisoning, and scenarios necessitating postoperative surveillance. Various factors inherent to the ICU environment can precipitate stress and anxiety among patients. These factors include the intense atmosphere of the unit, restricted opportunities for family visitation, limited mobility, reliance on medical devices, the complexity of equipment, painful medical procedures, exposure to a cacophony of sounds, and often insufficient information provided to the patient.[1] The experience of being in an ICU can

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evoke significant anxiety not only in patients themselves but also for their families. The gravity of patients' health conditions can fluctuate rapidly, thereby amplifying feelings of uncertainty and distress. Additionally, transitions such as discharge from the ICU or transfer to a general ward can similarly induce anxiety. Patients and their families may perceive such transitions as potentially negative due to concerns over diminished care and monitoring, as well as apprehensions regarding the safety of the new environment.[2] Family members of ICU patients frequently experience anxiety exacerbated by restricted access to the ICU, limited visitation times, insufficient communication from healthcare providers, perceived security threats, and the overarching atmosphere of uncertainty.[3] Specific factors that may negatively influence families in this context include environmental stimuli (such as electrocardiogram monitors and ventilators), invasive medical procedures, inadequate information, insufficient communication, and fears pertaining to mortality.

Despite the profound implications of these experiences, literature focusing on the anxiety levels of relatives of ICU patients remains scarce. Notably, research has evaluated the anxiety levels of parents of adolescents undergoing surgical procedures, relatives of individuals slated for surgery, and those of cancer patients.[4] Literature suggests that understanding and addressing the needs of family members or patient relatives positively influences the recovery trajectory of the patient.[3]

The anxiety degree for patients' relatives have been appraised using the State-Trait Anxiety Inventory (STAI) developed by Spielberger. The STAI differentiates between two categories of anxiety: state anxiety (S-anxiety) and trait anxiety.[5] This inventory comprises two distinct scales, each encompassing 20 items, and is designed for self-administration, facilitating ease of application. For the aim of present study, the S-anxiety scale was employed. The validity and reliability of this scale for measuring situational anxiety in Türkiye were established by N. Öner in 1977.[6] Scores for S-anxiety are assessed as follows: low anxiety is indicated by scores less than 35 points, moderate anxiety is defined as those scoring between 36 to 46 points, and high anxiety corresponds to scores exceeding 47 points (Table 1). In present study, we aimed to evaluate the anxiety degrees experienced by the relatives of patients residing in the resuscitation ICU.

MAIN POINTS

- This study has shown that as the level of education of the relatives of the patients decreases, they become more concerned about their patients.
- The anxiety levels of the relatives of the patients are higher, especially for the patients who are hospitalized at night.
- It has been concluded that the fact that the patients are admitted to the intensive care unit, regardless of their health status, is a sufficient reason to cause concern in the relatives of the patients.

MATERIAL AND METHODS

The ethical approval for this study was granted by the Clinical Research Ethics Committee of Atatürk University Faculty of Medicine (approval no.: 40; date: 30.06.2022). The primary objective of the present study was to determinate and compare the anxiety levels of relatives of patients in the Reanimation ICU on the 1st-7th and 10th days of hospitalization.

The study population comprised the relatives of patients age 18 and over 18 years old patients who were accepted to the Reanimation ICU between March 2023 and May 2024. It was ensured that the same relative completed the survey for each patient. Participation of different relatives for the same patient was excluded from the present study to maintain data consistency. Relatives who were illiterate or under the age of 18 were also excluded from participation. The sample size was determined based on existing literature relating to the correlation between acute physiological changes in intensive care (IC) patients and the associated anxiety and sleep disorders in their relatives. Using the Number Cruncher Statistical Systems/Power Analysis & Sample Size-NCSS/PASS program, a total sample of 175 patients was calculated to be necessary to identify a correlation coefficient (r) of 0.62 between the STAI scores of the patients' relatives and the IC scores of the patients, with a statistical power of 80% and a confidence level of 95%. A total of 185 patient relatives were approached for inclusion in the study. However, five relatives were excluded due to illiteracy, and an additional five were excluded for being under 18 years of age, resulting in a final dataset of 175 evaluated patients. The relatives were asked to complete questionnaire forms on the 1st, 2nd, 3rd, 4th, 5th, 7th, and 10th days of hospitalization. The questionnaire comprised three sections:

Demographic Information: This section collected data on the relatives, including the date of form completion, contact information, degree of relationship to the patient, frequency of visits, profession, income level, education level, and prior experiences in IC settings.

Patient Demographic Information: This section encompassed details related to the patient, such as their demographic information, educational background, file number, age, duration of IC hospitalization, and clinical scores [Glasgow Coma Scale (GCS), Acute Physiology and Chronic Health Evaluation II (APACHE II), Sequential Organ Failure Assessment (SOFA), Simplified Acute Physiology Score II (SAPS-2). GCS ranges from 3 to 15 points, and as the score decreases, the prognosis worsens. APACHE II is a maximum of 71 points, SOFA is a maximum of 24 points, SAPS-2 is a maximum of 163 points. As the score increases in these three scoring systems, the patient's prognosis worsens.

STAI Assessment: The final section enabled the assessment of anxiety levels among the patients' relatives through the STAI forms. The total score for the STAI scale is 80. Scores for S-anxiety are assessed as follows: low anxiety is indicated by scores less than 35 points, moderate anxiety is defined as those scoring between 36 to 46 points, and high anxiety corresponds to scores exceeding 47 points.

Table 1. Spielberger Anxiety State Scale: STAI FORM TX-1

	Not at all (1)	A little (2)	Very Much (3)	Completely (4)
1. I'm feeling calm				
2. I'm feeling secure				
3. I'm feeling tense at the moment				
4. I'm feeling regretful				
5. I'm feeling peaceful				
6. I'm not feeling cheerful				
7. I feel worried for what's waiting for me				
8. I'm feeling rested				
9. At the moment, I'm anxious				
10. I'm feeling comfortable				
11. I'm feeling confident				
12. At the moment, I'm feeling upset				
13. I'm very angry				
14. I'm feeling my nerves are very tense				
15. I'm feeling relieved				
16. At this moment, I feel content				
17. At this moment, I'm nervous				
18. I'm feeling baffled with excitement				
19. I'm joyful				
20. At the moment, I'm in a good mood				

The translated version of the scale in Turkish that was adapted by N. Öner in 1977.

Relatives were instructed to complete the first and second sections during hospitalization, and they were specifically prompted to fill out the STAI form on the designated days: 1, 2, 3, 4, 5, 7, and 10.

Statistical Analysis

Data were evaluated with using the IBM SPSS Statistics version 20. Descriptive statistics. Mean, standard deviation, median, percentage, and count provided for numerical variables as descriptive statistics. Normality of continuous variables was evaluated using the Shapiro-Wilk test, Kolmogorov-Smirnov test, Q-Q plots, as well as Skewness and Kurtosis assessments. Independent Samples t-test was used for data that were normally distrubuted for two independent groups while Mann-Whitney U test was used for of the data. Kruskal-Wallis test was used to compare continuous variables between more than two independent groups. A P value < 0.05 was considered statistically significant.

RESULTS

Clinical and demographic data of both patients and their relatives are outlined in (Table 2). When analyzing the education level of the patient relatives, there was a statistical difference between the illiterate and middle school education groups, compared to those with primary school, high school, and university education, favoring the illiterate and middle school education cohorts (P < 0.05), as detailed in (Table 3). Further analysis revealed a statistical difference in hospitalization anxiety scores between relatives with prior IC experience and those without, with the findings favoring the group possessing prior IC experience (P < 0.05) (Table 4). Additionally, significant differences were found in the anxiety scores of patient relatives on the 2nd, 4th, and 5th days of hospitalization for patients admitted during the hours of 20:00-08:00 compared to those admitted between 08:00-20:00, with the former group displaying lower anxiety degree (P < 0.05) (Table 5). On the 5th and 10th days, a statistical difference was noted between the patient groups classified by their GCS scores. Specifically, relatives of patients with a good GCS monstrated lower anxiety levels compared to those with moderate and poor GCS scores, and all of the differences were difference (P < 0.05) (Table 6).

DISCUSSION

ICU patients are critically ill patients who have a very extended hospital stay and a high risk of morbidity and mortality.[7] Many factors, especially the fear of losing their patients, can cause advanced degree of anxiety and sleep disorders for patients' relatives in IC.[8] Establishing and maintaining communication with the relatives of these patients, who are mainly unconscious and in need of more care, also poses difficulties when viewed by healthcare personnel. The training of healthcare personnel, especially for patient needs and patient care, results in ignoring the existing conditions of the patient's relatives. The patients' relatives in IC often have increased levels of anxiety, and their quality of life decreases.[9]

Table 2. Demographic Data of the Patients and Their Relatives

		n	(%)
Relative's gender	**Male**	116	(66)
	Female	59	(34)
Relative's age	**18-30**	28	(16)
	30-50	109	(62)
	>50	38	(22)
Type of relation	**Spouse**	25	(14)
	Mother-Father-Siblimg	26	(14)
	Daughter	38	(22)
	Son	86	(50)
How frequent does the relative see the patient?	**Day**	137	(78)
	Week	28	(16)
	Month-Year	10	(6)
Relative's monthly income	**0-5000**	27	(15)
	5000-10000	32	(18)
	10.000-20.000	68	(39)
	>20000	48	(28)
Relative's degree of education	**Illiterate**	8	(5)
	Primary school	44	(25)
	Middle school	25	(14)
	High school	43	(25)
	College	55	(31)
Relative's history of ICU	**Patient's experienced**	8	(5)
	Relative's experienced	60	(34)
	None	107	(61)
Patient's gender	**Male**	111	(63)
	Female	64	(37)
Patient's age	**18-50**	25	(15)
	>50	150	(85)
Patient's degree of education	**Illiterate**	41	(23)
	Primary school	76	(43)
	Middle school	25	(14)
	High school	23	(14)
	College	10	(6)
Time of hospitalisation during the day			
	08.00-20.00	81	(46)
	20.00-08.00	94	(54)

All data are represented as n (number) and % (percentage).

Informing the relatives of patients about the interventions and treatments to be applied to their patients and the decisions they will make further increases their anxiety levels.[10] Relatives of patients monitored in ICUs should be supported psychosocially. Anxiety, social isolation, physical dysfunction, sleep disorders, and depression are psychological disorders that can be seen in people with patients in IC.[11] The resulting sleep disorders and anxiety can cause changes such as decreased tolerance to stress, irritability, decreased attention, impaired immunity and decision-making ability.[12] Although studies have examined anxiety and sleep disorders in patients, few studies have examined the anxiety and sleep problems of patients' relatives treated in the ICU in detail. Purposes of the present study to investigate the relationship between the patient's age, education level, gender, hospitalization time, and the patient's relative's age, gender, income status, degree of closeness, frequency of visits, level of education, past IC experiences, and the acute physiological state changes of the patients and the stress and anxiety disorder seen in patients' relatives treated in ICU. Our study sample was created by accepting the article published by Opuş et al.[13] in 2020 as a reference. While the number of relatives who would fill out the survey according to the sample was determined to be 175, a total of 185 relatives of patients were included in the present study. Five relatives of patients participating in the study were excluded because they were illiterate, and five other relatives were under 18.

Our study evaluated the anxiety levels of patients' relatives for their patients in the resuscitation ICU. Up to now on the literature screening process, anxiety levels have primarily been compared with the characteristics of relatives of patients.

The number of studies investigating the characteristics of both patients and relatives and the anxiety degree of patients' relationships according to a comprehensive acute physiological condition change is quite limited.

66% of the patients' relatives participating in the present study were male and 34% were female, and these percentages were 37% female and 63% male for the patients included in the present study.

The mean score of the State Anxiety Scale of individuals with patients in the ICU was found to be 39.45 ± 6.81. When the lowest and highest scores obtained from the scale are considered, it can be said that the S-anxiety levels of the individuals participating in the study are above the moderate level.

In our study, when comparing the groups based on the age and gender of the patient relatives, the degree of closeness to the patient, the frequency of visits, the income level of the patient relatives, as well as patient age, gender, education level, and APACHE II score, no statisticall differences were monitored in anxiety scores across the groups.

When the anxiety scores due to the age of the relatives of patients were examined, no statistical difference was found between the groups in our study. However, as the patient's relative's age increased, the anxiety scores increased, although not statistically significant. Again, in the group where the patient's relative's age was >50, the anxiety scores increased as the number of days of hospitalization increased.

In their study, Türedi[14] found that anxiety scores increased as the patient's relative's age increased, consistent with our study.

Table 3. Anxiety Level According to the Education Degree of Patients' Relatives

	Illiterate (n=8)	Primary school degree (n=44)	Middle school degree (n=25)	High school degree (n=43)	College degree (n=55)	*P**
Day of hospitalisation in the ICU STAI	41.25 ± 10.17;42	40.18 ± 7.24;40	38.38 ± 5.91;38	38.36 ± 5.02;39	38.60 ± 6.13;37	0.481
Day 1 STAI	36.71 ± 8.40;37	39.85 ± 7.86;38	40.38 ± 8.94;38	37.92 ± 5.51;37.5	39.63 ± 5.44;38.5	0.596
Day 2 STAI	36.14 ± 8.23;35	40.16 ± 8.23;39.5	41.00 ± 6.96;42	39.27 ± 6.64;39	38.98 ± 5.51;39	0.589
Day 3 STAI	41.29 ± 9.21;42	38.88 ± 6.35;38.5	41.45 ± 5.96;40	39.89 ± 7.86;40	38.11 ± 5.65;38	0.519
Day 4 STAI	43.00 ± 10.4;48.5[α]	37.50 ± 5.96;38	44.44 ± 6.11;43[α]	38.41 ± 5.60;37	38.53 ± 7.15;38	**0.047**
Day 5 STAI	43.80 ± 7.79;47	39.00 ± 10.42;37.5	42.00 ± 6.65;41	41.06 ± 6.01;40.5	38.91 ± 7.05;38	0.399
Day 7 STAI	42.67 ± 4.93;45	36.43 ± 4.61;36	38.67 ± 3.27;39	40.31 ± 7.22;40	39.62 ± 7.37;39	0.613
Day 10 STAI	45.50 ± 4.95;45.5	35.33 ± 5.13;34	39.60 ± 2.61;40	40.15 ± 6.69;40	39.29 ± 7.77;38	0.371

Data are represented as mean ± standard deviation; Median
*Kruskal-Wallis H test
[α]*P* < 0.05 Kruskal-Wallis H test favors the groups of being illiterate and having middile school degree
ICU, intensive care unit; STAI, State-Trait Anxiety Inventory score.

Table 4. Anxiety Levels According to History of ICU Experience

	Patient's experienced (n=8)	Relative's experienced (n=60)	None (n=107)	*P**
Day of hospitalisation in the ICU STAI	40.04 ± 5.97;39[α]	37.38 ± 5.85;37	39.25 ± 11.83;38.5	**0.009**
Day 1 STAI	38.87 ± 6.22;38	39.46 ± 7.46;39	42.00 ± 8.83;38	0.626
Day 2 STAI	39.35 ± 6.13;39	39.10 ± 7.70;38.5	43.00 ± 7.48;42	0.430
Day 3 STAI	38.52 ± 6.10;38	40.05 ± 7.45;40	41.83 ± 6.65;45	0.246
Day 4 STAI	39.30 ± 7.53;38	38.86 ± 6.24;39	39.75 ± 4.03;40	0.886
Day 5 STAI	40.53 ± 8.07;40	39.88 ± 7.05;39	40.67 ± 1.53;41	0.861
Day 7 STAI	39.87 ± 6.67;40	38.90 ± 6.73;38	39.5 ± 0.71;39.5	0.890
Day 10 STAI	39.09 ± 5.55;40	40.16 ± 8.46;38	40.00 ± 1.41;40	0.961

Data are represented as mean ± standard deviation; Median
*Kruskal-Wallis H test
[α]*P* < 0.05 Kruskal-Wallis H test. favors the group of experienced patient
ICU, intensive care unit; STAI, State-Trait Anxiety Inventory score.

Table 5. Relatives Anxiety Levels According to the Time of Hospitalisation During the Day

	08:00-20:00 (n=81)	20:00-08:00 (n=94)	*P**
Day of hospitalisation in the ICU STAI	38.28 ± 6.37;38	39.67 ± 6.32;39	0.129
Day 1 STAI	38.42 ± 6.12;37.5	39.95 ± 7.33;38	0.281
Day 2 STAI	38.15 ± 6.80;37	40.48 ± 6.72;40[α]	**0.049**
Day 3 STAI	38.08 ± 5.86;38	40.25 ± 7.17;40	0.053
Day 4 STAI	37.54 ± 6.25;37	40.52 ± 7.14;40[β]	**0.026**
Day 5 STAI	38.76 ± 7.33;37	41.45 ± 7.42;41.5[γ]	**0.031**
Day 7 STAI	38.05 ± 5.36;37	40.41 ± 7.10;40	0.157
Day 10 STAI	39.11 ± 8.07;37.5	39.92 ± 5.89;40	0.332

Data are represented as mean ± standard deviation; Median
*Mann-Whitney U test
[α]*P* < 0.05 Mann-Whitney U test, favors the group 20:00-08:00
[β]*P* < 0.05 Mann-Whitney U test, favors the group 20:00-08:00
[γ]*P* < 0.05 Mann-Whitney U test, favors the group 20:00-08:00
STAI: State-Trait Anxiety Inventory score, ICU: intensive care unit.

Table 6. Relatives Anxiety Levels According to the Patients GCS on the Time of Hospitalisation

	Bad	Moderate	Good	*P**
Day of hospitalisation in the ICU GCS	38.45 ± 6.05;38	39.52 ± 7.08;41	39.60 ± 6.53;39	0.421
Day 1 GCS	38.53 ± 5.79;37	39.65 ± 7.24;38	39.97 ± 7.80;39	0.536
Day 2 GCS	39.02 ± 6.58;37	41.86 ± 8.49;39.5	39.25 ± 6.64;40	0.611
Day 3 GCS	38.60 ± 5.34;38	41.22 ± 8.21;41	39.63 ± 7.60;39	0.514
Day 4 GCS	38.48 ± 5.23;37.5	39.50 ± 7.17;37.5	39.81 ± 8.39;39	0.852
Day 5 GCS	38.44 ± 6.34;37.5	37.56 ± 5.22;39	44.41 ± 8.38;42.5[α]	**0.009**
Day 7 GCS	38.24 ± 6.62;38	39.00 ± 4.93;40	43.17 ± 6.18;42	0.052
Day 10 GCS	39.32 ± 7.28;38	36.25 ± 5.42;35.5	42.64 ± 5.55;42[β]	**0.035**

Data are represented as mean ± standard deviation; Median
*Kruskal-Wallis H test
[α]*P* < 0.05 Kruskal-Wallis H test, favors the Group-Good
[β]*P* < 0.05 Kruskal-Wallis H test, favors the Group-Good
GCS, Glasgow Coma scale; ICU, intensive care unit.

Bilgin and Türkleş[15] could not find a significant relationship between the patient's relative's age and anxiety scores in their study. When we looked at the gender of the patient relatives in our study, no statistically significant difference was found between the groups in terms of anxiety scores. However, although the anxiety levels of female patient relatives were not statistically significant, they increased as the patient's hospitalization days increased. Opuş et al.[13] also did not find a difference between the genders in their study, where they looked at the anxiety scores of patient relatives who had patients in IC, as in our study. Türedi[14] also found a difference between the gender of the patient relatives and anxiety scores in their study, which is consistent with our study. Maruiti et al.[16] also stated that anxiety was not related to gender with the data they obtained from their study covering 39 patient relatives. Pochard et al.,[17] on the other hand, found that the anxiety level was higher in women than in men in their study conducted with 920 patient relatives. When the degree of closeness of the patient relative to the patient in IC was examined, no statisticall difference was discovered between the anxiety scores between the groups in our study. However, it was observed that the patient's mother, father, and siblings, although not statistically significant, felt more anxious than their spouse and children. Again, when the groups were evaluated within themselves, it was observed that the anxiety scores increased as the days of hospitalization increased, although not statistically significant. Baltalı and Turkoz,[18] in their study in which they grouped the patients with and without first-degree relatives, could not find a significant difference between the degree of closeness and anxiety levels, similar to our study. In other studies conducted on the anxiety symptoms of patients' relationships in the ICU, contrary to our study, it was stated that the stress level of spouses was higher than other family members. Paparrigopoulos et al.[10] reported that spouses showed more anxiety symptoms. No statisticall difference was established between the groups in our study when the anxiety scores of the patients' relationships were examined according to the frequency of seeing the patient in the ICU in normal life. However, as the patient's hospitalization period increased, a decrease in anxiety scores was observed in the group with a lower frequency of seeing the patient, although not statistically significant. Since no study in the literature review examined the anxiety scores according to the frequency of seeing the patient in the ICU in normal life, a comparison could not be made. When the anxiety scores of the patients' relatives were examined according to their income level, significant difference was not established between the groups in our study. However, the anxiety score was discovered to be lower in the groups with high-income levels than in the groups with low-income levels, although not significant. In two different studies, it was found that the relatives of patients with lower income levels were more worried about their patients in IC and had significantly higher anxiety scores.[15,19] This supports the findings in our study. When the anxiety scores of the patient relatives were compared between the groups in terms of education level, a statisticall difference was found between the illiterate and middle school education groups and the primary school, high school, and university education groups in favor of the illiterate and middle school education groups. In addition, although there was no statistical difference, the anxiety scores in the low-educated groups increased with the number of days the patient stayed. This showed that the level of education was also connected to the anxiety levels of the individuals. In a study including 133 patient relatives, Chui and Chan[20] found that the anxiety levels of women with low education levels were significantly higher. In another study, it was reported that relatives of patients with lower levels of education were more reluctant to be involved in decisions that needed to be made about the patient and, therefore, experienced anxiety. However, significant relationship was not discovered between anxiety and level of education.[21] In another study investigating the degree of anxiety in patients' relationships, it was discovered that the anxiety scores of patients' relationships with higher levels of education were lower, consistent with our study. This suggested that as the level of education increases, patients' relationships can better understand the information given to them about their patients and can create adequate protection mechanisms.[16]

In our study, the patients' relationships were also questioned about their past IC experiences for themselves and other patients. The anxiety scores of the patients' relationships who had previous IC experience were discovered to be statistically significantly higher only on the day of admission compared to the other two groups, namely, the groups without experience and the groups with relatives. The anxiety scores of the group who had no previous IC experience for themselves or any relatives were higher than the other two groups with IC experience except for the day of admission. However, it was not statistically significant. In their study, Baltalı and Turkoz[18] only asked whether the patient's relatives had previous IC experience, but they did not publish any data on the effect of this on their anxiety. Since no other study on the experience of patients in ICU was established in the literature review, no comparison could be made. When the patients' relatives anxiety scores were evaluated to according to the patient's age, no statisticall difference was found between the groups. However, for the younger patient group, the anxiety scores of the patients' relatives increased as the patients' hospitalization period increased. However, it was not statistically significant. Similarly, when the anxiety scores of the patients' relatives were examined according to the patient's gender, no significant difference was established between the anxiety scores for male or female patients in our study. Since no study was found in the literature review measuring patient relatives' anxiety levels according to patient age and gender, no comparison could be made.

When the anxiety scores of the patients were evaluated to according to their hospitalization hours in our study, it was seen that the relatives of the patients were more worried about the patients they admitted at night. Anxiety scores were found to be statisticall higher on days 2, 4, and 5 in the relatives of the patients admitted to the ICU at night and on all other days, compared to those revealed during the day. In their study, Bilgin and Türkleş[15] only provided numerical information about the patients' emergency or planned admissions to the ICU and did not present data on the anxiety scores of the patients' relatives according to these situations. Other studies were no showed in the literature review regarding anxiety scores according to the time of admission to the ICU, so no comparison could be made.

When the patient relatives' anxiety scores were examined according to the patient's education level, no statisticall difference was found between all groups. However, although the patients relatives' anxiety scores increased as the patient's education level increased, these values were not statisticall significant. Since other studies was no showed in the literature review regarding the anxiety status of relatives of patients hospitalized in ICU according to their level of education, a comparison could not be made.

Informing patients' relatives hospitalized in ICU was very important in terms of providing comprehensible intelligence about the patient's condition that day. Pure knowledge about the patient's condition that day can only be obtained by calculating the patient's acute physiological scores.[22] In our study, the patient's physiological scores with SAPS-2, APACHE II, and organ system status with SOFA were calculated, and the relatives of the patients were informed about their patients. As the patients' physiological and organ system scores improved, the anxiety scores of the relatives of the patients also increased. Tok et al. [23] showed in their study that, contrary to our study, the anxiety scores of the patients' relatives increased as the patients' acute physiological scores increased. In other studies, contrary to our study, it was shown that if there was an increase in the patient's acute physiological scores, the anxiety symptoms of the relatives increased.[10,24,25]

When the anxiety scores of the patients' relatives were examined according to the GKS, the patients were in the 5th and 10th. It was observed that the anxiety scores of the patients' relatives with better GCS on the days were statisticall higher. When we look at our data in general, the better the patien's GCS, the higher the anxiety scores of the patients' relatives. Bilgin and Türkleş[15] stated that as the patients' GCS increased, the anxiety scores of the patients' relatives increased, similar to our study.

Study Limitations

The fact that the study was single-centered and that other ICUs in the same hospital were not included limits the study. This study has shown that as the level of education of the relatives of the patients decreases, they become more concerned about their patients. The anxiety levels of the relatives of the patients are higher, especially for the patients who are hospitalized at night. It has been concluded that the fact that the patients are admitted to the ICU, regardless of their health status, is a sufficient reason to cause concern in the relatives of the patients.

Ethics

Ethics Committee Approval: The ethical approval for this study was granted by the Clinical Research Ethics Committee of Atatürk University Faculty of Medicine (approval no.: 40; date: 30.06.2022).

Informed Consent: Written informed consent was obtained from persons who participated in this study.

Footnotes

Author Contributions

Concept - H.A., Ö.Ö.; Design - H.A., Ö.Ö.; Supervision - H.A., Ö.Ö.; Fundings - H.A.; Materials - H.A.; Data Collection and/or Processing - H.A.; Analysis and/or Interpretation - Ö.Ö.; Literature Search - Ö.Ö.; Writing - H.A., Ö.Ö.; Critical Review - Ö.Ö.

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REFERENCES

1. Kutlu R, Işıklar-Özberk D, Gök H, Demirbaş N. Frequency of anxiety and depression and affecting factors in inpatients in cardiology intensive care unit. *Turkish Journal of Thoracic and Cardiovascular Surgery*. 2016;24(4):672-679. [CrossRef]
2. Tel H, Tel H. Transfer anksiyetesi; transfer anksiyetesi; yoğun bakım hastası ve ailesinin ortak duygusal deneyimi. *Yoğun Bakım Hemşireliği Dergisi*. 2009;13(1):24-29. [CrossRef]
3. Ozbayir T, Tasdemir N, Ozseker E. Intensive care unit family needs. Nurses' and families' perceptions. *East J Med*. 2014;19:137-140. [CrossRef]
4. Hacıhasanoğlu G. *Ameliyata alınan hastaların yakınlarının kaygı düzeylerinin belirlenmesi*. Yakın Doğu Üniversitesi Hemşirelik Yüksek Lisans Tezi; 2011. [CrossRef]
5. Spielberger CD, Auerbach SM, Wadsworth AP, Dunn TM, Taulbee ES. Emotional reactions to surgery. *J Consult Clin Psychol*. 1973;40(1):33-38. [CrossRef]
6. Aydemir Ö, Köroğlu E. Psikiyatride kullanılan klinik ölçekler. *Ankara*: *Hekimler Yayın Birliği*; 2000. [CrossRef]
7. Akpir K. Yoğun bakım temel ilkeleri. Tüzüner F, editör. Anestezi, yoğun bakım, ağrı. 1. baskı. Ankara: Nobel Tıp Kitabevi; 2010:1199-1208. [CrossRef]
8. Leske JS. Interventions to decrease family anxiety. *Crit Care Nurse*. 2002;22(6):61-65. [CrossRef]
9. Wartella JE, Auerbach SM, Ward KR. Emotional distress, coping and adjustment in family members of neuroscience intensive care unit patients. *J Psychosom Res*. 2009;66(6):503-509. [CrossRef]
10. Paparrigopoulos T, Melissaki A, Efthymiou A, et al. Short-term psychological impact on family members of intensive care unit patients. *J Psychosom Res*. 2006;61(5):719-722. [CrossRef]
11. Hickman RL Jr, Douglas SL. Impact of chronic critical illness on the psychological outcomes of family members. *AACN Adv Crit Care*. 2010;21(1):80-91. [CrossRef]
12. Davidson JE, Jones C, Bienvenu OJ. Family response to critical illness: postintensive care syndrome-family. *Crit Care Med*. 2012;40(2):618-624. [CrossRef]
13. Opuş B, Gök F, Kılıçaslan A, Yosunkaya A. Yoğun bakım hastalarının akut fizyolojik durum kayıtları ile hasta yakınlarında görülen anksiyete ve uyku bozukluğu ilişkisi. *Selçuk Tıp Derg*. 2020;36(4):333-337. [CrossRef]
14. Türedi D. *Yoğun bakım hastalarının akut fizyolojik durum değişikliklerinin hasta yakınlarının psikolojileri üzerine etkileri*. Çukurova Üniversitesi Tıp Fakültesi Anesteziyoloji ve Reanimasyon Ana Bilim Dalı Uzmanlık Tezi; 2011. [CrossRef]
15. Bilgin F, Türkleş S. *The anxiety levels of the individuals who have the patients in the intensive care unit*. [Master's thesis] 2020. [CrossRef]
16. Maruiti MR, Galdeano LE, Dias Farah OG. Anxiety and depressions in relatives of patients admitted in intensive care units. *Acta Paul Enferm*. 2008;21(4):636-642. [CrossRef]
17. Pochard F, Azoulay E, Chevret S, et al. Symptoms of anxiety and depression in family members of intensive care unit patients: ethical hypothesis regarding decision-making capacity. *Crit Care Med*. 2001;29(10):1893-1897. [CrossRef]
18. Baltali S, Turkoz A, Bozdogan N, et al. The efficacy of intravenous patient-controlled remifentanil versus morphine anesthesia after coronary artery surgery. *J Cardiothorac Vasc Anesth*. 2009;23(2):170-174. [CrossRef]
19. İlbaşı AR. *İzole edilen hastaların izolasyon sonrası anksiyete, depresyon durumları ile izole edilemeyen hastaların anksiyete, depresyon durumlarının değerlendirilmesi ve izole edilen hasta yakınlarının, sağlık personelinin anksiyete durumlarının incelenmesi*, Uludağ Üniversitesi Tıp Fakültesi Enfeksiyon ve Klinik Mikrobiyoloji Ana Bilim Dalı Uzmanlık Tezi, Bursa. [CrossRef]
20. Chui WYY, Chan SWC. Stress and coping of Hong Kong Chinese family members during a critical illness. *J Clin Nurs*. 2007;16(2):372-381. [CrossRef]
21. Anderson WG, Arnold RM, Angus DC, Bryce CL. Passive decision-making preference is associated with anxiety and depression in relatives of patients in the intensive care unit. *J Crit Care*. 2009;24:249-254. [CrossRef]
22. Ball JAS, Redman JW, Grounds RM. *Severity of illness scoring systems general information*. Berlin: Springer; 2002:911-933 [CrossRef]
23. Tok G, Ok G, Erbüyün K, Aydemir Ö, Tok D. Yoğun bakım ünitesinde yatan hastaların yakınlarında görülen anksiyete ve depresyon. Türk Yoğun Bakım Derneği Dergisi. [Master's thesis] 2009;7:1-5. [CrossRef]
24. Day A, Haj-Bakri S, Lubchansky S, Mehta S. Sleep, anxiety and fatigue in family members of patients admitted to the intensive care unit: a questionnaire study. *Crit Care*. 2013;17(3):R91. [CrossRef]
25. Bolosi M, Peritogiannis V, Tzimas P, Margaritis A, Milios K, Rizos DV. Depressive and anxiety symptoms in relatives of ıntensive care unit patients and the perceived need for support. *J Neurosci Rural Pract*. 2018;9(4):522-528. [CrossRef]

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Research Article

Evaluation of Healthy Lifestyle Behaviors of Healthcare Workers; A Single Center Experience

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ABSTRACT

Objective: The aim was to evaluate the healthy lifestyle behaviors of healthcare professionals and to reveal the factors affecting these behaviors.

Methods: Research data were collected using the Health-Promoting Lifestyle Profile II (HPLP II) questionnaire and a 23-question social-demographic survey form (including gender, age, marital status, body weight, and height, occupational group as a health worker, years of experience at the profession, weekly working hours, working style, socioeconomic level, living status, health status, presence of chronic disease, having routine health check-ups, sleep duration, sleep quality, daytime sleeplessness, number of meals per day, appetite alterations in stress, smoking and drinking habits, professional satisfaction and occupational stress). Various groups were structured according to the answers given to the survey form, and then they were analyzed regarding the HPLP II questionnaire scores.

Results: A total of 296 participants were enrolled. The average HPLP II total score of healthcare workers was 121.29 ± 20.88. Participants obtained the highest score from the spiritual growth dimension of the HPLP II questionnaire and the lowest score from the physical activity dimension. Our results show that those with better socio-economic status, better sleep quality, a meal count of 3 or more, a sleep duration of 7 hours or more, and job satisfaction present better health-promoting lifestyle behaviors.

Conclusion: Considering their role in promoting public health, it is important to improve healthcare professionals' awareness. The data obtained during this current study are expected to make a valuable contribution and guide health policymakers in adapting their interventions.

Keywords: Health, lifestyle, medical staff, promotion of health, healthy lifestyle

INTRODUCTION

The definition and meaning of health have changed throughout history.[1] In 1948, the World Health Organization (WHO) expressed that health is not only the absence of disease, and discomfort but also a state of social, mental, and physical well-being.[2] Later, it was stated that since WHO's definition of health has limited aspects, health should be redefined to include concepts such as quantity, quality, and spirituality.[3] Today's understanding of health envisages a holistic care approach with health at its center, which ensures, develops, and protects the continuity of health of the society, family, and individual.[4]

In terms of the holistic approach, the behavior of protecting and promoting health has been considered an integral part of a healthy lifestyle. Improving the health status in our society and providing primary health care services are the main strategies for health promotion.[5] As Pender stated, one of the components that define a healthy lifestyle is health-protective behavior, while the other is health-promoting behavior necessary for the individual to increase his or her level of well-being and self-actualization and maintain personal satisfaction.[6] According to Pender's model, Healthy Lifestyle Behaviors II (HPLP II) consists of a total scale and six sub-scales coming together to measure behaviors in the theoretical dimensions of a health-

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promoting lifestyle, including nutrition, physical activity, health responsibility, interpersonal relationships, spiritual growth and stress management.[7]

Lifestyle behaviors influenced by social and environmental factors are the daily routine practices that directly affect the frequency of chronic diseases.[8] Behaviors like using alcohol, cigarettes, and addictive substances that threaten health, inadequate and unbalanced nutrition, and insufficient physical activity are responsible for most of the diseases and deaths.[9] Therefore, health services need to be developed in a way that prevent diseases and encourage HPLP rather than an acute treatment approach.[10] To prevent diseases, a health-promoting lifestyle is needed, defined as spontaneous, versatile behavioral habits that enable individuals to realize themselves to improve health and quality of life.[11] Therefore, protective, preventive, and individualized medicine to be applied in primary care should be cost-effective, affordable, and comprehensive. In this way, healthcare services should be implemented with a holistic approach, allowing healthcare professionals to recognize and understand the health-related behaviors of their patients and their families.[12] Sometimes, healthcare professionals prioritize ensuring the well-being of their patients over maintaining their own health because of factors such as low motivation to work, fatigue, inadequate knowledge about promoting a healthy lifestyle obtained during training, and lack of time.[13] It has been shown that healthcare professionals who engage in and exhibit healthy behaviors are more likely to provide preventive counseling and have higher self-efficacy and confidence while motivating their patients to avoid health-risk behaviors.[14] The health-related habits of healthcare professionals, who are expected to be role models, also influence the lifestyle attitudes of their patients.[13] Developing skilled, motivated, and supported healthcare workers is essential to overcoming obstacles in achieving national and global health goals because the workforce is central to advancing health in every health system.[15] This investigation aimed to analyze the healthy lifestyle behaviours of healthcare professionals by using social-demographic factors, occupation, living status, health, and habit-related factors obtained from the 23-question survey form. These factors were compared in terms of the HPLP II questionnaire scores.

MAIN POINTS

- The healthcare workers were studied using a 23-item socio-demographic questionnaire and analyzed for the Health Promoting Lifestyle Profile II (HPLP II) scores.
- Although our study results reveal that health-promoting behaviors of healthcare workers are at a moderate level, highest mean score was obtained from spiritual growth followed by interpersonal relations, while the lowest mean score was obtained from physical activity followed by stress management in terms of six dimensions of the HPLP II questionnaire.
- No significant relationship between body mass index, occupational groups as healthcare workers, weekly working hours, working styles, appetite changes under stress and total HPLP II scores or its six dimensions scores have been shown in this research.

MATERIAL AND METHODS

Study Design

This study was approved by the Medical Ethics Committee of Kafkas University (approval no.: 80576354-050-99/138, date: 23.09.2022, Session 7). This cross-sectional study was conducted between September 2022 and March 2023 at Kafkas University Health Research and Application Hospital after obtaining ethical approval. Study data were collected by asking participants, who could be reached individually, to read the printed forms and mark the answers. Participants who could not be reached individually were asked to fill out the forms presented online using the Google Forms platform. A survey form, which questions the sociodemographic characteristics, individual characteristics, and working conditions of healthcare workers, along with the Health-Promoting Lifestyle Profile II (HPLP II) questionnaire, were used to collect data. An anonymous survey was conducted with each participant's informed consent, both electronic and printed, consent, and the questionnaires were self-administered.

Our inclusion criteria were: 1- Working as a full-time healthcare worker at Kafkas University Faculty of Medicine Health, Research and Application Hospital; 2- Being over 18 years old; 3- Voluntarily requesting to participate in the study after being informed; 4- Filling out the questionnaires completely. Our exclusion criteria were: 1. Not being a full-time healthcare worker at Kafkas University Faculty of Medicine Health, Research and Application Hospital, 2. Not agreeing to participate in the study after being informed, and 3. Incomplete completion of questionnaires. The study was completed with a total of 296 valid surveys. Nine of the surveys were not included in the study because they were incompletely filled out.

Measurements and Instruments-Independent Variables

Sociodemographic data were obtained with a 23-question survey form which's content includes gender, age, marital status, body weight and height, occupational group as a healthcare worker, time spent in the profession, weekly working hours, working style, perception of socioeconomic level, living status, perception of health status, presence of chronic disease, having routine health check-ups, sleep duration, perception of sleep quality, daytime sleeplessness, number of meals, experiencing changes in appetite in case of stress, smoking and drinking habits, job satisfaction status and experiencing stress due to occupation. Some of the answers to the survey form questions were evaluated in their original form, while the remaining answers were evaluated by creating categories. Gender was evaluated in two groups: male and female. The ages of the participants were evaluated in 4 groups: 1=18-29 years, 2=30-39 years, 3=40-49 years, and 4= ≥ 50. Marital status was evaluated in two groups: 1= married and 2= single. Using the weight and height data of the participants, body mass index (BMI) was calculated with the formula weight (kg)/ height (m^2). The results were grouped based on the WHO's BMI classification, namely: BMI <18.5, underweight; 18.5≤ BMI <24.99, normal weight; 25.0≤ BMI <29.99, overweight (pre-obesity); and BMI ≥30.0, obese.[16] Participants were divided into four groups according to their professional groups: 1=

doctor, 2= nurses, 3= technicians, and 4= others (pharmacist, microbiologist, caregiver). Years of experience in the profession were evaluated in two groups: 1= ≤ 10 years, 2= >10 years. Weekly working hours were evaluated in two groups: Group 1: 40 hours and Group 2: more than 40 hours. Working style was evaluated in two groups: 1: permanent regular daytime working hours, and 2: other (permanent night shift, rotational/shift, sometimes being on guard duty in addition to regular daytime working). Perception of the socioeconomic level was evaluated in three groups: 1= low, 2= medium, and 3= high. The living status of the participants was evaluated as two groups: 1= living alone and 2= not living alone. Perception of health status was evaluated in three groups: 1= good, 2= moderate, and 3= poor. The presence of chronic disease was evaluated in two groups: 1= yes (with chronic disease) and 2= no (not with chronic disease). The timing of routine health check-ups was evaluated in three groups: 1= in the last 1 year; 2= more than 1 year ago; 3= never had a check-up. Sleep duration was evaluated in two groups: 1= < 7 hours, 2= ≥ 7 hours. Perception of sleep quality was evaluated in three groups: 1= good, 2= average, and 3= bad. Experiencing daytime sleeplessness was evaluated in two groups: 1= those having daytime sleeplessness, and 2= those without daytime sleeplessness. The daily meals consumed were evaluated in two groups: 1= < 3 meals and 2= ≥ 3 meals. Appetite change due to stress was categorized into three groups: 1= increases, 2= decreases, and 3= stable. The smoking status of the participants was evaluated based on whether they were smokers or non-smokers. The severity of smoking was calculated as packs/year, and the total duration of smoking (in years) was also calculated. The responses were evaluated based on yes and no for alcohol use. Additionally, the stated amount of alcohol consumption was assessed whether the participants had moderate alcohol consumption or high-risk drinking habits. Furthermore, the total alcohol consumption duration in years was evaluated. Professional satisfaction status was evaluated in three groups. 1= dissatisfied, 2= undecided, and 3= satisfied. Occupational stress was evaluated in three groups: 1= never, 2= sometimes, and 3= always.

Measurements and Instruments-Dependent Variables

The original HPLP was developed by Walker et al.[6] in 1987, based on Pender's health promotion model, and in 1996, Walker and Hill-Polerecky[7] developed HPLP II. The HPLP II questionnaire measures health promotion behavior, a multidimensional model of individually created perceptions and activities that help individuals reveal their potential and improve their health level. The questionnaire consists of 52 items and six dimensions, all of which have been designed with a positive approach. Therefore, as the scores obtained from the scale increase, the level of health behavior stated also increases. In this questionnaire, these subscales are stress management (8 items), spiritual growth (9 items), physical activity (8 items), health responsibility (9 items), nutrition (9 items), and interpersonal relations (9 items). Each item is rated on a 4-point Likert-type scale: 1 indicates "never," 2 indicates "sometimes," 3 indicates "often," and 4 indicates "routinely". Evaluation of the health-promoting lifestyle according to its theoretical dimensions, consists of evaluating the total score from the 52 items of HPLP II and calculating the scores of its subscales. The highest total score that can be obtained for the overall HPLP II Scale is 208, while the lowest score is 52.[7]

Statistical Methods

All statistical calculations were performed using IBM SPSS Statistics for Windows version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics are expressed as number, percentage, mean, standard deviation, median, and min.-max. values. The Shapiro-Wilk test was performed to examine whether the data were normally distributed. Data were analyzed using parametric (Independent Samples t-test or one-way ANOVA,) or nonparametric (Mann-Whitney U test or Kruskal-Wallis variance analysis,) tests, depending on the data distribution. Pearson's r and Spearman's rho correlation tests were used for examining the relationship between two variables, and Bonferroni test was used to determine the source of the difference between groups. The results were evaluated within the 95% confidence interval, and $P < 0.05$ was considered statistically significant.

RESULTS

This study included 296 healthcare workers. According to the results, 52.7% of participants were women, 62.5% were between the ages of 20 and 29, 62.5% were not married, and 82.4% had been working for less than 10 years. Table 1 summarizes the participants' characteristics regarding multiple parameters. Participants' average age was 29.36 ± 6.84, BMI was 24.67 ± 4.48, sleep duration was 7.13 ± 1.30 hours, and their average number of meals was 3.00 ± 1.25 per day. One hundred seven people who stated they were smoking had consumed an average of 7.68 ± 7.87 packs per year of cigarettes for approximately 8.02 ± 5.59 years. Moreover, 61 people who stated that they consumed alcohol less than moderately had been using it for 7.59 ± 7.04 years. Participants' lowest HPLP II total score was 73, the highest HPLP II total score was 186, and the average score was 121.29 ± 20.88. The mean scores from the subscales of the questionnaire, from highest to lowest, were found to be 24.63 ± 4.91 in spiritual growth, 24.20 ± 4.81 in interpersonal relations, 19.80 ± 4.53 in health responsibility, 18.82 ± 4.25 in nutrition, 17.66 ± 3.74 in stress management, and 16.19 ± 5.23 in physical activity (Table 2). Correlations between participants' age, BMI, sleep duration, daily meal number, amount of smoking (pack/year), duration of smoking (years), duration of alcohol consumption (years), and HPLP II scores were presented in Table 3. The participants' physical activity increased in correlation as their age decreased ($\rho \geq 0.147$, Sig.: 0.012). As their daily sleep duration increases, they exhibit higher levels of health responsibility ($r > 0.115$, Sig.: 0.048) and stress management ($r = 0.148$, Sig.: 0.011). Participants with greater daily meal numbers tend to have better eating behavior ($\rho = 0.136$, Sig.: 0.019), and those with more prolonged smoking habits had better interpersonal relationships ($r = 0.192$, Sig.: 0.047). No statistically significant correlation was found between BMI, amount of smoking (pack/year), duration of alcohol consumption (year), and HPLP II scores.

The statistically significant differences between participants' characteristics and HPLP II and its six dimensions are listed in Table 4. It was determined that those aged between 20-

Table 1. Participants' Characteristics

Variable	Cathegory	n	%
Age group (years)	20-29	185	62.5
	30-39	84	28.4
	40-49	22	7.4
	≥ 50	5	1.7
Gender	Female	156	52.7
	Male	140	47.3
Marital status	Married	110	37.2
	Not married	186	62.8
BMI	<18,5 (underweight)	11	3.7
	18.5-24.99 (normal weight)	163	55.1
	25-29.99 (overweight)	92	31.1
	≥ 30 (obese)	30	10.1
Occupational group as a healthcare worker	Doctor	108	36.5
	Nurse	110	37.2
	Technician	46	15.5
	Other	32	10.8
Years of professional experience	≤ 10 years (0-5 years, 5-10 years)	244	82.4
	> 10 years (10-15 years, 15 years and over)	52	17.6
Weekly working hours	40 hours	125	42.2
	> 40 hours (40-50 hours, ≥ 50 hours)	171	57.8
Working style	Regular daytime working	103	34.8
	Other (permanent night shift, rotational/shift, being on guard duty from time to time in addition to regular daytime working)	193	65.2
Perception of socioeconomic level	Low	81	27.4
	Medium	200	67.6
	High	15	5.1
Living status	Living alone	111	37.5
	Not living alone (living with family, living with spouse and children, living only with children, other)	185	62.5
Perception of health status	Good (excellent, very good, good)	186	62.8
	Moderate	91	30.7
	Poor	19	6.4
Chronic desease	Yes	51	17.2
	No	245	82.8
Time of routine health check-up	In the last 1 year	205	69.3
	In more than 1 year (in the last 2 years, in the last 3 years, in the last 4 years or more)	49	16.6
	Never	42	14.2
Sleep duration	< 7 hours	97	32.8
	≥ 7 hours	199	67.2
Perception of sleep quality	Good (very good, good)	109	36.8
	Average	118	39.9
	Bad (bad, very bad)	69	23.3
Daytime sleeplessness	Having daytime sleeplessness (always, often, sometimes, rarely)	285	96.3
	Not having daytime sleeplessness	11	3.7

Table 1. Continued

Variable	Category	n	%
Daily number of meals	< 3 meals	58	19.6
	≥ 3	238	80.4
Apetite change due to stress	Increases	114	38.5
	Decreases	147	49.7
	Stable	35	11.8
Smoking status	No	189	63.9
	Yes	107	36.1
Alcohol consumption status	No	235	79.4
	Yes	61	20.6
Professional satisfaction	Dissatisfied (very dissatisfied, dissatisfied)	76	25.7
	Undecided	69	23.3
	Satisfied (satisfied, very satisfied)	151	51.0
Having occupational stress	Never	6	2.0
	Sometimes	175	59.1
	Always	115	38.9

Table 2. Mean, Median, Minimum, Maximum, and Standard Deviation of The HPLP II Scale and Subscales of All Participants

	HPLP II total score	Health responsibility	Physical activity	Nutrition	Spiritual growth	Interpersonal relations	Stress management
n	296	296	296	296	296	296	296
Mean	121.29	19.80	16.19	18.82	24.63	24.20	17.66
Median	121.00	19.00	16.00	19.00	25.00	24.00	17.00
SD* (±)	20.88	4.53	5.23	4.25	4.91	4.81	3.74
Minimum	73	10	8	9	10	11	10
Maximum	186	36	32	32	36	36	27

*SD, standard deviation; HPLP II, Health- Promoting Lifestyle Profile II.

29, compared to those aged between 40-49 (P = 0.003), and men, compared to women (P = 0.001), exhibited significantly higher physical activity levels. Those with less than 10 years of experience in the profession exhibited higher levels of physical activity (P = 0.044) than more experienced healthcare professionals; in addition, the physical activity level of those living alone was significantly higher (P = 0.013) than those who do not live alone. Moreover, alcohol users exhibited better physical activity (P = 0.009) than non-users.

While the physical activity scores of single people were found to be higher than those of married people (P = 0.002), married people had higher spiritual growth scores (P = 0.045) than single people.

HPLP II total score (P = 0.022) and spiritual development score (P = 0.030) of those who stated their socio-economic status as high were significantly higher than those who reported their socioeconomic status as low. Both high and medium socioeconomic levels are more successful in terms of health responsibility (P = 0.004). On the other hand, stress management of individuals with low socioeconomic levels was more successful (P = 0.048) than that of individuals with higher socioeconomic levels. The stress management behaviors of the participants with good health were better (P = 0.025) than those with moderate health, and the individuals with chronic disease were more successful in interpersonal relations (P = 0.041) than those who did not have a chronic disease. The nutrition subscale score was found to be significantly higher (P = 0.012) for those who had a routine health check-up both within the last year and more than a year ago those who had never gone for a routine health check-up.

It was determined that healthcare workers with a daily sleep duration of 7 hours or more were more successful in interpersonal relations (P = 0.027) and stress management (P = 0.010) than those who slept less than 7 hours. Regarding HPLP II total (P < 0.001), health responsibility (P < 0.001), nutrition (P = 0.005), spiritual development (P = 0.004), and stress management (P < 0.001), the scores obtained from the scale by healthcare professionals who have good sleep quality were found to be higher than those whose sleep quality was average or poor. Participants with good sleep quality exhibited higher levels of physical activity (P < 0.001) than those with average sleep quality. Additionally, individuals with high sleep quality were more successful in interpersonal relations (P =0.044) than those with poor sleep quality. Healthcare workers who do not have sleeplessness during the day indicated higher levels of healthy lifestyle behavior in health responsibility (P = 0.039),

stress management (P = 0.038), and nutrition (P = 0.005) compared to those who experienced daytime sleeplessness. The study population who consumed 3 or more meals daily had significantly higher scores on the nutrition (P = 0.004) and stress management (P =0.006) subscales than healthcare workers who consumed less than 3 meals. Healthcare workers who are satisfied with their professions have significantly higher scores in The HPLP II total score (P = 0.010), interpersonal relations score (P = 0.001), and stress management score (P = 0.016) compared to those who are dissatisfied. The participants who were satisfied with their profession had higher scores in the spiritual growth subscale (P < 0.001) than those who were undecided and those who were dissatisfied with their professions. Healthcare professionals who sometimes experience stress due to their professions have been found to have better stress management (P = 0.006) than those who always experience occupational stress.

There were no significant relationships between occupational groups, such as healthcare professionals, weekly working hours, working styles, changes in appetite under stress, smoking status, amount of smoking (pack/year), duration of alcohol use (years), and the HPLP II scores.

DISCUSSION

The aim of this study is to identify the level of health-promoting lifestyle behaviors among healthcare professionals. Moreover, we aimed to determine how sociodemographic factors related to individual and working life affect these lifestyle behaviors. While the total score obtained from the HPLP II questionnaire varies between 52 and 208, the average total score of 121.29 ± 20.88 obtained in this study indicates a medium-level health-promoting lifestyle. Our result was consistent with the outcomes of these studies, which found the average total score at a medium level. In addition, the result we presented is similar to studies conducted using the same scale with healthcare professionals in different countries, where the average score was found to be at a medium level of 131 ± 23,[17] 139.82 ± 21.27.[18] and 122.42 ± 44.22.[19] Healthcare professionals with sufficient knowledge about health-promoting behaviors and their effects on health, and who encounter patients with chronic diseases every day due to the patients' health-risking habits, are expected to have a higher level of healthy lifestyle behavior.[13] However, in our study, the average HPLP II total score of healthcare workers does not meet this expectation. Although research supports that having adequate knowledge can affect attitudes toward health, this does not necessarily

Table 3. Correlation Between Participants' Age, BMI, Sleep Duration, Daily Meal Number, Amount of Smoking (Pack/Year), Duration of Smoking (years), Duration of Alcohol Consumption (Years) and Healthy Lifestyle Behaviors II Scores

Variable		HPLP II total score	Health responsibility	Physical activity	Nutrition	Spiritual growth	Interpersonal relations	Stress management
Age	ρ*	-0.024	-0.059	-0.147	0.088	0.099	-0.044	-0.050
	Sig.**	0.680	0.308	0.012	0.130	0.090	0.446	0.391
BMI**	ρ*	0.061	0.014	0.020	0.042	0.072	0.084	0.047
	Sig.**	0.293	0.810	0.726	0.467	0.220	0.149	0.418
Sleep duration	r***	0.044	0.115	-0.059	0.026	-0.035	0.046	0.148
	Sig.**	0.447	0.048	0.309	0.656	0.552	0.433	0.011
Number of meals	ρ*	0.093	0.078	0.083	0.136	0.039	0.024	0.086
	Sig.**	0.111	0.179	0.153	0.019	0,509	0.685	0.138
Smoking amount (pack/year)	ρ*	-0.008	-0.131	-0.129	-0.064	0.151	0.141	-0.002
	Sig.**	0.935	0.180	0.184	0.512	0.120	0.147	0.981
Smoking duration (years)	r***	-0.004	-0.137	-0.189	-0.029	0.185	0.192	-0.018
	Sig.**.	0.966	0.159	0.052	0.763	0.056	0.047	0.850
Alcohol consumption duration (years)	ρ*	-0.009	-0.133	-0.064	0.089	0.135	0.024	-0.055
	Sig.**	0.943	0.308	0.622	0.494	0.299	0.856	0.675

*ρ, Spearman's rank correlation coefficient
**Sig., significance level (P) (2-tailed)
***r, Pearson correlation coefficient
****BMI, body mass index; HPLP II, Health- Promoting Lifestyle Profile II.

Table 4. Statistical Relationship Between Participants' Characteristics and HPLP II and Its Six Dimensions

Variable		n	Mean	Standart deviation (±)	P
HPLP II total score		**n**	**Mean**	**Standart deviation (±)**	***P***
Socioeconomic level	Low	81	118.06	23.23	***P**:* **0.022**
	Medium	200	121.64	19.51	
	High	15	134.20	21.19	
Sleep quality	Good	109	128.56	20.84	***P***:* ≤ 0.001**
	Average	118	117.39	18.74	
	Bad	69	116.49	21.49	
Professional satisfaction	Dissatisfied	76	116.20	20.05	***P***:* 0.010**
	Undecided	69	119.48	22.76	
	Satisfied	151	124.69	19.87	
Health responsibility		**n**	**Mean**	**Standart deviation (±)**	***P***
Socioeconomic level	Low	81	18.93	4.82	***P**:* **0.004**
	Medium	200	19.97	4.36	
	High	15	22.27	4.30	
Sleep quality	Good	109	21.15	4.79	***P***:* ≤ 0.001**
	Average	118	19.08	4.28	
	Bad	69	18.90	4.07	
Daytime sleeplessness	Yes	285	19.72	4.55	***P*****:* 0.039**
	No	11	22.00	3.49	
Physical activity		**n**	**Mean**	**Standart deviation (±)**	***P***
Age group (years)	20-29 years	185	16.89	5.00	***P**:* **0.003**
	30-39 years	84	15.32	5.68	
	40-49 years	22	13.32	4.04	
	≥ 50 years	5	17.60	4.82	
Sleep quality	Good	109	17.53	4.94	***P***:* ≤ 0.001**
	Average	118	14.84	4.94	
	Bad	69	16.38	5.62	
Gender	Female	156	15.25	4.724	***P****:* 0.001**
	Male	140	17.24	5.577	
Marital status	Married	110	14.98	5.01	***P****:* 0.002**
	Single	186	16.90	5.23	
Years of experience	≤ 10 years	244	16.47	5.15	***P****:* 0.044**
	> 10 years	52	14.87	5.44	
Living status	Living alone	111	17.16	4.88	***P****:* 0.013**
	Nnot living alone	185	15.61	5.35	
Alcohol consumption	No	235	15.79	5.14	***P****:* 0.009**
	Yes	61	17.74	5.32	
Nutrition		**n**	**Mean**	**Standart deviation (±)**	***P***
Time of routine health check-ups	In the last 1 year	205	19.12	4.27	***P***:* 0.012**
	In more than 1 year	49	19.14	4.03	
	Never	42	17.02	4.09	
Sleep quality	Good	109	19.87	4.04	***P***:* 0.005**
	Average	118	18.15	4.39	
	Bad	69	18.32	4.08	
Daily number of meals	< 3 meals	58	17.40	4.495	***P****:* 0.004**
	≥ 3 meals	238	19.17	4.135	

Table 4. Continued

Variable		n	Mean	Standart deviation (±)	P
HPLP II total score		**n**	**Mean**	**Standart deviation (±)**	***P***
Daytime sleeplessness	Yes	285	18.71	4.27	***P****: 0,005***
	No	11	21.73	2.49	
Spiritual growth		**n**	**Mean**	**Standart deviation (±)**	***P***
Socioeconomic level	Low	81	23.64	5.82	***P*: 0,030***
	Medium	200	24.83	4.46	
	High	15	27.27	4.20	
Sleep quality	Good	109	25.85	4.87	***P**: 0,004***
	Average	118	24.01	4.36	
	Bad	69	23.75	5.49	
Professional satisfaction	Dissatisfied	76	23.07	4.85	***P**: ≤ 0,001***
	Undecided	69	23.97	4.95	
	Satisfied	151	25.72	4.67	
Interpersonal relations		**n**	**Mean**	**Standart deviation (±)**	***P***
Sleep quality	Good	109	24.87	4.98	***P**: 0,044***
	Average	118	24.25	4.43	
	Bad	69	23.03	5.02	
Professional satisfaction	Dissatisfied	76	22.50	4.49	***P**: 0,001***
	Undecided	69	24.20	5.10	
	Satisfied	151	25.05	4.63	
Chronic disease	Yes	245	23.93	4.70	***P***: 0,041***
	No	51	25.45	5.15	
Sleep duration	< 7 hours	97	23.31	4.53	***P***: 0,027***
	≥ 7 hours	199	24.63	4.89	
Stress management		**n**	**Mean**	**Standart deviation (±)**	***P***
Socioeconomic level	Low	81	17.30	4.22	***P*: 0,048***
	Medium	200	17.65	3.49	
	High	15	19.73	3.73	
Health status	Good	186	18.05	3.54	***P*: 0,025***
	Moderate	91	16.95	3.62	
	Poor	19	17.1	5.47	
Having occupational stress	Never	6	18.50	5.95	***P*: 0,006***
	Sometimes	175	18.17	3.66	
	Always	115	16.83	3.61	
Sleep quality	Good	109	19.28	3.52	***P**: ≤ 0,001***
	Average	118	17.05	3.34	
	Bad	69	16.12	3.80	
Professional satisfaction	Dissatisfied	76	16.84	3.32	***P**: 0,016***
	Undecided	69	17.25	4.31	
	Satisfied	151	18.25	3.57	
Sleep duration	< 7 hours	97	16.86	3.68	***P***: 0,010***
	≥ 7 hours	199	18.05	3.71	
Daily number of meals	< 3 meals	58	16.45	3.560	***P***: 0,006***
	≥ 3 meals	238	17.95	3.732	
Daytime sleeplessness	Yes	285	17.57	3.74	***P****: 0,038***
	No	11	19.82	3.06	

*P**, Kruskal-Wallis test
*P***, One-way ANOVA
*P****, Independent Sample t-test
*P*****, Mann-Whitney U test; HPLP II, Health- Promoting Lifestyle Profile II.

mean that awareness will lead to correct health behaviors and habits.[20] because participants' different sociodemographic characteristics, health conditions, and work environments affect these behaviors.[13]

Considering the six dimensions of the questionnaire, the highest average score received by the participants was in spiritual growth, however, the lowest average score was obtained from physical activity. Similar results have been encountered in some studies in the literature,[17,18,21] where the highest score was spiritual growth, and the lowest score was physical activity. There are other studies conducted with healthcare professionals, such as Mustafaei Najaf-Abadi and Rezaei's[19] study. Their highest score was in health responsibility, followed by spiritual development. The lowest was in stress management, followed by physical activity.[19] Cho and Han's[22] study indicated that interpersonal relations had the highest score, and the lowest score was in physical activity. Kurnat-Thoma et al.'s[23] highest score was in interpersonal relations, and the lowest score was in health responsibility. While Tsai and Liu's[24] highest score was in interpersonal relations, the lowest score was in physical activity. Even though some studies have reached entirely different results from ours, we saw that the results of most of these studies were consistent with this study. Spiritual growth involves the ability to gain the life experience of individuals who develop themselves, and they change positively to maximize their efforts to live a healthy life. Spiritual growth enables individuals to analyze the meaning and consequences of their traumatic experiences, allowing them to increase mental maturation and self-efficacy.[25] Given that healthcare workers received the lowest score for physical activity, this might result from longer shifts and tiredness due to their heavy workload.[13] Therefore, reducing obstacles such as lack of time, excessive fatigue, shift work, and lack of resources is important to support the engagement in physical activity.[18]

This study indicated that physical activity levels decrease with aging. According to the study results, those between the ages of 20-29 showed significantly higher levels of physical activity compared with the 40-49 age group, and the physical activity scores of those with 10 years or less of professional experience were higher than those with more than 10 years. There were other findings related to sociodemographic status of the participants. Our statistical analysis found that men scored significantly higher than women in physical activity. In addition, physical activity levels decrease with aging. Moreover, the physical activity score of those living alone was significantly higher than that of those who did not live alone. According to this study's results, the total HPLP II and spiritual growth scores of individuals with high socioeconomic levels were higher than the scores of those with low socioeconomic levels among our participants. There was a significant positive, low-level correlation between the number of meals our participants consumed and nutritional intake in this study. This study showed a statistically significant, positive yet very low correlation between health responsibility, stress management scores, and daily sleep duration. Unlike the known adverse effects of smoking on health, there was no relationship between either smoking status or the amount of smoking (packs/year) and HPLP II scores in the current investigation.

Based on the well-known adverse effects of alcohol consumption on health, this current investigation unexpectedly revealed that the physical activity score of alcohol users was higher than that of non-users, and the duration of alcohol consumption did not have a significant relationship with HPLP II. The amount of alcohol consumption reported by the participants was less than moderate, and they were mainly young individuals (with an average age of 29.93 ± 8.77). Therefore, the alcohol-consuming participants' low-level drinking habits and average age, which is considerably younger, might play a role in this outcome. The current study's findings were similar to the literature, in that the scores of those who were satisfied with their profession were significantly higher in HPLP II total, interpersonal relations, and stress management than those of the individuals who were dissatisfied.

Considering the previous studies on marital status and HPLP II, various relationships have been reported. Moghimi et al.[17] reported that married people have better nutrition and experience spiritual growth. Some researchers stated that single people have low nutritional scores.[21] Married people have been reported to have lower HPLP II scores.[26] In another study by Mustafaei Najaf-Abadi and Rezaei[19], no significant relationship between marital status and HPLP II scores was found. In this study, the physical activity scores of singles were significantly higher than those of married people, and the spiritual growth scores of married people were significantly higher than those of singles. This current study showed a statistically significant, positive yet very low correlation between health responsibility, stress management scores, and daily sleep duration. The participants who slept 7 hours or more daily had significantly higher average interpersonal relations and stress management scores than those who slept less than 7 hours. In the study by Itani et al.,[27] the dose-response of short sleep duration in mortality was examined, finding that there was a linear relationship between a statistically significant increase in mortality and sleep duration under 6 hours. Hirshkowitz et al.'s[28] study evaluated the sleep duration recommended by the American National Sleep Foundation. In this systematic review, the acceptable duration for adults was concluded to be between 7 and 9 hours. These findings seem to support our conclusion. Moreover, the results of this current study indicated that the scores of participants with good sleep quality were significantly higher for physical activity than participants with medium sleep quality. For the interpersonal relations subscale, individuals with good sleep quality had higher scores on the subscale than those with poor sleep quality. Previous studies conducted with healthcare professionals reported that the higher the job stress, the poorer the health promotion behaviors, conversely, the lower the job stress, the better the health promotion behaviors.[26] Additionally, the more spiritual development scores increase, the more work stress decreases significantly.[29] The emergence of work stress may result from the person not having sufficient knowledge and skills to cope with the situations in the work environment. If it continues, it has the effect of worsening the balance between the person's abilities and job demands.[30] Considering that one of the most important factors of burnout is occupational stress,[31] working without stress can be associated with a healthy lifestyle, just

as being under stress at work is associated with an unhealthy lifestyle.[19] The current study concluded that the stress management scores of the participants who stated that they sometimes experienced occupational stress were significantly higher than those who stated that they always experienced occupational stress.

According to this the results of the current study conducted with the HPLP II survey, which we chose due to its benefits in assessing self-maintained health care behaviors in daily life, clearly demonstrate the need for specific health intervention. Since the study group consists of healthcare professionals, it is worrying that the HPLP II total score is at a medium level and the least successful health behavior in the overall evaluation is physical activity. We think that it is necessary to provide sports facilities and organize access to them, reduce the workload to provide sufficient time, and organize events that promote the health benefits of regular physical activity to support the population, especially, the elderly, women, married people, as well as those not living alone and who are not physically active in their lives. In addition, those who sleep an average of 7 hours or more can cope with stressors better. Moreover, those with good sleep quality performed significantly better in both the HPLP II total score and all six dimensions. As the authors of the current study, we think that educational interventions that encourage the development of sleep duration and sleep quality among healthcare professionals will support the development of health-promoting behaviors.

There were various subheadings studied in this investigation, and among them, some showed no statistical relationship with healthy lifestyle behaviours regarding the HPLP II questionnaire. No significant relationship between BMI, occupational groups of healthcare workers, weekly working hours, working styles, appetite changes under stress and total HPLP II scores or its six dimensions' scores has been shown in this research.

Study Limitations

This study has some limitations to discuss before interpreting the results of the investigation. Although this study highlights and clarifies the necessity of health-promoting behaviors, the cross-sectional design makes it difficult to interpret the causal relationships and time-dependent changes in the lifestyle patterns of healthcare professionals. Since the participants of our single-center study were selected from a university hospital, our findings may not represent community employees due to differences in the working environment and conditions. The sample size is another aspect to discuss since these results will not represent all healthcare professionals, and caution should be used when generalizing them to foreign countries, considering cultural differences. All data collected for the study consist of self-reported responses; it is possible that individuals may have reported fewer negative behaviors or vice versa due to social acceptance bias, and these responses may not reflect the truth. To reduce this bias, future studies examining life behaviors aimed at improving health should be designed as multicenter studies, with a larger sample group and using measurements as objective as possible.

CONCLUSION

In this cross-sectional study, we aimed to identify the factors affecting the health-promoting lifestyle behaviors of healthcare professionals. Although our study results reveal that health-promoting behaviors of healthcare workers are at a moderate level, we should also point out that, in terms of six dimensions, the highest mean score was obtained from spiritual growth, while the lowest mean score was obtained from physical activity. A significant relationship between the factors we examined, such as gender, age, marital status, time spent in the profession, socioeconomic level, living status, health status, chronic disease, routine health check-up, daily sleep duration, sleep quality, daytime sleeplessness, number of meals, alcohol use, professional satisfaction, occupational stress, and health-promoting lifestyle behaviors, has been indicated in this research. However, no significant relationship has been reached between BMI, occupational group, specifically as healthcare workers, weekly working hours, working style, appetite change under stress, smoking status, amount of smoking (pack/year), duration of alcohol use (years), and health-promoting life behaviors. Based on these findings, and considering the role of healthcare workers in providing health services, education, promoting public health, it is important to improve their lifestyle behaviors regarding physical activity, where they score the lowest. We advocate that multi-center studies should be conducted with larger sample groups and improved methodologies to increase the awareness of those serving in the health sector regarding health promotion. Additionally, these studies aim to reveal the reasons for the differences between the results of studies in the literature. These types of studies and meta-analyses that evaluate the cumulative data of these studies will provide essential data to guide health policymakers in adapting interventions for these professional groups and public health.

Ethics

Ethics Committee Approval: This study was approved by the Medical Ethics Committee of Kafkas University (approval no.: 80576354-050-99/138, date: 23.09.2022, Session 7).

Informed Consent: An anonymous survey was conducted with each participant's informed consent, both electronic and printed, consent, and the questionnaires were self-administered.

Footnotes

Author Contributions

Concept - B.K., H.Ç.; Design - B.K.; Literature search - B.K.; Supervision - H.Ç.; Data collection - B.K.; Materials - B.K.; Data Interpretation - B.K., H.Ç.; Statistical analysis - B.K.; Manuscript prepeation - B.K., H.Ç.; Critical Review - B.K., H.Ç.

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REFERENCES

1. Stokes J 3rd, Noren J, Shindell S. Definition of terms and concepts applicable to clinical preventive medicine. *J Community Health*. 1982;8(1):33-41. [CrossRef]
2. WHO. Alma-Ata Declaration, International Conference on Primary Health Care, *Alma-Ata*, USSR, 6-12 September. Geneva: WHO; 1978. [CrossRef]
3. Galloway RD. Health promotion: causes, beliefs and measurements. *Clin Med Res*. 2003;1(3):249-258. [CrossRef]
4. Sisk RJ. Caregiver burden and health promotion. *Int J Nurs Stud*. 2000;37(1):37-43. [CrossRef]
5. Salari S, Pilevarzadeh M, Daneshi F, Ahmadidarrehsima S. Examining the health-promoting lifestyle and its related factors among the nursing students of Jiroft university of medical sciences. *Indian J Public Health Res Dev*. 2017;8(1):342-346. [CrossRef]
6. Walker SN, Sechrist KR, Pender NJ. The health-promoting lifestyle profile: development and psychometric characteristics. *Nurs Res*. 1987;36(2):76-81. [CrossRef]
7. Walker SN, Hill-Polerecky DM. Psychometric evaluation of the health promoting lifestyle profile II. Omaha, NE: University of Nebraska Medical Center. 1996. [CrossRef]
8. Alothman SA, Al Baiz AA, Alzaben AS, Khan R, Alamri AF, Omer AB. Factors associated with lifestyle behaviors among university students-a cross-sectional study. *Healthcare (Basel)*. 2024;12(2):154. [CrossRef]
9. Örs M. Healthy lifestyle behaviors among teachers working in public primary schools and affecting factors. *Front Public Health*. 2024;12:1382385. [CrossRef]
10. Zhang SC, Tao FB, Ueda A, Wei CN, Fang J. The influence of health-promoting lifestyles on the quality of life of retired workers in a medium-sized city of Northeastern China. *Environ Health Prev Med*. 2013;18(6):458-465. [CrossRef]
11. Wang L, Wang Y, Luo Y, Li Y, Li J. The mediating and moderating effect of health-promoting lifestyle on frailty and depressive symptoms for Chinese community-dwelling older adults: a cross-sectional study. *J Affect Disord*. 2024;361:91-96. [CrossRef]
12. Kafadar D, Esen AD, Arıca S. Determining health-promoting behavior in smokers preparing to quit: a holistic and personalized approach. *EPMA J*. 2019;10(2):115-123. [CrossRef]
13. Profis M, Simon-Tuval T. The influence of healthcare workers' occupation on health promoting lifestyle profile. *Ind Health*. 2016;54(5):439-447. [CrossRef]
14. Lobelo F, Duperly J, Frank E. Physical activity habits of doctors and medical students influence their counselling practices. *Br J Sports Med*. 2009;43(2):89-92. [CrossRef]
15. Deriba BK, Sinke SO, Ereso BM, Badacho AS. Health professionals' job satisfaction and associated factors at public health centers in West Ethiopia. *Hum Resour Health*. 2017;15(1):36. [CrossRef]
16. World Health Organization. A healthy lifestyle – WHO recommendations. (Accessed 25 September 2024). [CrossRef]
17. Moghimi A, Saberi Isfeedvajani M, Javanbakht M, Khedmat L. Health-promoting lifestyle behaviors and its association with sociodemographic characteristics in hospital clinical staff. *Front Public Health*. 2024;12:1391094. [CrossRef]
18. Keele R. To role model or not? Nurses' challenges in promoting a healthy lifestyle. *Workplace Health Saf*. 2019;67(12):584-591. [CrossRef]
19. Mustafaei Najaf-Abadi H, Rezaei B. Health-promoting behaviours of Iranian nurses and its relationship with some occupational factors: a cross sectional study. *J Nurs Manag*. 2018;26(6):717-725. [CrossRef]
20. Karimian Z, Moradi M, Zarifsanaiey N. Exploring the relationship between contextual factors and health-promoting lifestyle profile (HPLP) among medical students: a cross-sectional study. *Health Sci Rep*. 2024;7(4):e2040. [CrossRef]
21. Al-Qahtani MF. Health-promoting lifestyle behaviors among nurses in private hospitals in Al-Khobar, Saudi Arabia. *J Egypt Public Health Assoc*. 2015;90(1):29-34. [CrossRef]
22. Cho H, Han K. Associations among nursing work environment and health-promoting behaviors of nurses and nursing performance quality: a multilevel modeling approach. *J Nurs Scholarsh*. 2018;50(4):403-410. [CrossrRef]
23. Kurnat-Thoma E, El-Banna M, Oakcrum M, Tyroler J. Nurses' health promoting lifestyle behaviors in a community hospital. *Appl Nurs Res*. 2017;35:77-81. [CrossRef]
24. Tsai YC, Liu CH. Factors and symptoms associated with work stress and health-promoting lifestyles among hospital staff: a pilot study in Taiwan. *BMC Health Serv Res*. 2012;12:199. [CrossRef]
25. Sun C, Zhu Z, Zhang P, et al. Exploring the interconnections of anxiety, depression, sleep problems and health-promoting lifestyles among Chinese university students: a comprehensive network approach. *Front Psychiatry*. 2024;15:1402680. [CrossRef]
26. Zhou Y, Ye L, Chen X, Zhang J. Factors associated with workplace stress and health promotion behaviours among Chinese emergency nurses: a cross-sectional study. *Int J Nurs Pract*. 2024;30(6):e13294. [CrossRef]
27. Itani O, Jike M, Watanabe N, Kaneita Y. Short sleep duration and health outcomes: a systematic review, meta-analysis, and meta-regression. *Sleep Med*. 2017;32:246-256. [CrossRef]
28. Hirshkowitz M, Whiton K, Albert SM, et al. National Sleep Foundation's sleep time duration recommendations: methodology and results summary. *Sleep Health*. 2015;1(1):40-43. [CrossRef]
29. Williams HL, Costley T, Bellury LM, Moobed J. Do Health promotion behaviors affect levels of job satisfaction and job stress for nurses in an acute care hospital? *J Nurs Adm*. 2018;48(6):342-348. [CrossRef]
30. Lee JH, Hwang J, Lee KS. Job satisfaction and job-related stress among nurses: the moderating effect of mindfulness. *Work*. 2019;62(1):87-95. [CrossRef]
31. Siegel TR, Nagengast AK. Mitigating burnout. *Surg Clin North Am*. 2019;99(5):1029-1035. [CrossRef]

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Research Article

Does Aortic Propagation Velocity Predict Subclinical Atherosclerosis in Prehypertensive Patients?

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ABSTRACT

Objective: Predictors of subclinical atherosclerosis include carotid intima-media thickness (cIMT) and epicardial adipose tissue (EAT). The risk of atherosclerosis increases owing to hypertension. The aim of the present research was to determine the association between aortic propagation velocity (APV), cIMT, and EAT in patients with prehypertension.

Methods: This research included 208 patients. Two groups were generated: prehypertensive and control. The APV, cIMT, and EAT values were also recorded. The correlations between these parameters were also analyzed.

Results: Statistically significant differences were found between the two groups in the EAT, cIMT, systolic blood pressure (SBP), diastolic blood pressure (DBP), and APV variables ($P < 0.05$). A statistically significant inverse association was found among EAT, cIMT, SBP, DBP, and APV and the atherosclerosis surrogate markers ($P < 0.05$). Linear regression analysis revealed a close relationship between the EAT, cIMT, and APV.

Conclusion: In prehypertensive patients, APV as a non-invasive method may be helpful in identifying individuals predisposed to atherosclerosis.

Keywords: Aortic propagation velocity, subclinical atherosclerosis, prehypertension

INTRODUCTION

Hypertension (HT) is correlated with elevated cardiac mortality and morbidity.[1] For diagnosing HT, staging is performed based on the current guidelines, and treatment management follows the staging.[2] It is known that even early-stage HT is associated with coronary artery disease (CAD). In addition, cardiovascular death and morbidity increase proportionally with increasing systolic blood pressure (SBP) pressure and diastolic blood pressure (DBP) values.[3] In this respect, it is important to identify individuals who may develop HT at an early stage and initiate appropriate lifestyle changes and treatment in terms of risk reduction.

Worldwide, CAD remains a principal cause of death.[3,4] Atherosclerosis, which plays an important role in CAD pathophysiology, becomes subclinical before the disease manifests.[5] Therefore, it is extremely important to diagnose diseases that cause such high mortality in the subclinical stage and to initiate lifestyle changes and various drug therapies to prevent atherosclerotic disease.[5-8] The link between epicardial adipose tissue (EAT) and CAD has been well established. Many studies have shown an association between EAT and CAD severity.[9-12] Increased carotid intima-media thickness (cIMT) is correlated with the onset of future cardiac events. It is considered an indirect parameter that indicates atherosclerosis

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burden and subclinical atherosclerosis.[9,13] In this context, EAT and cIMT are current non-invasive parameters that are used as predictors of atherosclerosis.

Atherosclerosis is an early onset, systemic, and progressive disease that affects the large muscular arteries. Atherosclerosis causes stiffening and thickening of the arterial wall, resulting in increased arterial resistance. Increasing arterial resistance results in a reduction in the blood flow within the arterial lumen. Studies have revealed that the color M-mode Doppler flow propagation speed of the descending aorta, namely, the aortic propagation velocity (APV), is associated with coronary atherosclerosis.[14-16] We aimed to evaluate cIMT and EAT, which are predictors of subclinical atherosclerosis, to investigate the association between these predictors and APV; and the ability of APV to predict atherosclerosis, in prehypertensive patients. This study represents the first effort to assess APV, cIMT, and EAT in prehypertensive patients, to the best of our knowledge.

MATERIAL AND METHODS

Our study included patients examined in a cardiology outpatient clinic between March and June 2019. A total of 101 apparently healthy volunteers with no known history of cardiovascular, renal, hepatic, or systemic inflammatory disease were prospectively enrolled as the control group. In addition, 107 patients aged 18-80 years who met the diagnostic criteria for prehypertension and had no other comorbidities were included in the prehypertensive group. Erzurum Regional Training and Research Hospital Ethical Committee provided approval for this study (approval no.: 2019/07-62, date: 15.09. 2019). All participants provided informed consent prior to enrollment. The exclusion criteria were a) diabetes mellitus, b) infection, c) chronic obstructive pulmonary disease, d) drug use for chronic disease, e) a history of cancer, f) peripheral arterial disease, and g) CAD.

Definitions

Patients were diagnosed with prehypertension based on the current 8th Joint National Committee criteria.[17] An ambulatory blood pressure measurement device was connected to all patients for 24 hours. The mean DBP values between 80-89 mmHg and mean SBP values between 120-139 mmHg were considered prehypertension. The mean values of the control group, i.e. those with normal blood pressure values, were <120/80 mmHg in the ambulatory blood pressure measurement.

MAIN POINTS

- Hypertension contributes to the risk of atherosclerotic cardiovascular disease. In this context, prehypertension is a clinically important condition.
- We found a negative correlation between aortic propagation velocity and predictors of subclinical atherosclerosis such as carotid intima-media thickness and epicardial adipose tissue.
- Finally, APV may be used as a predictor of subclinical atherosclerosis in prehypertension.

Participants' smoking habits were noted based on whether they were already active smokers. Body mass index measurements were obtained for all patients.

Analysis of Blood Samples

Blood samples collected for the study were drawn from the antecubital vein with minimal venous stasis after 12 hours of fasting. Blood samples for complete blood counts were stored in tubes containing potassium EDTA. Counts of white blood cells (WBC), hemoglobin concentrations, and platelet numbers were evaluated using the electrical impedance method with a fully automatic hematology analyzer (Beckman Coulter LH 780). Albumin, serum lipid profile, creatinine, glucose, sodium, potassium, and calcium levels were measured using standard laboratory methods.

Echocardiography

Echocardiographic measurements were performed using Vivid 7 GE (GE Healthcare, Little Chalfont, UK) and a 2.5 MHz frequency transducer. Echocardiographic recordings, were obtained from standard apical and parasternal views, in the left lateral position at the end of expiration in three cardiac cycles. Echocardiographic examinations were carried out following the American Society of Echocardiography (ASE) standards.[18] The left ventricular (LV) ejection fraction was calculated using the modified Simpson method. After routine echocardiographic evaluation, the "cursor" was positioned along the axis to the blood flow, in the descending aorta, and colored M-mode records were obtained from the suprasternal window. The flame-shaped M-mode velocity records were obtained (Figure 1). An appropriate aliasing velocity was selected for each patient to evaluate the velocity slope clearly. APV values were obtained by plotting the velocity slope and dividing the time between the beginning and end of this slope into intervals. The mean of the three measurements was considered the APV.

cIMT and EAT Measurement

For cIMT measurements, patients were positioned supine with their head tilted backward. The bilateral carotid arteries were imaged using the Vivid S5 ultrasound device (GE Vingmed Ultrasound AS, Norten, Norway) with a 7.5 MHz linear probe. cIMT was obtained according to the protocol published by ASE.[19] The main carotid artery, internal carotid artery, and carotid bulb were examined in all the patients. cIMT measurements were made from the distal posterior wall, approximately 1 cm from the bifurcation, using the echogenicity of the lumen-intima and media-adventitia surfaces of both main carotid arteries. At least three measurements were performed. Segments with atherosclerotic plaques were not used for measurements. The EAT was measured from the hypoechoic gap between the visceral pericardium and outermost border of the right ventricular (RV) myocardium from the parasternal long-axis view at end-diastole. The largest diameter of the EAT, which was located on the RV free wall, was determined as previously described.

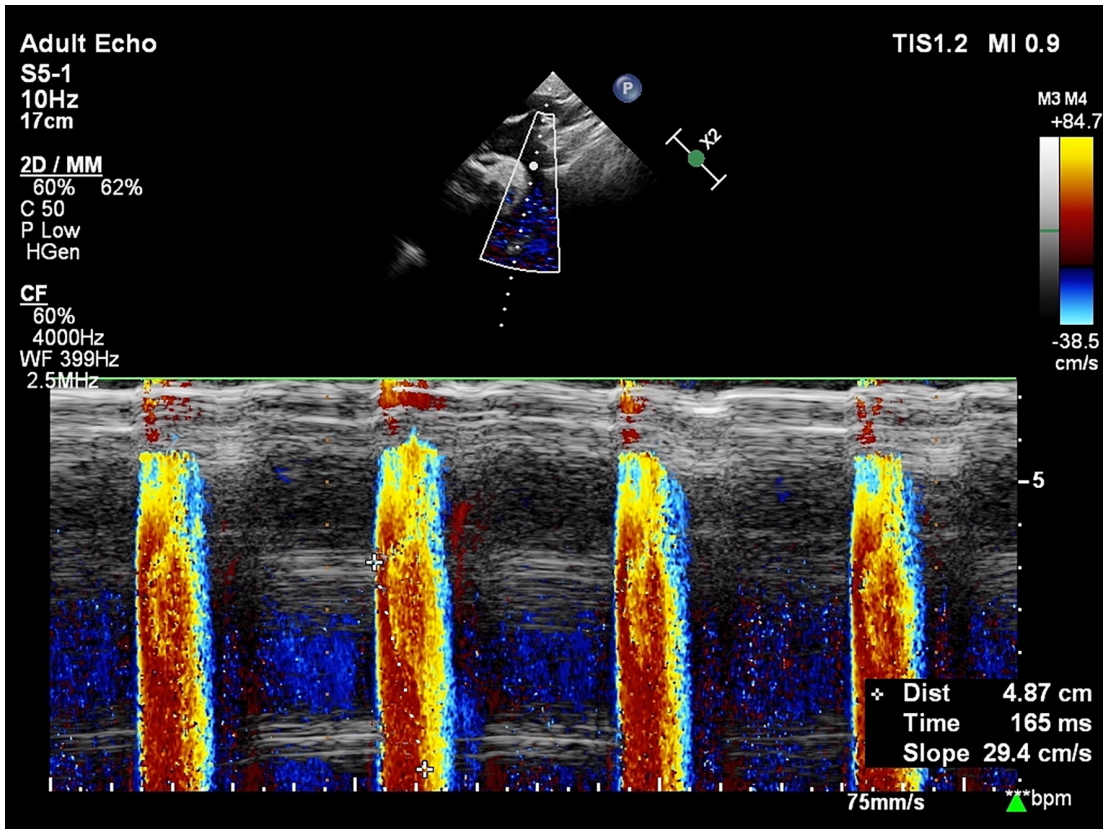

Figure 1. An example image for M-mode velocity record aortic propagation velocity.

Statistical Analysis

Data analysis was conducted using SPSS version 22 (IBM, Chicago, IL, USA). Data are expressed as continuous variables with mean ± standard deviation and as categorical variables with frequency and percentage. The compatibility of continuous variables with a normal distribution was tested using the Kolmogorov-Smirnov test. In the evaluation of continuous variables between the patient and control groups, Student's t-test was used for those meeting parametric assumptions, and the Mann-Whitney U test was used for data not meeting parametric assumptions. Categorical variables between the two study groups were assessed using Pearson's chi-square test. Correlations between two continuous variables were tested using Pearson's correlation test. Variables that were significant in the univariate analyses, were subjected to multivariate linear regression analysis to determine whether the EAT, SBP, DBP, and cIMT values were independently associated with APV. Statistical significance was set at $P < 0.05$.

RESULTS

This study comprised 208 patients in total. Patient characteristics and laboratory and echocardiographic findings are displayed in Table 1. The mean age of the prehypertensive group was 55.5 ± 7.7, 65% were male, while the mean age of the control group was 54.3 ± 6.1 and 62% were male. Comparisons between the two groups revealed no significant differences in age, gender, smoking habits, body mass index, or serum electrolyte levels (all $P > 0.05$). Nonetheless, multiple clinical parameters showed statistically significant differences between the groups. Prehypertensive patients had significantly higher EAT,cIMT, SBP, and DBP than controls ($P = 0.004$, the others $P < 0.001$ respectively). The APV was significantly lower in the prehypertensive group compared to controls (42.5 ± 12.5 cm/s vs. 55.2 ± 10.3 cm/s, $P < 0.001$), indicating increased aortic stiffness in the prehypertensive patients. The comparison revealed no significant differences between the groups in LV ejection fraction, interventricular septal thickness, LV end-diastolic diameter , LV systolic dimension, or systolic pulmonary artery pressure (all $P > 0.05$). Laboratory tests, including glucose, albumin, total cholesterol, LDL, HDL, and triglyceride levels, exhibited no significant variation between the two groups (all $P > 0.05$). Hematological parameters, such as hemoglobin, platelet count, and WBC count, also showed no significant differences (all $P > 0.05$).As shown in Table 2, correlation analysis showed that APV was inversely correlated with EAT ($r = -0.38$, $P < 0.001$), cIMT ($r = -0.48$, $P < 0.001$), SBP ($r = -0.31$, $P < 0.001$), and DBP ($r = -0.30$, $P < 0.001$). These findings suggest that increased EAT, cIMT, and elevated blood pressures are linked with reduced APV, which indicates a relationship between increased vascular stiffness and lower APV. This finding highlights the potential utility of APV as an indicator of subclinical vascular changes, particularly in patients with prehypertension and early signs of arterial stiffness. In univariate analysis, EAT ($P = 0.004$) and cIMT ($P < 0.001$) were significantly associated with reduced APV. Specifically, for each 1 mm increase in EAT, the odds of reduced APV increased by a factor of 4.3 (OR = 4.3, 95% CI: 1.2-8.1), and for each 1

mm increase in cIMT, the odds of reduced APV increased by a factor of 3.6 (OR = 3.6, 95% CI: 1.2-7.3). SBP and DBP also showed significant associations with APV, with odds ratios of (OR = 1.6, 95% CI: 1.1-2.5) and (OR = 1.3, 95% CI: 1.1-2.1), respectively. As shown in Table 3, in the multivariate analysis, significant associations persisted for EAT and cIMT, with EAT remaining a significant predictor of APV (*P* = 0.046, OR = 2.6, 95% CI: 0.9-4.17), and cIMT (*P* = 0.009, OR = 1.9, 95% CI: 1.1-3.3). However, SBP and DBP were not statistically significant in the multivariate model (SBP: *P* = 0.128; DBP: *P* = 0.389).

Table 1. Comparison of Baseline Characteristics, Laboratory and Echocardiographic Findings of the Study Population Between Study Groups

Variables	Prehypertensive (n=107)	Control (n=101)	*P*
Age, years	55.5 ± 7.7	54.3 ± 6.1	0.821
Gender, male %	65	62	0.418
Smoking, %	41	39	0.369
EAT, mm	7.8 ± 2	5.9 ± 2	**0.004**
cIMT, mm	1.1 ± 0.3	0.7 ± 0.2	**< 0.001**
Systolic blood pressure, mmHg	131 ± 5.7	119 ± 5.1	**< 0.001**
Diastolic blood pressure, mmHg	83 ± 7.1	75 ± 6.3	**< 0.001**
LV-EF, %	60 ± 5.9	62 ± 5.4	0.239
IVS, mm	11.3 ± 0.4	10.4 ± 0.3	0.683
LVEDD, mm	45 ± 8.9	44 ± 5.5	0.394
LVSDD, mm	27 ± 6.2	26 ± 8.7	0.691
sPAB,mm Hg	23 ± 6.3	21 ± 4.7	0.831
APV, cm/s	42.5 ± 12.5	55.2 ± 10.3	**< 0.001**
BMI, kg/m^2	24 (21-29)	24 (20-28)	0.621
GFR, mL/min/1.73 m^2	89 (73-115)	86 (71-116)	0.407
Glucose, mg/dL	88 (79-104)	92 (81-101)	0.528
Na	141 ± 4.9	140 ± 4.1	0.372
K	3.9 ± 0.5	3.8 ± 0.4	0.815
Ca	8.9 ± 1.3	8.7 ± 1.4	0.228
AST	35 (21-45)	37 (22-46)	0.393
ALT	33 (24-40)	33 (25-41)	0.459
Albumin	3.5 ± 1.1	3.5 ± 1.2	0.156
Total cholesterol, mg/dL	150 (120-189)	145 (114-174)	0.409
LDL-cholesterol, mg/dL	93 (72-118)	91 (71-121)	0.832
HDL-cholesterol, mg/dL	36 (31-42)	32 (29-35)	0.281
Triglyceride, mg/dL	102 (81-123)	99 (80-120)	0.125
Hemoglobin, g/dL	15.3 ± 3.2	15.6 ± 3.7	0.916
Platelet count, 10^3/L	342 (230-420)	304 (221-412)	0.609
White blood cell count, 10^3/L	6.3 (3.4-8.3)	5.1 (3.1-8.1)	0.791

EAT, epicardial adipose tissue; cIMT, carotid intima-media thickness; LV-EF, left ventricular ejection fraction; cIMT, carotid intima-media thickness; IVS, interventricular septum; LVEDD, left ventriculer end diastolic diameter; LVSDD, left ventriculer systolic dimension; sPAB, systolic pulmonary artery pressure; APV, aortic propagation velocity; BMI, body mass index; GFR, glomerular filtration rate; Na, sodium; K, potassium; Ca, calcium; AST, aspartat aminotransferaz; ALT, alanin aminotransferaz; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

Table 2. Correlation of Aortic Propagation Velocity with Blood Pressure and Surrogate Markers

Variables	APV	
	***r* value**	***P* value**
EAT; mm	-0.38	**< 0.001**
cIMT,mm	-0.48	**< 0.001**
Systolic blood pressure	-0.31	**< 0.001**
Diastolic blood pressure	-0.30	**< 0.001**

APV, aortic propagation velocity; EAT, epicardial adipose tissue; cIM, carotid intima-media thickness.

Table 3. Association of APV with Atherosclerotic Surrogate Markers and Blood Pressure in Linear Regression Analysis

Variables	Univariate *P* value	Univariate OR	Multivariate *P* value	Multivariate OR
EAT, mm	0.004	4.3 (1.2-8.1)	**0.046**	2.6 (0.9-4.17)
cIMT, mm	< 0.001	3.6 (1.2-7.3)	**0.009**	1.9 (1.1-3.3)
SBP	< 0.001	1.6 (1.1-2.5)	0.128	1.3 (0.89-1.6)
DBP	< 0.001	1.3 (1.1-2.1)	0.389	1.3 (0.82-1.9)

OR, odds ratio; EAT, epicardial adipose tissue; cIMT, carotid intima-media thickness; SBP, systolic blood pressure; DBP, diastolic blood pressure.

DISCUSSION

The findings of our study can be summarized as follows:

The prehypertensive group had significantly higher EAT and cIMT values. In this context, there was a higher tendency for atherosclerosis in the prehypertensive patients versus the control group.

APV is intimately related to the surrogate markers of atherosclerosis in patients with prehypertension. In our study, APV was used as a surrogate marker for atherosclerosis in this patient group.

HT is a key risk factor for the development of atherosclerotic heart disease.[20] Its pathophysiology includes conditions such as endothelial dysfunction and activation of the sympathetic system. HT is a leading cause of chronic renal failure and cardiovascular disorders (coronary artery-peripheral vascular disease and cardiac failure) in developed and developing countries. The risk of cardiovascular fatality and myocardial infarction is threefold higher in patients compared to those without the condition.[21] Prehypertension was defined as SBP between 120-139 mmHg and DBP between 80-89 mmHg.[17] Both HT incidence and cardiovascular (mortality and morbidity) rates have increased in the long term in patients with prehypertension. A study by Uçar et al.[22] showed that coronary complexity may be increased in patients with HT. Another study showed that cardiovascular morbidity and mortality increased directly proportional to the increase in blood pressure values.[23]

Ultrasonographic quantification of cIMT is an inexpensive, reliable, and repeatable method that can be used to evaluate subclinical atherosclerosis. It has been suggested that cIMT is closely linked to conventional cardiovascular risk factors and may predict future cardiac diseases such as myocardial infarction and stroke.[24,25]

Atherosclerosis is a systemic and intensifying disease that starts at an early age and affects large muscular arteries such as the thoracic aorta. Atherosclerosis causes condensation and stiffening of the arterial wall, resulting in amplified arterial resistance. Increased arterial resistance results in a decreased rate of blood flow propagation within the arterial lumen, which can be measured using non-invasive methods.[14,26] Among these measurements, the APV is the most widely studied. APV is a Doppler echocardiographic measure indicates the elasticity and compliance of the descending aorta. A reduction in APV suggests increased stiffness of the aorta, which has been linked to negative cardiovascular outcomes, such as LV diastolic dysfunction, myocardial ischemia, and a heightened risk of arrhythmias due to changes in ventricular-arterial coupling. In the literature, there is evidence suggesting that atheroma plaque in the aorta may be a marker of generalized atherosclerosis. Tribouilloy et al.[27] described a strong relationship between the presence and amount of CAD and the manifestation of atherosclerotic plaques detected by transesophageal echocardiography in the thoracic aorta. Arterial resistance increases due to the thickening and hardening of the arterial wall caused by atherosclerosis. Increased aortic resistance due to atherosclerosis in the descending aorta decreased the flow propagation rate. Thus, as the severity of atherosclerosis in the descending aorta increases, APV values decrease. Various studies indicate that APV may have a close association with cardiovascular conditions, notably coronary atherosclerosis. In an observational case-control study by Oğuz et al.[14], decreased aortic flow propagation velocity was associated with increased epicardial adipose thickness. Similarly, in our study, APV values decreased and EAT values increased. In addition, Vasudeva Chetty et al.'s [15] cross-sectional comparative study of 100 patients showed that APV and cIMT were associated with CAD burden. In a study of 93 patients by Sen et al.[28], it was shown that APV can help in the non-invasive assessment of cardiovascular risks and in identifying high-risk individuals for CAD. We found that the cIMT and EAT values were higher in patients with prehypertension. In other words, patients with prehypertension may be indirectly prone to atherosclerosis. In addition, there was a relationship between APV and predictors of atherosclerosis in prehypertensive patients. This finding is valuable because it shows that prehypertension may be an atherosclerotic precursor and demonstrates the utility of APV as a surrogate marker of atherosclerosis in prehypertensive individuals. The study's limitations involve a small sample size and the lack of coronary computed tomography and angiography, which are instrumental in diagnosing CAD.

In conclusion, in patients with prehypertension, APV is closely associated with cIMT and EAT, which are surrogate markers of atherosclerosis. In this patient group, APV as a non-invasive method may be helpful in predicting atherosclerosis.

Ethics

Ethics Committee Approval: Erzurum Regional Training and Research Hospital Ethical Committee provided approval for this study (approval no.: 2019/07-62, date: 15.09. 2019).

Informed Consent: All participants provided informed consent prior to enrollment.

Footnotes

Author Contributions

Concept - K.K. H.K.; Design - K.K. H.K.; Supervision - K.K. H.K.; Fundings - K.K. H.K.; Materials - K.K. H.K.; Data Collection and/or Processing - K.K. H.K.; Analysis and/or Interpretation - K.K. H.K.; Literature Search - K.K. H.K.; Writing - K.K. H.K.; Critical Review - K.K. H.K.

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REFERENCES

1. Tang L, Zhao Q, Han W, Li K, Li J. Association of cardiovascular risk factor clustering and prehypertension among adults-results from the China health and retirement longitudinal study baseline. *Clin Exp Hypertens*. 2020;42(4):315-321. [CrossRef]
2. Huang XB, Zhang Y, Wang TD, et al. Prevalence, awareness, treatment, and control of hypertension in Southwestern China. *Sci Rep*. 2019;9(1):19098. [CrossRef]
3. Timmis A, Townsend N, Gale CP, et al. European Society of Cardiology: Cardiovascular Disease Statistics 2019. *Eur Heart J*. 2019. [CrossRef]
4. Anderson JL, Le VT, Min DB, et al. Comparison of three atherosclerotic cardiovascular disease risk scores with and without coronary calcium for predicting revascularization and major adverse coronary events in symptomatic patients undergoing positron emission tomography-stress testing. *Am J Cardiol*. 2020;125(3):341-348. [CrossRef]
5. Wilkins JT, Gidding SS, Robinson JG. Can atherosclerosis be cured? *Curr Opin Lipidol*. 2019;30(6):477-484. [CrossRef]
6. Khan SS, Ning H, Wilkins JT, et al. Association of body mass index with lifetime risk of cardiovascular disease and compression of morbidity. *JAMA Cardiol*. 2018;3(4):280-287. [CrossRef]
7. Srivastava RAK. Life-style-induced metabolic derangement and epigenetic changes promote diabetes and oxidative stress leading to NASH and atherosclerosis severity. *J Diabetes Metab Disord*. 2018;17(2):381-391. [CrossRef]
8. Kohlman-Trigoboff D. Hypertension management in patients with vascular disease: an update. *J Vasc Nurs*. 2016;34(3):87-92. [CrossRef]
9. Kalkan K, Hamur H, Yildirim E, et al. The comparison of angiographic scoring systems with the predictors of atherosclerosis. *Angiology*. 2018;69(2):158-163. [CrossRef]
10. Nappi C, Ponsiglione A, Acampa W, et al. Relationship between epicardial adipose tissue and coronary vascular function in patients with suspected coronary artery disease and normal myocardial perfusion imaging. *Eur Heart J Cardiovasc Imaging*. 2019;20(12):1379-1387. [CrossRef]
11. Bakirci EM, Degirmenci H, Hamur H, et al. New inflammatory markers for prediction of non-dipper blood pressure pattern in patients with essential hypertension: serum YKL-40/Chitinase 3-like protein 1 levels and echocardiographic epicardial adipose tissue thickness. *Clin Exp Hypertens*. 2015;37(6):505-510. [CrossRef]
12. Mancio J, Oikonomou EK, Antoniades C. Perivascular adipose tissue and coronary atherosclerosis. *Heart*. 2018;104(20):1654-1662. [CrossRef]
13. Balta S, Aparci M, Ozturk C, Yildirim AO, Demir M, Celik T. Carotid intima media thickness and subclinical early atherosclerosis. *Int J Cardiol*. 2016;203:1146. [CrossRef]
14. Oğuz D, Ünal HÜ, Eroğlu H, Gülmez Ö, Çevik H, Altun A. Aortic flow propagation velocity, epicardial fat thickness, and osteoprotegerin level to predict subclinical atherosclerosis in patients with nonalcoholic fatty liver disease. *Anatol J Cardiol*. 2016;16(12):974-979. [CrossRef]
15. Vasudeva Chetty P, Rajasekhar D, Vanajakshamma V, Ranganayakulu KP, Kranthi Chaithanya D. Aortic velocity propagation: a novel echocardiographic method in predicting atherosclerotic coronary artery disease burden. *J Saudi Heart Assoc*. 2017;29(3):176-184. [CrossRef]
16. Karaman K, Arisoy A, Altunkas A, et al. Aortic flow propagation velocity in patients with familial mediterranean fever: an observational study. *Korean Circ J*. 2017;47(4):483-489. [CrossRef]
17. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. 2014;311(5):507-520. Erratum in: *JAMA*. 2014;311(17):1809. [CrossRef]
18. Mitchell C, Rahko PS, Blauwet LA, et al. Guidelines for performing a comprehensive transthoracic echocardiographic examination in adults: recommendations from the American Society of Echocardiography. *J Am Soc Echocardiogr*. 2019;32(1):1-64. [CrossRef]
19. Stein JH, Korcarz CE, Hurst RT, et al. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American Society of Echocardiography carotid intima-media thickness task force. Endorsed by the Society for Vascular Medicine. *J Am Soc Echocardiogr*. 2008;21(2):93-111; quiz 189-190. Erratum in: *J Am Soc Echocardiogr*. 2008;21(4):376. [CrossRef]
20. Hurtubise J, McLellan K, Durr K, Onasanya O, Nwabuko D, Ndisang JF. The different facets of dyslipidemia and hypertension in atherosclerosis. *Curr Atheroscler Rep*. 2016;18(12):82. [CrossRef]
21. Kannel WB. Framingham study insights into hypertensive risk of cardiovascular disease. *Hypertens Res*. 1995;18(3):181-196. [CrossRef]
22. Uçar H, Gür M, Börekçi A, et al. Relationship between extent and complexity of coronary artery disease and different left ventricular geometric patterns in patients with coronary artery disease and hypertension. *Anatol J Cardiol*. 2015;15(10):789-794. [CrossRef]
23. Gosmanova EO, Mikkelsen MK, Molnar MZ, et al. Association of systolic blood pressure variability with mortality, coronary heart disease, stroke, and renal disease. *J Am Coll Cardiol*. 2016;68(13):1375-1386. [CrossRef]
24. Johri AM, Behl P, Hetu MF, et al. Carotid ultrasound maximum plaque height-a sensitive imaging biomarker for the assessment of significant coronary artery disease. *Echocardiography*. 2016;33(2):281-289. [CrossRef]
25. Davis PH, Dawson JD, Riley WA, Lauer RM. Carotid intimal-medial thickness is related to cardiovascular risk factors measured from childhood through middle age: the muscatine study. *Circulation*. 2001;104(23):2815-2819. [CrossRef]
26. Stefanadis C, Dernellis J, Tsiamis E, et al. Aortic stiffness as a risk factor for recurrent acute coronary events in patients with ischaemic heart disease. *Eur Heart J*. 2000;21(5):390-396. [CrossRef]
27. Tribouilloy C, Peltier M, Andrejak M, Rey JL, Lesbre JP. Correlation of thoracic aortic atherosclerotic plaque detected by multiplane transesophageal echocardiography and cardiovascular risk factors. *Am J Cardiol*. 1998;82(12):1552-1555, a8. [CrossRef]
28. Sen T, Tufekcioglu O, Ozdemir M, et al. New echocardiographic parameter of aortic stiffness and atherosclerosis in patients with coronary artery disease: aortic propagation velocity. *J Cardiol*. 2013;62(4):236-240. [CrossRef]

ABCResearch

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Research Article

Comparison of Cumulative Antibiogram Results of Trakya University Hospital for the Years 2015-2016 and 2022-2023

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ABSTRACT

Objective: A cumulative antibiogram serves as a critical tool in guiding the selection of appropriate empirical therapy, facilitating de-escalation based on susceptibility results, and shaping institutional policies to combat antibiotic resistance effectively. This study aimed to evaluate changes in antimicrobial susceptibility over the years and provide guidance to clinicians in the selection of empirical therapies.

Methods: A retrospective analysis was conducted on the *in vitro* antimicrobial susceptibility test results of bacterial isolates obtained from clinical samples submitted to the Medical Microbiology Laboratory at Trakya University Hospital during the periods of 2015-2016 and 2022-2023. Cumulative antibiogram data were compiled in accordance with the guidelines outlined in the "Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data" (CLSI 2014, M39-A4).

Results: A total of 7524 isolates (5009 Gram-negative, 2515 Gram-positive) were analyzed during the 2015-2016 period, while 5880 isolates (4202 Gram-negative, 1678 Gram-positive) were analyzed during the 2022-2023 period. In both timeframes, the most commonly isolated microorganisms were isolated from urine, blood/catheter, and wound/aspirate/tissue samples. The predominant isolates included *Escherichia coli (E.coli)*, *Klebsiella* spp., and *Enterococcus* spp. Based on the findings, the following antimicrobials were identified as suitable for empirical treatment for *E. coli* infections: carbapenems and amikacin. For *Klebsiella* spp. infections: amikacin. For *Enterococcus* spp. infections: vancomycin, teicoplanin, linezolid, and tigecycline. For *Acinetobacter* spp. infections: combination therapy. Carbapenem susceptibility among *Klebsiella* spp., isolates decreased notably in 2022-2023, ranging between 55% and 62%, in contrast to higher rates observed during 2015-2016.

Conclusion: The regular evaluation of hospital-based antibiogram data and the revision of empirical treatment protocols based on these findings represent a crucial strategy for effectively combating antimicrobial resistance.

Keywords: Antibiogram, cumulative antimicrobial susceptibility testing report, empirical treatment, resistance

INTRODUCTION

According to the World Health Organization (WHO), antimicrobial resistance (AMR) has become one of the most urgent global public health challenges, significantly increasing morbidity and mortality worldwide.[1,2] In 2019, approximately 3.57 million deaths were attributed to antibiotic resistance. Projections by WHO estimate that this number could rise to 10 million annually by 2050.[3,4] The coronavirus disease-2019 pandemic has exacerbated the AMR crisis. During the pandemic, the inappropriate and excessive use of antibiotics, treatments that induce immunosuppression, and prolonged hospital stays have accelerated the development of antibiotic resistance.[5] Additionally, financial constraints in healthcare systems and reductions in healthcare personnel have negatively impacted surveillance and control efforts aimed at combating AMR.[6] The widespread use of hand sanitizers and surface disinfectants

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during the pandemic may further worsen resistance patterns in the coming years.[7] AMR renders first-line antibiotics ineffective, leading to the replacement of these drugs with more expensive alternatives. This situation prolongs disease duration, increases healthcare costs, and imposes significant economic burdens on individuals and societies. According to the World Bank, resistant infections could trigger a global economic crisis. It is estimated that by 2050, AMR could push 28 million people into poverty each year and cost the global economy over $1 trillion annually.[8] Under these circumstances, it is essential to develop effective global strategies to combat AMR, raise public awareness, and promote the judicious use of antibiotics. These measures are critical for mitigating the far-reaching impacts of AMR.

In community -or hospital-acquired infections, the rapid initiation of effective antibiotic therapy targeting the causative microorganisms is critical for improving survival rates.[9-12] However, the isolation and identification of the pathogen in culture, as well as the determination of its antimicrobial susceptibility profile, typically require 24-48 hours. Therefore, particularly in severe infection cases, ensuring an appropriate and broad-spectrum empirical antimicrobial therapy is of vital importance.[13,14]

One of the most essential tools guiding clinicians in the selection of empirical therapy are cumulative antibiogram reports. These reports were standardized for the first time in 2000 with the publication of the M39 guideline by the Clinical and Laboratory Standards Institute (CLSI). CLSI defines a cumulative antibiogram as an analysis and reporting method that reflects the percentage susceptibility of the first isolates per patient to tested antimicrobial agents, collected from a specific institution over a defined time period.[15] Cumulative antibiograms provide clinicians with critical guidance for empirical therapy decisions before the antimicrobial susceptibility results of the patient's isolated pathogen are available. Furthermore, these reports can be compiled at national and international levels, enabling the detection of regional antimicrobial susceptibility patterns and the emergence of new resistance trends.

The aim of this study is to compare the cumulative antibiogram data of bacterial isolates obtained from patient samples submitted to the Medical Microbiology Laboratory at Trakya University Hospital during the periods of 2015-2016 and 2022-2023. The study seeks to evaluate changes in antimicrobial susceptibility over the years and provide guidance to clinicians in the selection of empirical therapies.

MAIN POINTS

- A notable rise in resistance rates was observed among Gram-negative bacteria, including *Klebsiella* spp., *Acinetobacter* spp., and *Pseudomonas* spp. In particular, *Klebsiella* spp. demonstrated a significant decline in carbapenem susceptibility, while *Acinetobacter* spp. exhibited the lowest overall susceptibility rates (S%).
- Recommended empirical therapies include carbapenems, amikacin, tigecycline, vancomycin, and linezolid, depending on the pathogen.
- Given the variations in antimicrobial S% over time, regularly updating and implementing empirical treatment protocols based on antibiogram data is crucial for combating resistance and improving clinical outcomes.

MATERIAL AND METHODS

Ethics Approval and Consent to Participate

The study received ethical approval from the Non-interventional Scientific Research Ethics Committee of the Faculty of Medicine of Trakya University with the protocol code 2024/207 (approval no: 09/35, date: 06.05.2024).

In this study, the *in vitro* antimicrobial susceptibility test results of bacterial strains isolated from clinical samples submitted to the Medical Microbiology Laboratory at Trakya University Hospital during the periods of 2015-2016 and 2022-2023 were evaluated.

Identification of Bacterial Species and Susceptibility Testing

Bacterial identification and antimicrobial susceptibility testing were performed using both conventional methods and the automated VITEK-2 system (bioMérieux, France). Conventional methods included the evaluation of colony morphology, Gram staining, and basic biochemical tests such as catalase, oxidase, and coagulase when appropriate. Antimicrobial susceptibility test results were interpreted according to the current annual recommendations of the European Committee on Antimicrobial Susceptibility Testing (EUCAST).[16]

Data Collection and Processing

The data used in this study were retrospectively retrieved from the laboratory information system. The collected data were organized according to the guidelines outlined in the Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data (CLSI 2014, M39-A4), based on criteria.[15]

Only verified test results from samples submitted for clinical diagnostic purposes were included in the study; samples submitted for surveillance or screening purposes were excluded.

Susceptibility rates (S%) were calculated exclusively for antimicrobial agents routinely tested in the laboratory.

When multiple isolates of the same bacterial species were identified from the same patient, only the first isolate was included in the study; subsequent isolates were excluded from the analysis.

While calculating S%, data categorized as "intermediate" (I) were included in the percentage of susceptible isolates (S%).

Antimicrobial Agents

The selection of which antimicrobial agents should be tested for each pathogen was determined based on the "Turkish Society of Microbiology Restricted Antimicrobial Notification Table".[17] This table aims to promote rational antimicrobial use and stewardship by recommending targeted antibiotic panels based on organism group, infection site, and clinical relevance. In line with these guidelines, agents were selected to include

first-line, commonly used antibiotics, as well as critical agents for multidrug-resistant pathogens. The antibiotics tested were standardized across isolates of the same species and clinical significance. The susceptibility of the isolates included in the study was evaluated for the following antimicrobial agents:

Beta-lactams: ampicillin (AM), amoxicillin/clavulanic acid (AMC), piperacillin-tazobactam (TZP), cefuroxime (CXM), ceftazidime (CAZ), ceftriaxone (CRO), cefepime (FEP), ertapenem (ETP), imipenem (IPM), meropenem (MEM).

Aminoglycosides: gentamicin (GN), amikacin (AN).

Fluoroquinolones: ciprofloxacin (CIP), levofloxacin (LVX).

Other agents: trimethoprim-sulfamethoxazole (SXT), nitrofurantoin (F), tigecycline (TGC), erythromycin (E), clindamycin (CC), vancomycin (VA), teicoplanin (TEC), linezolid (LZD), tetracycline (TE).

The selection of antimicrobials should be guided by the S% rate based on the severity of the infection. For severe infections such as meningitis or sepsis, the WHO recommends a S% (percent susceptible) rate of ≥90% for penicillin in empirical treatment.[18] In cases where the risk of mortality or severe morbidity is high, antimicrobials with a S% rate of at least 90-95% should be preferred. For milder infections, a S% rate of 80-85% may be acceptable. When no alternatives are available and the S% rate is below 80%, the agent with the highest S% rate or combination therapy should be considered. Local antimicrobial policies and guidelines must also be taken into account when making treatment decisions[19-21]. In this study, we evaluated antimicrobials with a S% rate of ≥90% as suitable options for empirical treatment.

Statistical Analysis

The data were analyzed using IBM SPSS (Statistical Package for Social Sciences) Statistics 21.0. Descriptive statistics were presented as frequencies and percentages. The analyses were performed using descriptive statistics, the chi-square test, and Fisher's Exact test. Results with *P* values < 0.05 were considered statistically significant.

RESULTS

Sample Types and Distribution of Bacteria

This study evaluated isolates from the periods of 2015-2016 and 2022-2023. A total of 7524 isolates (5009 Gram-negative, 2515 Gram-positive) were analyzed during 2015-2016, and 5880 isolates (4202 Gram-negative, 1678 Gram-positive) were analyzed during 2022-2023. In both periods, the most frequently isolated microorganisms were obtained from urine, blood, catheter, and wound, aspirate, and tissue samples. In 2015-2016, microorganisms were most commonly isolated from patients aged 18-65 years, whereas in 2022-2023, isolates were predominantly obtained from patients older than 65 years. For both time periods, the highest number of isolates came from samples submitted by the Internal Medicine department. The most frequently isolated microorganisms during 2015-2016 were *Escherichia coli (E. coli)*, coagulase-negative *Staphylococcus* (CoNS), and *Enterococcus* spp. In 2022-2023, the most common isolates were *E. coli*, *Klebsiella* spp., and *Enterococcus* spp. (Table 1). *E. coli* was the most frequently isolated microorganism from urine samples, while CoNS was predominantly isolated from blood/catheter samples (Table 2). In intensive care units (ICUs), the most frequently isolated microorganisms during 2015-2016 were CoNS, *Acinetobacter* spp., and *Klebsiella* spp. In 2022-2023, the most common ICU isolates were *Acinetobacter* spp., *Klebsiella* spp., and *Enterococcus* spp. Among ICU samples, bacteria were most frequently isolated from blood/catheter samples (48.3%), respiratory samples (tracheal aspirate, sputum, bronchoalveolar lavage) (31.5%), and urine samples (12.8%). The highest bacterial isolation rate in ICUs was observed in Surgical ICUs, with *Acinetobacter* spp. being the most frequently isolated microorganism (Table 3).

Antimicrobial Susceptibility Findings

For *E. coli* isolates, S% exceeding 90% were observed for ETP, IMP, MEM, and AN in both urine and non-urine samples, as well as across outpatient, inpatient, and ICU settings, during both the 2015-2016 and 2022-2023 periods. Additionally, susceptibility to F in urine samples was found to be above 90%.

For *Klebsiella* spp. isolates, S% exceeding 90% were observed only for AN in both study periods. In 2022-2023, susceptibility to carbapenems ranged from 55% to 62%, representing a significant decline compared to the 2015-2016 period.

For *Acinetobacter* spp. isolates, no single antimicrobial agent demonstrated a susceptibility rate exceeding 90% in either study period. Given the limited susceptibility observed across the tested agents, empirical treatment of suspected *Acinetobacter* infections may require the use of combination therapy, especially in settings with high rates of multidrug resistance. For *Pseudomonas* spp. isolates, S% above 90% were observed for FEP and AN during 2015-2016, while in 2022-2023, only AN maintained a susceptibility rate above 90%.

For *Staphylococcus aureus* isolates, S% exceeding 90% were observed for LVX, VA, TEC, LZD, TGC, SXT, and GN. In methicillin-resistant *S. aureus* (MRSA) isolates, a significant decrease in susceptibility to E and CC was detected. Additionally, susceptibility to LVX, SXT, and GN fell below 90% in MRSA isolates. For CoNS, S% above 90% were observed for VA, LZD, and TGC. Similarly, for *Enterococcus* spp., VA, TEC, LZD, and TGC demonstrated S% exceeding 90%. Cumulative antimicrobial susceptibility percentages for Gram-negative and Gram-positive bacteria are presented in Table 4 and Table 5. Notably, the MRSA rate increased from 12.9% to 24.1%, while the vancomycin-resistant *Enterococcus* (VRE) rate rose from 2.5% to 4.2% (Table 6).

DISCUSSION

Cumulative antibiogram reports, regularly and systematically updated, serve as a critical guide for clinicians in selecting empirical antibiotic therapy. Monitoring the S% of commonly used antibiotics through cumulative antibiograms is an essential component of antibiotic stewardship programs.[22,23] This approach allows for the identification of regional resistance patterns and highlights areas requiring targeted interventions.

Table 1. Characteristics of Samples Included in the Study

	2015-2016		2022-2023		Total	
	n	%	n	%	n	%
Sample Type						
Urine	2901	38.6	2110	35.9	5011	37.4
Blood/catheter	2095	27.8	1538	26.2	3633	27.1
Wound/aspirate/tissue	1363	18.1	1118	19.0	2481	18.5
Respiratory sample	937	12.5	945	16.1	1882	14.0
Sterile body fluid	228	3.0	169	2.9	397	3.0
Age						
>65	3068	40.8	3000	51.0	6068	45.3
18-65	3553	47.2	2356	40.1	5909	44.1
0-18	903	12.0	524	8.9	1427	10.6
Microorganism						
E. coli	2124	28.2	1358	23.1	3482	26.0
Klebsiella spp.	879	11.7	890	15.1	1769	13.2
Enterococcus spp.	969	12.9	748	12.7	1717	12.8
CoNS	1070	14.2	510	8.7	1580	11.8
Pseudomonas spp.	687	9.1	625	10.6	1312	9.8
Acinetobacter spp.	589	7.8	559	9.5	1148	8.6
S. aureus	476	6.3	420	7.1	896	6.7
Proteus spp.	220	2.9	268	4.6	488	3.6
Enterobacter spp.	234	3.1	215	3.7	449	3.3
S. maltophilia	98	1.3	107	1.8	205	1.5
Morganella spp.	97	1.3	83	1.4	180	1.3
Serratia spp.	81	1.1	97	1.6	178	1.3
Department						
Internal medicine	1996	26.5	1405	23.9	3401	25.4
General surgery	1112	14.8	838	14.3	1950	14.5
Emergency medicine	1069	14.2	735	12.5	1804	13.5
Pediatrics	794	10.6	479	8.1	1273	9.5
Urology	405	5.4	499	8.5	904	6.7
Pulmonology	224	3.0	514	8.7	738	5.5
Anesthesiology	296	3.9	245	4.2	541	4.0
Plastic surgery	176	2.3	258	4.4	434	3.2
Orthopedics	242	3.2	189	3.2	431	3.2
Cardiology	256	3.4	146	2.5	402	3.0
Infectious diseases	208	2.8	136	2.3	344	2.6
Neurosurgery	109	1.4	51	0.9	160	1.2
Neurology	111	1.5	46	0.8	157	1.2
Physical therapy and rehabilitation	105	1.4	51	0.9	156	1.2
Cardiovascular surgery	101	1.3	54	0.9	155	1.2
Obstetrics and gynecology	70	0.9	76	1.3	146	1.1
Dermatology	28	0.4	84	1.4	112	0.8
Radiation oncology	111	1.5	1	0.0	112	0.8
Thoracic surgery	44	0.6	26	0.4	70	0.5
Pediatric surgery	25	0.3	15	0.3	40	0.3
Ophthalmology	12	0.2	20	0.3	32	0.2
Otolaryngology	18	0.2	12	0.2	30	0.2
Psychiatry	12	0.2	0	0.0	12	0.1
Total	**7524**	**100.0**	**5880**	100.0	13404	100.0

CoNS, coagulase-negative *Staphylococcus*.

Additionally, cumulative antibiograms facilitate the analysis of resistance trends over successive years, providing valuable insights into the evolution of AMR.[24] However, caution is warranted when interpreting these reports at the patient level. Patient-specific factors play a crucial role in antibiotic selection and in determining whether an isolated microorganism is a true pathogen or a colonizer. A notable limitation of cumulative antibiogram reports in the literature is their qualitative nature, as they typically lack minimum inhibitory concentration (MIC) values, which are critical for more nuanced decision-making, as noted in study.[24] In Türkiye, comprehensive cumulative antibiogram data are scarce. For this reason, the findings of this study have been compared with surveillance data from broad-scale programs. These include the 'National Antimicrobial Resistance Surveillance System (NAMRSS)' by the Ministry of Health Turkish Public Health Institute, the 'Central Asian and European Surveillance of Antimicrobial Resistance (CEASER)', and the 'European Centre for Disease Prevention and Control's 'Antimicrobial Resistance Surveillance in Europe report (ECDC)'. These sources are considered valuable references for reflecting national and regional resistance patterns.

According to the CDC's National Healthcare Safety Network surveillance, the most frequently isolated bacteria in healthcare-associated infections during 2015-2017 were *E. coli* (17.5%), *Enterococcus* spp. (14.8%), *S. aureus* (11.8%), *Klebsiella* spp. (8.8%), and *Pseudomonas* spp. (8.0%).[25] In Türkiye, the NAMRSS surveillance system, established in 2011, included 105 centers from 59 provinces by 2016, forming a nationwide surveillance network. Although the system continues to operate, no data have been published since 2016. The NAMRSS 2016 report, which included only blood and cerebrospinal fluid samples, indicated that the most frequently

Table 2. Distribution of Microorganisms by Sample Type (n)

Sample Type	*E. coli*	*Klebsiella spp.*	*Enterococcus spp.*	CoNS	*Pseudomonas spp.*	*Acinetobacter spp.*	*S. aureus*	*Proteus spp.*	*Enterobacter spp.*	*S. maltophilia*	*Morganella spp.*	*Serratia spp.*	Total
Urine	2507	755	764	100	306	98	62	179	142	15	42	41	**5011**
Blood/Catheter	360	437	547	1165	200	320	278	93	99	64	24	46	**3633**
Wound/Aspirate/Tissue	406	214	328	209	297	164	388	176	126	29	102	42	**2481**
Respiratory Sample	137	319	21	6	475	549	140	32	67	87	6	43	**1882**
Sterile Body Fluid	72	44	57	100	34	17	28	8	15	10	6	6	**397**
Total	**3482**	**1769**	**1717**	**1580**	**1312**	**1148**	**896**	**488**	**449**	**205**	**180**	**178**	**13404**

CoNS, coagulase-negative *Staphylococcus.*

Table 3. Distribution of Microorganisms Isolated from Intensive Care Units (n)

ICU Type	*Acinetobacter spp.*	CoNS	*Klebsiella spp.*	*Enterococcus spp.*	*Pseudomonas spp.*	*E. coli*	*S. aureus*	*Proteus spp.*	*S. maltophilia*	*Enterobacter spp.*	*Serratia spp.*	*Morganella spp.*	Total
Surgical ICU	262	166	216	200	174	69	33	53	27	34	21	19	**1274**
Medical ICU	220	175	181	158	131	96	51	38	34	28	16	10	**1138**
Anesthesia ICU	85	82	86	85	70	37	22	29	19	13	10	3	**541**
Respiratory ICU	71	33	61	43	33	17	12	11	15	7	7	3	**313**
Coronary ICU	33	54	35	47	11	42	21	8	6	14	1	3	**275**
Neonatal ICU	3	104	39	18	10	13	18	0	12	15	9	0	**241**
Pediatric ICU	20	26	10	8	13	8	5	0	4	4	4	0	**102**
Cardiovascular Surgery ICU	0	0	0	1	0	0	0	0	0	0	0	1	**2**
Total	**694**	**640**	**628**	**560**	**442**	**282**	162	139	117	115	68	39	3886

ICU, intensive care unit; CoNS, coagulase-negative *Staphylococcus.*

Table 4. Comparison of Susceptibility Percentages (%S) for Gram-negative Bacteria

Bacteria	Year	Source	n	AM	AMC	TZP	CXM	CAZ	CRO	FEP	ETP	IMP	MEM	GN	AN	CIP	SXT	F
E. coli	2015-2016	Outpatient clinic	1203	39	69	91	71	83	73	84	100	100	100	83	100	74	61	96
		Ward	773	23	52	82	58	74	59	74	98	100	99	72	100	59	46	96
		ICU	148	14	40	73	53	69	55	69	94	99	98	65	99	54	46	**
		Total	2124	32	61	86	65	79	67	78	99	100	99	78	100	67	54	96
	2022-2023	Outpatient clinic	784	37	65	87	58	64	65	69	98	98	99	88	99	50	62	98
		Ward	440	27	51	78	48	52	55	58	95	99	99	84	99	40	52	100
		ICU	134	26	42	71	58	55	57	69	91	97	99	80	97	51	56	100
		Total	1358	33	58	82	55	59	61	66	96	99	99	87	99	47	58	98
		p§		0.616	0.085	**0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	0.225	**<0.001**	**<0.001**	**<0.001**	**0.015**	**<0.001**
E. coli (urine)	2015-2016	Total	1523	36	67	91	68	80	70	82	100	100	100	80	100	70	58	96
	2022-2023		984	38	68	87	60	65	64	70	98	98	99	88	99	51	62	99
		p§		0.471	0.579	**0.007**	**<0.001**	**<0.001**	**0.004**	**<0.001**	**<0.001**	**<0.001**	0.101*	**<0.001**	**0.004**	**<0.001**	**0.021**	**<0.001**
E. coli (non-urine)	2015-2016	Total	601	21	45	76	58	74	59	72	96	100	99	74	100	60	45	
	2022-2023		374	19	33	72	41	48	53	55	92	99	99	78	98	36	47	
		p§		0.580	**<0.001**	0.207	**<0.001**	**<0.001**	0.050	**<0.001**	**0.003**	0.163	0.970	0.163	**0.032***	**<0.001**	0.579	
Klebsiella spp.	2015-2016	Outpatient clinic	255	0	63	72	55	63	58	69	79	82	85	83	97	67	67	77
		Ward	360	0	48	64	54	66	60	68	76	74	82	81	98	71	71	71
		ICU	264	0	28	34	27	33	30	41	41	35	43	59	98	51	51	**
		Total	879	0	48	59	48	56	52	59	60	66	72	76	98	74	65	74
	2022-2023	Outpatient clinic	247	0	65	66	54	59	65	65	80	88	89	85	98	60	64	75
		Ward	279	0	49	51	45	46	55	49	63	69	73	77	94	52	61	77
		ICU	364	0	24	31	28	32	33	30	35	43	38	59	89	36	44	42
		Total	890	0	43	46	40	43	49	45	55	57	62	75	93	48	55	76
		p§		-	0.063	**<0.001**	**0.002**	**<0.001**	0.160	**<0.001**	**0.029**	**<0.001**	**<0.001**	0.500	**<0.001**	**<0.001**	**<0.001**	0.407

Table 4. Continued

Bacteria	Year	Source	n	AM	AMC	TZP	CXM	CAZ	CRO	FEP	ETP	IMP	MEM	GN	AN	CIP	SXT	F
Acinetobacter spp.	2015-2016	Outpatient clinic	46			17						20	27	48	59	43	43	
		Ward	225			16						17	19	47	42	37	37	
		ICU	318			2						2	2	33	42	17	17	
		Total	589			9						10	12	41	41	13	28	
	2022-2023	Outpatient clinic	32			39						43	45	60	48	52	52	
		Ward	151			13						13	17	36	25	19	28	
		ICU	376			2						3	3	30	12	4	17	
		Total	559			7						8	9	34	17	10	22	
		p§				0.106						0.104	0.112	**0.037**	**<0.001**	0.183	**0.017**	
Pseudomonas spp.	2015-2016	Outpatient clinic	141			90		90		96		86	92		92	90		
		Ward	341			80		87		94		78	85		93	89		
		ICU	205			65		80		95		54	60		89	85		
		Total	687			78		85		95		73	81		92	88		
	2022-2023	Outpatient clinic	145			83		90		89		90	89		100	87		
		Ward	243			83		87		85		85	78		97	83		
		ICU	237			68		81		83		67	67		97	83		
		Total	625			77		85		85		79	76		98	84		
		p§				0.694		0.858		**<0.001**		**0.017**	0.051		**<0.001**	**0.041**		
Enterobacter spp.	2015-2016	Outpatient clinic	65		0	77		71	69	97	97	93	97	95	100	97	94	
		Ward	119		0	76		64	59	91	94	89	96	93	99	93	93	
		ICU	50		0	78		73	66	93	95	94	98	93	100	98	89	
		Total	234		0	77		68	63	93	95	91	96	94	100	92	92	
	2022-2023	Outpatient clinic	54		4	76		79	69	80	81	91	96	95	100	89	85	
		Ward	96		1	73		73	67	77	81	90	91	95	98	92	86	
		ICU	65		0	72		70	69	82	79	91	91	93	95	94	89	
		Total	215		2	73		73	68	79	80	91	92	95	98	92	87	
		p§			0.110*	0.356		0.192	0.288	**<0.001**	**<0.001**	0.917	0.068	0.702	0.199*	0.945	**0.047**	

Table 4. Continued

Bacteria	Year	Source	n	AM	AMC	TZP	CXM	CAZ	CRO	FEP	ETP	IMP	MEM	GN	AN	CIP	SXT	F
Proteus spp.	2015-2016	Outpatient clinic	73	49	85	99	80	95	91	100	99	34	100	84	100	85	59	
		Ward	92	53	88	97	79	96	98	94	99	**	99	80	100	81	55	
		ICU	55	41	74	96	67	88	81	91	98	**	100	57	100	72	48	
		Total	220	49	84	97	77	94	91	95	99	32	100	76	100	80	55	
	2022-2023	Outpatient clinic	97	36	65	90	76	79	68	74	88	80	94	61	97	40	25	
		Ward	87	49	76	95	84	86	83	81	92	80	95	84	98	57	43	
		ICU	84	36	70	84	74	74	75	69	82	85	87	63	93	54	43	
		Total	268	40	70	89	78	79	75	75	87	81	92	68	96	50	37	
		p§		**0.047**	**<0.001**	**<0.001**	0.763	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.042**	**0.001**	**<0.001**	**<0.001**	
Morganella spp.	2015-2016		97	0	0	98		61	62	98	99		100	64	100	52	52	
	2022-2023	Total	83	2	0	95		58	87	91	98		98	84	98	63	64	
		p§		0.214*		0.418*		0.726	**<0.001**	**0.046***	1.000*		0.464*	**0.003**	0.464*	0.154	0.112	
Serratia spp.	2015-2016		81	4	5	100		88	86	95	100		100	95	100	95	95	
	2022-2023	Total	97	13	4	95		96	95	96	99		99	100	100	94	98	
		p§		**0.026**	1.000*	0.065*		**0.017**	**0.047**	1.000*	1.000*		1.000*	**0.040***		1.000*	0.412*	
S. maltophilia	2015-2016	Total	98														88	
	2022-2023		107														94	
		p§															0.093	

Fisher's Exact test
**Insufficient Data
§The 'total' groups were compared.
ICU, intensive care unit, AM, ampicillin, AMC, amoxicillin-clavulanate, TZP, piperacillin-tazobactam, CXM, cefuroxime, CAZ, ceftazidime, CRO, ceftriaxone, FEP, cefepime, ETP, ertapenem, IMP, imipenem, MEM, meropenem, GN, gentamicin, AN, amikacin, CIP, ciprofloxacin, SXT, trimethoprim-sulfamethoxazole, F, nitrofurantoin.

isolated bacteria in Türkiye were *E. coli* (23.8%), *Enterococcus* spp. (18.9%), *Klebsiella spp.* (17.6%), *S. aureus* (15.5%), and *Acinetobacter* spp. (15.1%).[26] In a study conducted in Saudi Arabia, the most frequently isolated Gram-negative bacteria were *E. coli*, *Klebsiella* spp., and *Pseudomonas* spp.[27] Similarly, a U.S.-based study focusing exclusively on Gram-negative bacteria found that *Pseudomonas aeruginosa*, *E. coli*, and *Klebsiella pneumoniae* were the three most frequently isolated microorganisms in both ICU and non-ICU settings. These three bacteria accounted for 56.7% of Gram-negative isolates in ICUs and 70% in non-ICU settings.[28] Our study also identified similar microorganisms, albeit with variations in their rankings across different periods. This underscores the critical importance of regularly and systematically monitoring surveillance data to track trends and inform infection control strategies.

A study conducted under the 'International Network for Optimal Resistance Monitoring' program involving 70 centers from the United States separately evaluated isolates from ICUs and non-ICU settings. In this study, the most frequently isolated bacterium from ICU samples was *Pseudomonas* spp., while *E. coli* was most commonly isolated from non-ICU samples. Furthermore, antimicrobial S% were found to be significantly lower in isolates from ICUs compared to those from non-ICU settings.[28] In a study conducted in Türkiye, the most frequently isolated bacteria from ICU samples were *Acinetobacter* spp. and *Klebsiella* spp.[29] Similarly, in our study, *E. coli* was the most frequently isolated microorganism from outpatient and inpatient ward samples, whereas *Acinetobacter* spp. and *Klebsiella* spp. were predominant in ICU samples. The observed differences in bacterial species between ICU and non-ICU isolates are likely due to the varying infection types common to these patient groups. In ICUs, bacterial growth was most frequently observed in blood/catheter and respiratory samples, whereas non-ICU infections were predominantly associated with urine samples.

Consistent with our findings, a large-scale study also reported that isolates from ICUs exhibited lower antimicrobial susceptibility compared to those from other units, such as outpatient clinics and inpatient wards.[28] In general, it is well-documented that isolates from ICUs tend to have lower S% than those from outpatient or inpatient ward settings. The higher rates of AMR observed in ICUs are attributed to several factors. These include the more intensive use of antimicrobial agents, prolonged hospital stays, and the increased risk of acquiring hospital-associated infections caused by resistant organisms.[23,25] This highlights the critical role of ICUs as hotspots for the development and proliferation of AMR, emphasizing the need for targeted infection control measures in these settings.

In a study conducted by Sader et al. [28] in the United States, S% for *E. coli* isolates from ICUs were reported as follows: TZP 92.1%, CAZ 81.3%, CRO 76.9%, MEM 99.8%, GN 87.6%, and AN 99.4%. For non-ICU *E. coli* isolates, S% were higher: TZP 97.4%, CAZ 90.2%, CRO 88.1%, MEM 99.8%, GN 90.2%, and AN 99.7%. According to the NAMRSS report, S% for *E. coli* in Türkiye were as follows: AM 21.5%, AMC 35.4%, TZP 72.3%, CRO 48.9%, CAZ 45.8%, GN 70.7%, AN 91.3%, CIP 45.5%, IMP/MEM 95%, and ETP 91.8%.[26] Similarly, the CEASER report for Türkiye reported the following rates: AMC 39%, TZP 78%, CAZ 53%, ETP 91%, IMP/MEM 97%, GN 74%, AN 98%, and CIP 48%.[30] The ECDC report indicated that in Türkiye, fluoroquinolone resistance in *E. coli* exceeded 25%, carbapenem resistance ranged between 1-5%, and third-generation cephalosporin resistance exceeded 50%.[31] In another study conducted in Türkiye, *E. coli* isolates from urine samples demonstrated S% exceeding 90% for ETP, MEM and F. For non-urine samples, ETP and MEM also showed S% above 90% 29. In our study, antimicrobial S% were found to be higher than NAMRSS and CEASER reports. However, the S% reported by Sader et al.,[28] even for ICU isolates -particularly for beta-lactam antibiotics- were higher than our findings. While our results were consistent with the ECDC report, third-generation cephalosporin resistance in our study was below 50%. In conclusion, ETP, MEM, IMP, and AN were identified as effective empirical treatment options for *E. coli*-related infections in our study. However, it is important to note the significant decline in S% for ETP, IMP, and AN over time.

According to a study conducted by Sader et al.[28], *Klebsiella* spp. isolates from ICUs exhibited the following S%: TZP 89.1%, CAZ 82.7%, CRO 82.2%, MEM 97.6%, GN 91.5%, and AN 99.2%. For non-ICU Klebsiella spp. isolates, S% were higher: TZP 93.6%, CAZ 88.4%, CRO 87.6%, MEM 98.3%, GN 93.2%, and AN 99.3%. The NAMRSS report indicated that Klebsiella spp. isolates showed S% of 23.2% for AMC, 33.4% for TZP, 31.5% for CRO, 24.7% for CAZ, 50.8% for GN, 70% for AN, 37.3% for CIP, 59.9% for IMP/MEM, and 51.1% for ETP.[26] Similarly, the CEASER report for Türkiye: reported S% of 25% for AMC, 40% for TZP, 30% for CAZ, 49% for ETP, 61% for IMP/MEM, 55% for GN, 73% for AN, and 35% for CIP.[30] The ECDC report highlighted that in Türkiye, third-generation cephalosporin resistance in *Klebsiella* spp. exceeded 50%, while carbapenem resistance ranged between 10-25%.[31] In our study, S% for carbapenems in *Klebsiella* spp. isolates were similar to those reported by NAMRSS and CEASER. However, higher S% were observed for other antibiotics. Sader et al.'s[28] findings demonstrated higher S% overall compared to our results. In our study, carbapenem resistance was found to be between 25% and 50%, which deviates from the range reported in the ECDC report. The high carbapenem resistance observed in *Klebsiella* spp. isolates is particularly concerning and underscores the critical need for stringent antibiotic stewardship strategies to mitigate resistance and improve treatment outcomes.

A study reported that antimicrobial S% for *Klebsiella* spp. isolates were lower than *E. coli* isolates. 27. Our findings align with these results. In our study, significant reductions in S% were observed for *Klebsiella* spp. isolates against TZP, CXM, CAZ, FEP, ETP, IMP, MEM, AN, CIP, and SXT. From an empirical therapy perspective, AN was identified as the only effective option for *Klebsiella* spp. infections. Notably, carbapenem S% were approximately 80% in outpatient settings but declined sharply to 30% in ICUs. This highlights the increasing resistance rates in ICUs and underscores the necessity of a more cautious approach when selecting empirical therapies in these settings.

In a study conducted by Sader et al.,[28] *Acinetobacter* spp. isolates from ICUs exhibited S% of 61.0% for TZP, 69.4%

Table 5. Comparison of Susceptibility Percentages (%S) for Gram-Positive Bacteria

Bacteria	Year	Source	n	AM	E	CC	LVX	VA	TEC	LZD	TGC	TE	SXT	GN
S. aureus	2015-2016	Outpatient clinic	148		91	92	96	100	100	100	100	86	99	98
		Ward	256		86	92	97	100	100	100	100	88	98	98
		ICU	72		78	86	95	98	98	100	100	80	98	92
		Total	476		87	91	96	100	100	100	100	86	99	97
	2022-2023	Outpatient clinic	134		71	83	93	100	100	98	100	85	96	100
		Ward	196		69	81	95	100	100	100	99	74	96	98
		ICU	90		82	84	93	100	97	100	100	81	98	93
		Total	420		72	82	94	100	99	99	100	79	96	98
		p§			**<0.001**	**<0.001**	0.109	1.000*	0.195*	0.106*	0.224*	**0.004**	**0.047**	0.542
MSSA	2015-2016	Outpatient clinic	126		93	93	97	100	100	100	100	90	100	99
		Ward	217		91	95	98	100	100	100	100	91	100	99
		ICU	62		83	90	100	98	98	100	100	95	98	98
		Total	405		91	94	98	100	100	100	100	91	99	99
	2022-2023	Outpatient clinic	102		76	88	95	100	100	100	100	96	98	100
		Ward	159		80	87	100	100	100	100	99	89	99	98
		ICU	76		92	94	98	100	100	100	100	93	98	100
		Total	337		81	89	98	100	100	100	100	92	99	98
		p§			**0.001**	**0.028**	0.779*	1.000*	1.000*	-	0.357*	0.705	0.354	0.705
MRSA	2015-2016	Total	71		69	73	84	100	100	100	100	56	92	85
	2022-2023		83		44	46	86	100	97	97	100	43	87	84
		p§			**0.007**	**0.002**	0.877	-	0.500*	0.500*	-	0.139	0.425	0.943
CoNS	2015-2016	Outpatient clinic	178		35	67	73	100	99	99	100	44	83	78
		Ward	482		26	61	68	100	100	99	100	35	81	70
		ICU	410		21	39	48	100	99	97	100	36	72	41
		Total	1070		22	54	62	100	99	98	100	40	77	61
	2022-2023	Outpatient clinic	92		36	74	65	98	**	98	98	51	82	75
		Ward	188		22	57	48	100	92	99	99	53	71	70
		ICU	230		11	28	21	99	68	99	100	71	65	35
		Total	510		19	46	39	99	74	99	99	61	70	53
		p§			**0.144**	**0.002**	**<0.001**	**0.026***	**<0.001**	0.683	**0.026***	**<0.001**	**0.002**	**0.001**

Table 5. Continued

Bacteria	Year	Source	n	AM	E	CC	LVX	VA	TEC	LZD	TGC	TE	SXT	GN
MSCoNS	2015-2016	Outpatient clinic	80		47	79	88	100		100	100	54	94	
		Ward	147		46	84	95	100		99	100	65	93	
		ICU	59		64	91	100	100		100	100	76	98	
		Total	286		50	84	94	100		100	100	64	94	
	2022-2023	Outpatient clinic	40		50	87	90	100		100	100	59	97	
		Ward	51		45	79	91	100		97	100	58	82	
		ICU	33		54	86	81	100		100	100	70	82	
		Total	124		49	83	88	100		99	100	62	86	
		p§			0.894	0.755	0.104	-		0.484*	-	0.675	**0.020**	
MRCoNS	2015-2016	Outpatient clinic	98		25	55	54	100	99	99	100	35	74	
		Ward	335		16	50	54	100	100	99	100	31	73	
		ICU	351		13	30	39	100	99	96	100	30	68	
		Total	784		16	43	48	100	99	98	100	31	71	
	2022-2023	Outpatient clinic	52		25	73	45	97	**	97	97	45	77	
		Ward	137		12	45	35	100	89	100	99	46	72	
		ICU	197		5	21	11	99	66	98	100	69	62	
		Total	386		10	35	23	99	70	99	99	59	67	
		p§			**0.008**	**0.020**	**<0.001**	**0.032***	**<0.001**	0.308	0.101*	**<0.001**	0.210	
Enterococcus spp.	2015-2016	Outpatient clinic	224	79				99	99	100	100			70
		Ward	488	49				97	98	99	100			71
		ICU	257	41				97	97	100	100			64
		Total	969	55				98	98	99	100			69
	2022-2023	Outpatient clinic	146	86				97	96	98	99			71
		Ward	299	56				96	96	100	97			59
		ICU	303	50				95	96	98	90			45
		Total	748	60				96	96	98	94			54
		p§		**0.038**				**0.044**	**0.007**	0.081	**<0.001**			**<0.001**
E. faecalis	2015-2016	Outpatient clinic	174	97				99	100	100	100			69
		Ward	221	100				100	100	100	100			68
		ICU	105	98				100	100	100	100			79
		Total	500	98				100	100	100	100			70
	2022-2023	Outpatient clinic	116	97				99	99	99	100			73
		Ward	163	89				98	98	99	98			78
		ICU	163	88				100	100	98	85			55
		Total	442	91				99	99	98	94			67
		p§		**<0.001**				0.201*	0.053*	**0.032***	**<0.001**			0.323

Table 5. Continued

Bacteria	Year	Source	n	AM	E	CC	LVX	VA	TEC	LZD	TGC	TE	SXT	GN
E. faecium	2015-2016	Outpatient clinic	42	7				96	96	100	100			**
		Ward	259	6				95	96	99	100			73
		ICU	144	1				95	94	100	100			56
		Total	445	4				95	95	99	100			68
	2022-2023	Outpatient clinic	21	**				**	**	**	**			**
		Ward	124	8				94	92	100	96			31
		ICU	136	2				91	90	97	94			31
		Total	281	5				92	91	98	95			31
		p§		0.650				0.120	**0.017**	0.277*	**<0.001**			**<0.001**

* Fisher's exact test
**Insufficient Data
§The "total"groups were compared.
MSSA, Methicillin-Susceptible *Staphylococcus aureus*; MRSA, Methicillin-Resistant *Staphylococcus aureus*; MSCoNS, Methicillin-Susceptible Coagulase-Negative *Staphylococcus*; MRCoNS, Methicillin-Resistant Coagulase-Negative Staphylococcus; ICU, ıntensive care unit; AM, ampicillin; E, erythromycin; CC, clindamycin; LVX, levofloxacin; VA, vancomycin; TEC, teicoplanin; LZD, linezolid; TGC, tigecycline; TE, tetracycline, SXT,trimethoprim-sulfamethoxazole; GN, gentamicin.

for CAZ, 70.1% for MEM, 70.8% for LEV, and 74.3% for GN. For non-ICU *Acinetobacter* spp. isolates, S% were slightly different: TZP 61.9%, CAZ 62.4%, MEM 72.2%, LEV 69.8%, and GN 79.4%.[28] According to the NAMRSS report, *Acinetobacter* spp. isolates showed S% of 22.7% for GN, 27.6% for AN, 8.8% for CIP, and 7.7% for IMP/MEM.[26] Similarly, the CEASER report indicated S% of 10% for IMP/MEM, 20% for GN, 30% for AN, and 9% for CIP in Türkiye.[30] The ECDC report highlighted carbapenem resistance exceeding 50% in *Acinetobacter* spp. isolates in Türkiye.[31] The findings of our study were consistent with the NAMRSS, CEASER, and ECDC reports. However, the S% reported by Sader et al.[28] were notably higher than our results. Among Gram-negative bacteria, *Acinetobacter* spp. isolates exhibited the lowest antimicrobial S%. In our study, a significant decrease in S% was observed for GN, AN, and SXT over time. Notably, no single antimicrobial agent demonstrated sufficiently high susceptibility to be recommended alone for empirical treatment of *Acinetobacter* spp. infections. Given the overall low susceptibility profile, particularly in the context of multidrug resistance, the use of combination therapy may be considered a more appropriate empirical treatment strategy until definitive culture and susceptibility results are available.

In a study by Sader et al.[28], *Pseudomonas* spp. isolates from ICUs demonstrated S% of 76.9% for TZP, 81.7% for CAZ, 76.1% for MEM, 69.5% for LEV, and 88.1% for GN. For non-ICU isolates, S% were higher: TZP 83.4%, CAZ 87%, MEM 83.7%, LEV 68.4%, and GN 87.4%. According to the NAMRSS report, *Pseudomonas* spp. isolates showed S% of 69.9% for TZP, 76.5% for CAZ, 69.5% for FEP, 73.9% for GN, 62.3% for CIP, and 53.9% for IMP/MEM. Similarly: the CEASER report indicated S% of 66% for TZP, 72% for CAZ, 69% for FEP, 62% for IMP/MEM, 79% for GN, and 65% for CIP in Türkiye 30. The ECDC report noted that carbapenem resistance in *Pseudomonas* spp. isolates in Türkiye ranged between 10-25%.[31] The findings of our study showed that S% were higher compared to the NAMRSS and CEASER reports and were consistent with the ECDC report. Among antimicrobials, AN was identified as the most effective option for empirical therapy in *Pseudomonas* spp. infections. While S% for other antimicrobials were below 90%, rates for CAZ, FEP, and CIP were above 80%. A significant decrease in susceptibility to FEP was observed, alongside a notable increase in susceptibility to IMP. However, it is crucial to consider that S% are even lower in ICU settings, which should be carefully accounted for when planning empirical therapy for critically ill patients.

According to the NAMRSS report, *S. aureus* isolates exhibited S% of 85.5% to CIP and 94% to LZD, with no resistance detected to VA or an unspecified agent, TEC.[26] Similarly, the CEASER report from Türkiye also reported no resistance to VA and LZD in *S. aureus* isolates.[30] Our study findings are consistent with these reports, indicating high S% for most antimicrobials in *S. aureus* isolates. However, a significant reduction in susceptibility was observed for E, CC, and TE. From an empirical therapy perspective, LVX, VA, TEC, LZD, TGC, SXT, and GN are viable options. Notably, susceptibility differences between methicillin-susceptible *S. aureus* (MSSA) and MRSA isolates are significant. For MSSA isolates, all antimicrobials except E and CC are appropriate for empirical therapy. In contrast, for MRSA isolates, empirical therapy should be limited to VA, TEC, LZD, and TGC. These findings underscore the importance of carefully tailored treatment strategies to ensure the effective management of *S. aureus* infections.

CoNS isolates were found to have lower S% than *S. aureus*. Significant reductions in susceptibility were observed for all antimicrobials except LZD and TE. From an empirical therapy perspective, only VA, LZD, and TGC were identified as effective treatment options. Methicillin-susceptible CoNS (isolates demonstrated higher S% than methicillin-resistant CoNS (MRCoNS) isolates. However, SXT, which was a viable empirical therapy option in 2015-2016, showed a significant decline in S% by 2022-2023, rendering it unsuitable for empirical use. In MRCoNS isolates, notable reductions in susceptibility were

Table 6. Distribution of MRSA and VRE Rates Across Outpatient clinic, Ward, and ICU (%)

MRSA	**2015-2016**	Outpatient clinic	14.2
		Ward	9.6
		ICU	20.6
		Total	12.9
	2022-2023	Outpatient clinic	19.2
		Ward	25.7
		ICU	26.1
		Total	24.1
VRE	**2015-2016**	Outpatient clinic	1.4
		Ward	2.8
		ICU	2.9
		Total	2.5
	2022-2023	Outpatient clinic	2.9
		Ward	4.3
		ICU	4.6
		Total	4.2

MRSA, methicillin-resistant *Staphylococcus aureus;* VRE, vancomycin-resistant *Enterococcus* rate; ICU, intensive care unit.

observed for E, CC, LVX, and TEC. Conversely, a significant increase in susceptibility to TE was recorded. Despite this, only VA, LZD, and TGC were deemed suitable for empirical therapy in MRCoNS infections. These findings highlight the importance of carefully assessing resistance patterns when planning treatment strategies for CoNS infections, ensuring that therapeutic choices are guided by the most current susceptibility data.

According to the NAMRSS report, *Enterococcus faecalis* isolates demonstrated S% of 94% for AM, 42.8% for GN, and 98.7% for VA. For *Enterococcus faecium*, S% were 8.4% for AM, 38.3% for GN, 84% for VA, and 99% for LZD 26. Similarly, the CEASER report indicated S% of 95% for AM, 66% for GN, 100% for VA, and 100% for LZD in *E. faecalis* isolates in Türkiye. For *E. faecium* isolates, S% were 11% for AM, 45% for GN, 87% for VA, and 100% for LZD. In our study, the findings were consistent with the NAMRSS and CEASER reports, except for VA susceptibility, which was slightly lower. In addition to VA, TEC, LZD, and TGC were identified as effective empirical therapy options. A significant decrease in susceptibility was observed for AM, LZD, and TGC in *E. faecalis* isolates. Despite this decline, AM, in addition to VA, TEC, LZD, and TGC, remains a viable option for empirical treatment of *E. faecalis* infections. However, AM susceptibility in *E. faecium* isolates is substantially lower than in E. faecalis. Furthermore, significant reductions in susceptibility to TEC, TGC, and GN were noted for *E. faecium* isolates. For *E. faecium* infections, only VA, TEC, LZD, and TGC were deemed suitable for empirical therapy. These findings underscore the critical importance of carefully evaluating resistance patterns in the management of *Enterococcus* infections to optimize therapeutic outcomes.

According to the NAMRSS report, the MRSA rate was reported as 23.6%. The CEASER report for Türkiye indicated a slightly higher rate of 31%,[30] while the ECDC report stated that MRSA rates in Türkiye range between 25 and 50%.[31] In our study, MRSA rates were found to be consistent with the NAMRSS report but lower than the rates reported in the CEASER and ECDC reports. The observed increase in MRSA rates was primarily attributed to samples originating from inpatient wards. This highlights the need for enhanced infection control measures specifically targeting ward-based infections to mitigate the spread of MRSA.

According to the CEASER report, the VRE rate in Türkiye was reported as 1%. In contrast, the ECDC report indicated a higher VRE rate, ranging between 10-25%.[31] In our study, the observed VRE rate was higher than the CEASER report, but lower than the range reported in the ECDC data. This increase in VRE rates was largely attributed to samples collected from outpatient clinics and ICU patients. These findings emphasize the critical importance of strengthening infection control measures, particularly in these settings, to effectively manage and reduce the spread of VRE.

According to ECDC reports, AMR rates are lower in Northern and Western Europe, while significantly higher rates are observed in Eastern and Southern Europe, as well as in Türkiye.[31] In our study, the resistance rates at our hospital were found to be lower compared to the NAMRSS and CEASER reports, indicating the implementation of an effective antimicrobial stewardship program within our institution. However, the persistence of high resistance rates underscores that AMR cannot be fully mitigated through measures at the level of a single hospital or region alone. Addressing this global challenge requires comprehensive nationwide strategies and enhanced international collaboration and coordination to effectively combat AMR on a broader scale.

When comparing our findings with national and international surveillance data, we observed some differences in S%. These variations may be attributed to several factors, including differences in patient populations, hospital-specific antimicrobial stewardship strategies, local infection control practices, diagnostic methodologies, and sample selection criteria. As this study was conducted in a single tertiary care center, the observed resistance patterns may reflect the unique characteristics of the institution. These findings underscore the importance of cumulative antibiogram data tailored to specific regions or healthcare settings, because they provide more clinically relevant guidance for empirical therapy decisions than generalized national estimates.

In accordance with current WHO recommendations, antimicrobials with a susceptibility rate of ≥90% are considered appropriate for empirical treatment in severe infections.[18] In this study, some antimicrobial agents demonstrated S% below this threshold. These findings suggest that such agents may be less reliable for empirical use in serious infections, such as bloodstream infections or meningitis, and should be used with caution. However, in cases of mild or moderate infections-especially when supported by local antibiogram data or when alternative agents are limited-agents with S% between 80-90% may still be considered, provided that close clinical monitoring and follow-up microbiological testing are ensured. In instances where no suitable alternatives are available,

combination therapy or the agent with the highest S% rate may be considered, as reflected in local antimicrobial stewardship strategies. This underscores the importance of continually updating cumulative antibiograms and integrating them into institutional treatment guidelines.

Although empirical therapy suggestions in this study were based on antimicrobial agents with ≥90% S%, it is important to emphasize that such recommendations should not be generalized across all clinical contexts. The choice of empirical treatment must be guided not only by local susceptibility trends, but also by the specific clinical setting, infection site, severity of illness, and patient-related factors such as renal function, immune status, and comorbidities. Moreover, the pharmacokinetic and pharmacodynamic properties and toxicity profiles of antimicrobial agents should be carefully considered before empirical use. Therefore, the findings of this study should be viewed as a microbiological foundation to support, but not replace, individualized clinical decision-making and alignment with institutional treatment protocols.[18,32,33]

One of the limitations of this study is the absence of MIC distribution data. Only categorical susceptibility data (i.e., susceptible or resistant) were presented. In addition, molecular characterization of resistance mechanisms - such as the detection of extended-spectrum β-lactamase, *Klebsiella pneumoniae* carbapenemase, or oxacillinase-48 type carbapenemase genes- was not routinely performed in our laboratory and was, therefore, not available for analysis in this study. Furthermore, interpretive breakpoints defined by EUCAST were not uniform across the two study periods. Specifically, isolates from 2015-2016 were interpreted using EUCAST versions 5.0 to 6.0, while data from 2022-2023 were evaluated based on versions 12.0 to 13.0. Updates in clinical breakpoints for certain antimicrobial agents -particularly aminoglycosides and fluoroquinolones- may have led to reclassification of isolates with MIC values near the susceptibility thresholds. Although overall trends remained consistent, this methodological variation should be taken into account when comparing the two time periods.

In conclusion, the cumulative antibiogram data from our region demonstrate higher S% compared to those of the national average, in Türkiye. However, the growing resistance problem, particularly among Gram-negative bacteria, is a significant concern. This emphasizes the critical importance of accurately selecting empirical treatment options to effectively manage infections.

The recommended antimicrobials for empirical therapy are as follows:

For *E. coli* infections: carbapenems, and AN.

For *Klebsiella* spp. and *Pseudomonas* spp. infections: AN.

For *Acinetobacter* spp. infections: combination therapy.

For *S. aureus* infections: LVX, VA, TEC, LZD, TGC, SXT, and GN.

For CoNS infections: VA, LZD, and TGC.

For *Enterococcus* spp. infections: VA, TEC, LZD, and TGC.

These findings highlight the necessity of regularly assessing regional antibiogram data and updating empirical therapy protocols based on these data. Such an approach is essential for improving the effectiveness of infection management and combating AMR.

Ethics

Ethics Committee Approval: The study received ethical approval from the Non-interventional Scientific Research Ethics Committee of the Faculty of Medicine of Trakya University with the protocol code TÜTF-GOBAEK-2024/207(approval no: 09/35, date: 06.05.2024).

Informed Consent: Retrospective study, and permission was obtained from the hospital administration to collect the data used in the study.

Footnotes

Author Contributions

Concept - İ.D.; Design - İ.D., H.G.; Supervision - İ.D., H.G.; Materials - İ.D., H.G., E.Ç.; Data Collection and/or Processing - İ.D., H.G., E.Ç.; Analysis and/or Interpretation - İ.D., E.Ç.; Literature Search - İ.D., H.G., E.Ç.; Writing - İ.D., H.G., E.Ç.; Critical Review - İ.D., H.G.

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REFERENCES

1. Holmes AH, Moore LS, Sundsfjord A, et al. Understanding the mechanisms and drivers of antimicrobial resistance. *Lancet*. 2016;387(10014):176-187. [CrossRef]
2. WHO. Antibiotic Resistance. Accessed 15.09.2024. [CrossRef]
3. Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet*. 2022;399(10325):629-655. [CrossRef]
4. WHO. New report calls for urgent action to avert antimicrobial resistance crisis. Accessed 15.09.2024. [CrossRef]
5. Mirzaei R, Goodarzi P, Asadi M, et al. Bacterial co-infections with SARS-CoV-2. *IUBMB Life*. 2020;72(10):2097-2111. [CrossRef]
6. Tomczyk S, Taylor A, Brown A, et al. Impact of the COVID-19 pandemic on the surveillance, prevention and control of antimicrobial resistance: a global survey. *J Antimicrob Chemother*. 2021;76(11):3045-3058. [CrossRef]
7. Bengoechea JA, Bamford CG. SARS-CoV-2, bacterial co-infections, and AMR: the deadly trio in COVID-19? *EMBO Mol Med*. 2020;12(7):e12560. [CrossRef]
8. Group WB. By 2050, Drug-resistant infections could cause global economic damage on par with 2008 financial crisis. Accessed 15.09.2024. [CrossRef]
9. Harbarth S, Garbino J, Pugin J, Romand JA, Lew D, Pittet D. Inappropriate initial antimicrobial therapy and its effect on survival in a clinical trial of immunomodulating therapy for severe sepsis. *Am J Med*. 2003;115(7):529-535. [CrossRef]
10. Riccobene T, Ye G, Lock J, et al. Outcomes of inadequate empiric therapy and timing of newer antibacterial therapy in hospitalized adults with culture-positive Enterobacterales and Pseudomonas aeruginosa: a multicenter analysis. *BMC Infect Dis*. 2024;24(1):810. [CrossRef]

11. Puzniak L, Bauer KA, Yu KC, et al. Effect of Inadequate Empiric Antibacterial Therapy on Hospital Outcomes in SARS-CoV-2-Positive and -Negative US Patients With a Positive Bacterial Culture: A Multicenter Evaluation From March to November 2020. *Open Forum Infect Dis*. 2021;8(6):ofab232. [CrossRef]
12. Kollef MH, Ward S, Sherman G, et al. Inadequate treatment of nosocomial infections is associated with certain empiric antibiotic choices. *Crit Care Med*. 2000;28(10):3456-3464. [CrossRef]
13. Fridkin SK, Steward CD, Edwards JR, et al. Surveillance of antimicrobial use and antimicrobial resistance in United States hospitals: project ICARE phase 2. Project Intensive Care Antimicrobial Resistance Epidemiology (ICARE) hospitals. *Clin Infect Dis*. 1999;29(2):245-252. [CrossRef]
14. Goldmann DA, Weinstein RA, Wenzel RP, et al. Strategies to prevent and control the emergence and spread of antimicrobial-resistant microorganisms in hospitals. A challenge to hospital leadership. *JAMA*. 1996;275(3):234-240. [CrossRef]
15. PA W. Clinical and Laboratory Standards Institute, Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data. 4th Edition. Document M39-A4. ABD. [CrossRef]
16. Testing TECoAS. Breakpoint tables for interpretation of MICs and zone diameters. [CrossRef]
17. Cemiyeti TM. Kısıtlı Bildirim. [CrossRef]
18. Organization WH. Model prescribing information. Drugs used in bacterial infections. [CrossRef]
19. Simner PJ, Hindler JA, Bhowmick T, et al. What's new in antibiograms? Updating CLSI M39 guidance with current trends. *J Clin Microbiol*. 2022;60(10):e0221021. [CrossRef]
20. Gupta K, Hooton TM, Naber KG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for microbiology and infectious diseases. *Clin Infect Dis*. 2011;52(5):e103-120. [CrossRef]
21. Kalil AC, Metersky ML, Klompas M, et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis*. 2016;63(5):e61-e111. [CrossRef]
22. Kohlmann R, Gatermann SG. Analysis and presentation of cumulative antimicrobial susceptibility test data--the influence of different parameters in a routine clinical microbiology laboratory. *PLoS One*. 2016;11(1):e0147965. [CrossRef]
23. MacVane SH. Antimicrobial Resistance in the Intensive Care Unit: A Focus on Gram-Negative Bacterial Infections. *J Intensive Care Med*. 2017;32(1):25-37. [CrossRef]
24. Pakyz AL. The utility of hospital antibiograms as tools for guiding empiric therapy and tracking resistance. Insights from the Society of Infectious Diseases Pharmacists. *Pharmacotherapy*. 2007;27(9):1306-1312. [CrossRef]
25. Weiner-Lastinger LM, Abner S, et al. Antimicrobial-resistant pathogens associated with adult healthcare-associated infections: Summary of data reported to the National Healthcare Safety Network, 2015-2017. *Infect Control Hosp Epidemiol*. 2020;41(1):1-18. [CrossRef]
26. T.C. Sağlık Bakanlığı THSK. Ulusal antimikrobiyal direnç sürveyans sistemi 2016 yıllık raporu. [CrossRef]
27. Al-Tawfiq JA, Rabaan AA, Saunar JV, Bazzi AM. Antimicrobial resistance of gram-negative bacteria: A six-year longitudinal study in a hospital in Saudi Arabia. *J Infect Public Health*. 2020;13(5):737-745. [CrossRef]
28. Sader HS, Mendes RE, Streit JM, Carvalhaes CG, Castanheira M. Antimicrobial susceptibility of Gram-negative bacteria from intensive care unit and non-intensive care unit patients from United States hospitals (2018-2020). *Diagn Microbiol Infect Dis*. 2022;102(1):115557. [CrossRef]
29. Yürüyen C, Daldaban Dinçer Ş, Yanılmaz Ö, Boz ES, Aksaray S. Yoğun bakım ünitelerinde kümülatif antibiyogram ile antibiyotik direncinin izlenmesi [Surveillance of resistance in the intensive care units using a cumulative antibiogram]. *Mikrobiyol Bul*. 2018;52(4):329-339. [CrossRef]
30. Europe. WHOROf. Central Asian and European surveillance of antimicrobial resistance: annual report 2020. [CrossRef]
31. Organisation WH. Antimicrobial resistance surveillance in Europe 2023-2021 data. [CrossRef]
32. Tamma PD, Cosgrove SE, Maragakis LL. Combination therapy for treatment of infections with gram-negative bacteria. *Clin Microbiol Rev*. 2012;25(3):450-470. [CrossRef]
33. Roberts JA, Paul SK, Akova M, et al. DALI: defining antibiotic levels in intensive care unit patients: are current β-lactam antibiotic doses sufficient for critically ill patients? *Clin Infect Dis*. 2014;58(8):1072-1083. [CrossRef]

ABCResearch

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Research Article

Effect of Whitening Mouthrinses on Color Change of Stained Teeth: *In Vitro* Study

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ABSTRACT

Objective: This *in vitro* study aimed to evaluate the effectiveness of three different whitening mouthrinses on the color change and whiteness of stained teeth at different immersion times.

Methods: Thirty-two human incisors teeth were stained in black tea solution for seven days and randomly divided into four groups, which were control (artifical saliva) and three whitening mouthrinses (containing tetrapotassium pyrophosphate, hydrogen peroxide, charcoal powder) (n=8). Spectrophotometric measurements were performed at baseline, after staining, after 12 hours, and 120 hours after keeping in whitening mouthrinses. The color changes and whiteness indexes occurring at different immersion times and after teeth staining were calculated.

Results: The whitening mouthrinses tested showed similar changes in color change while exhibiting color change above the clinically acceptable threshold. Regarding whiteness index values, the highest value was obtained in the mouthrinse containing hydrogen peroxide with an immersion time of 120 hours ($P < 0.05$). While there was no significant difference in color change values at different immersion times, it was observed that the whiteness index values increased with increasing immersion time.

Conclusion: Whitening mouthrinses can provide a clinically noticeable color change in discolored teeth. It can be said that using mouthrinses containing peroxide can provide more effective whitening on stained teeth.

Keywords: Activated charcoal, hydrogen peroxide, tooth bleaching, whiteness index, whitening mouthrinse

INTRODUCTION

Today, as aesthetic appearance becomes increasingly essential, applications for restoring teeth color have developed, and tooth whitening treatments have become a popular treatment that supports improving aesthetic appearance. Teeth whitening treatments encompass a variety of methods, including different types of whitening agents, concentration levels and application protocols. Today, the over-the-counter (OTC) products are one of the most preferred whitening treatments applied to vital teeth.[1] OTC products are freely sold to consumers in many places such as in supermarkets, on the internet. Unlike professional teeth whitening methods, OTC products are not under the supervision of a physician and can be used at home without needing a prescription or guidance.[2,3] Products such as whitening toothpaste and mouthrinses, whitening strips, dental floss, and chewing gum marketed with various ingredients fall into this category.[4] One of the OTC products, whitening mouthrinse, has recently been introduced to prevent discoloration, combat plaque buildup, and provide a rapid whitening effect. The easy use and low cost of whitening mouthrinses have enabled to become widespread rapidly, resulting in the production of different

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products in terms of concentration, quantity, and content. The most commonly utilized bleaching agent in whitening mouthrinses is hydrogen peroxide. The whitening properties of agent occurs when the oxygen molecules released by its breakdown break down the pigmented structures in the tooth into smaller structures.[5] In the literature is examined, many studies may be found that have been conducted on products containing hydrogen peroxide (cHP), and the ability of hydrogen peroxide to cause color change in teeth has been demonstrated in previous studies.[6,7] There are also whitening mouthrinses with alternative ingredients such as sodium citrate, sodium hexametaphosphate, and tetrasodium pyrophosphate. These agents can chemically remove external colorations and prevent new chromogen adsorption by disrupting the pellicle structure.[8,9] One of the whitening agent ingredients recently introduced to the market is activated charcoal. Manufacturers state that because activated charcoal has a large surface area (>1000 m^2/g) besides porous structure, it can absorb chromogenic structures that cause tooth discoloration.[10] Although the use of activated charcoal is recommended with the claim that it can whiten teeth effectively, there is insufficient scientific data on its use as a whitening agent. Considering the results that may arise from patient-controlled use of whitening mouthrinses, there is a need to assess the efficacy of different ingredient-containing whitening mouthrinses on the teeth during different periods of use. Based on this, this research aims to evaluate the effects of three whitening mouthrinses on the color change and whiteness of stained teeth at different immersion times. The first null hypothesis tested was that there would be no difference between whitening mouthrinses in their effect on discoloration and whiteness on stained teeth. The second null hypothesis was that immersion time would not affect the color change and whiteness index of whitening mouthrinses.

MATERIAL AND METHODS

The study was approved by the Erzincan Binali Yıldırım University Non-invasive Clinic Ethics Committee (approval no.: 2023-23/12, date: 28.12.2023) and conducted in accordance with the Helsinki Declaration. Written informed consent was obtained from the patients who owned the extracted teeth used in this study.

Sample Size Calculation

The power of the sample size was calculated by G*Power software (G*Power Ver. 3.1.9.4, Heinrich-Heine Dusseldorf University, Dusseldorf, Germany) with a 95% confidence interval, an 95% power, and 0.50 effect size values for 32 samples according to one-way analysis of variance (ANOVA)-type power analysis. Eight samples per group were calculated as minimum sample size.

Preparation of Dental Specimens

In this study, a total of 32 permanent extracted human incisor teeth without cavities or enamel defects for orthodontic or periodontal reasons in last 6 months. Tissue residues remaining on the tooth surface were removed with the help of periodontal curettes and the surfaces were polished using a polishing rubber. Then, the teeth were divided into two parts, crown and root, from the enamel-cement junction with a low-speed diamond disk saw (Isomet, Buehler Ltd., Lake Bluff IL, USA) under water coolant. The crowns of the teeth were embedded in teflon molds (3 cm in diameter) with the help of self-hardening cold acrylic, leaving the root parts outside. The samples were kept in distilled water at room temperature for one day before starting the staining process.

Measuring Color Change Values (ΔE_{00})

The samples removed from distilled water were dried using an air-water spray. The first color measurements (T0) were made using a digital spectrophotometer (VITA Easyshade V; Vita Zahnfabrik, Bad Sackingen, Germany). The device was calibrated before measurements. In order to standardize the measurements, measurements were made in D65 standards on a white background. Each sample was measured three times, and the mean L*, a*, and b* values were recorded for each measurement. A single operator made all color measurements.

After the first color measurements, the samples were kept in a solution prepared by adding two bags (2 x 2g) of black tea (Yellow Label Tea, Lipton, London and Türkiye) into 300 mL of boiled water in closed containers for seven days in order to color them. The black tea solution was refreshed daily. At the end of the coloring procedure, color measurement (T1) was made for the second time after all samples were washed under running water and dried.

Experimental Groups

The samples were randomly divided into four groups based on their whitening mouthrinses composition (n=8):

Mouthrinse containing tetrapotassium pyrophosphate (cTP),

Mouthrinse cHP,

Mouthrinse containing charcoal powder (cCP),

Artifical saliva [control group (CG)].

The composition of each mouthrinse and artificial saliva were presented in Table 1. A previous study reported that keeping dental materials in continuous mouthrinse for 12 hours had the same clinical effect as using mouthrinse for one year (twice a day, one minute)[11]; in this study, samples were subjected to a 12-hour and 120-hour mouthrinse immersion procedure. In this way, it was aimed to simulate the effect of whitening mouthrinse for one and 10 years. Solutions were refreshed

MAIN POINTS

- The most important finding of the study is that discolored teeth can be affected by whitening mouthrinses.
- Whitening mouthrinses can be recommended to patients as a product that supports whitening treatments, which are in increasing demand today.
- The use of a whitening mouthrinse containing hydrogen peroxide will help achieve better results in terms of patient satisfaction.

every 24 hours. Samples removed from the solutions after 12 and 120 hours were washed in distilled water for five min and dried on blotting paper. The third (T2, following the 12 hours) and fourth (T3, following the 120 hours) color measurements were performed, respectively.

The color changes were assessed using the formula of CIEDE2000 (ΔE_{00}), which represents the distance of two colors to the three-dimensional space. While the color change that occurs after initial and staining is considered ΔE_{001} (T0-T1), between staining and 12-hour immersion is ΔE_{002} (T1-T2), and between staining and 120-hour immersion is ΔE_{003} (T1-T3). The following formulation was used to calculate ΔE_{00}:

$$\Delta E_{00}=\sqrt{\left(\frac{\Delta L}{K_L S_L}\right)^2+\left(\frac{\Delta C}{K_C S_C}\right)^2+\left(\frac{\Delta H}{K_H S_H}\right)^2+R_T\left(\frac{\Delta C}{K_C S_C}\right)\left(\frac{\Delta H}{K_H S_H}\right)}$$

The variations in hue, chroma, and lightness between the two measurements are expressed in the formulas ΔL, ΔC, and ΔH. The letter "S" represents the hue and chroma weight functions. KL, KC, and KH were designated as "1" in this investigation.[6]

Analysis of Whitening Efficacy

The whitening effectiveness of whitening mouthrinses was evaluated using the Whitening Index for Dentistry (WI_D) and was calculated as follows:

$WI_D = 0.511L^* - 2.324a^* - 1.100b^*$

The whiteness difference (ΔWI_D) between the two measurements was calculated with the following formula:[12]

$\Delta WI_D = WI_{D2} - WI_{D1}$

Whiteness differences were calculated to be the same as the time intervals indicated in the color change.

Statistical Analysis

Data were analyzed with IBM SPSS V23 and the JAMOVI program. Compliance with normal distribution was examined using the Shapiro-Wilk Test. Robust Two-Way ANOVA was used in the JAMOVI program to compare ΔE_{00} values. The generalized linear model method was used to compare WI_D values, and multiple comparisons were examined with the Tukey honestly significant difference test. The significance level was taken as $P < 0.05$.

RESULTS

ΔE_{00} values of whitening mouthrinses examined at different time intervals are presented in Table 2. In this study, the clinically acceptable limit for color change exceeded ΔE_{00}=2.25, as stated by Ghinea et al.[13] Accordingly, a clinically noticeable color change was seen in all whitening mouthrinse groups at all time intervals. The results showed that the whitening mouthrinse used and the immersion time did not have a statistically significant effect on the ΔE_{00} values representing the color change, and the interaction between the mouthrinse and the immersion time was not statistically significant. ($P > 0.05$) In contrast, the whitening mouthrinses tested appeared to increase color change compared to the CG ($P > 0.05$). Regardless of the time, the cTP group showed the most effect among whitening mouthrinses. The highest ΔE_{00} value was again seen in the cTP mouthrinse group in the T1-T2 time interval ($P > 0.05$). The lowest ΔE_{00} value was calculated in the T1-T3 time interval in the CG. The T1-T2 time interval was observed to have a higher ΔE_{00} value than the T1-T3 time interval in the

Table 1. The Compositions of Whitening Mouthrinses and Artificial Saliva

Whitening mouthrinse	Composition	Company
cTP	Aqua, alcohol, sorbitol, tetrapotassium pyrophosphate, pentasodium triphosphate, citric acid, Poloxamer 407, sodium benzoate, eucalyptol, thymol, menthol, sodium saccharin, sodium fluoride, tetrasodium pyrophosphate, propylene glycol, sucralose, aroma, disodium phosphate	Johnson& Johnson, Pomezia, Italy
cHP	Aqua, glycerin, propylene glycol, xylitol, Laminaria saccharina extract, PEG-40 Hydrogenated Castor Oil, PVP, aroma, sodium benzoate, benzoic acid, calcium glycerophosphate, sodium saccharine, magnesium chloride, hydrogen peroxide, limonede.	Eurocosmed-Stupino Ltd, 142800, Moscow, Russia
cCP	Aqua, glycerin, propylene glycol, sorbitol, tetrapotassium pyrophosphate, polysorbate 20, tetrasodium pyrophosphate, zinc citrate, PVM/MA Copolymer, aroma, benzyl alcohol, sodium fluoride, sodium saccharin, Bambusa vulgaris shoot extract, charcoal powder	Colgate-Palmolive, Guildford, GU2 8JZ
CG	Sodium chloride (0.4 g/L), potassium chloride (0.4 g/L), calcium chloride-H2O (0.795 g/L), sodium dihydrogen phosphate-H2O (0.69 g/L), sodium sulfur-9H2O (0.005 g/L), and 1000 mL distilled water	-

cTP, mouthrinse containing tetrapotassium pyrophosphate; cHP, mouthrinse containing hydrogen peroxide; cCP, mouthrinse containing charcoal powder; CG, control group (artificial saliva); PEG-40 Hydrogenated Castor Oil, polyethylene glycol-40 hydrogenated castor oil; PVM/MA Copolymer, polyvinyl methyl ether/maleic anhydride copolymer.

mouthrinse groups, except for the cHP group ($P > 0.05$). In the cHP group, the color change value in the T1-T3 time interval was seen to be higher than the color change value in the T1-T2 interval ($P > 0.05$).

The time-dependent average WI_D values of whitening mouthrinses are presented in Table 3. The analysis showed that the whitening mouthrinse and immersion time had a statistically significant effect on the WI_D values representing the whiteness index ($P = 0.046$). The highest WI_D value among whitening mouthrinses was seen in the T1-T3 time interval in the cHP group, and this value was statistically significant compared to all other groups ($P < 0.05$). The lowest WI_D value was obtained in the T1-T2 time interval in the same group, and there was no statistically significant difference between this value and the CG ($P > 0.05$). In all groups except the cCP group, it was observed that the WI_D values obtained in the T1-T3 time interval were statistically significantly higher than the WI_D values obtained in the T1-T2 time interval. ($P < 0.05$) There was no statistically significant difference between the WI_D values in the T1-T2 and T1-T3 time intervals in the cCP group ($P > 0.05$).

DISCUSSION

In vitro research conducted recently has concentrated on the impacts of bleaching agents other than hydrogen peroxide on restorations, enamel, and dentin. In this his study, the effectiveness of three whitening mouthrinses at different immersion times in improving tooth color on black tea-stained teeth was evaluated. According to the study results, while there was no significant interaction between the whitening mouthrinses in terms of their effects on the color change of the teeth at different immersion times, significant differences were found in their impact on the whiteness indexes of the teeth. Therefore, both null hypotheses were partially accepted. The human incisor tooth surfaces used in this study were carefully cleaned to mimic the natural structure, but no smoothing process was applied. The smoothing process causes the enamel thickness to decrease with the removal of the aprismatic layer, therefore the whitening agent penetrates more into the tooth structure.[14] Also, this process makes it more susceptible to pigment absorption.[15] As a result, problems might occur in terms of accurate measurement of color. Many studies have shown that black tea is used to create pigments that cause discoloration in teeth.[12,16,17] In this study, dental samples were stored in black tea for seven days. When the literature was examined, it was found that the formula of CIELAB was often used to evaluate the change in color. However, studies have proven that the CIEDE2000 formula is a better fit for the evaluation of color changes compared to the CIELAB formula.[2,18,19] In parallel with the literature, in this study, a digital spectrophotometer was used for color measurements and the CIEDE2000 formula for determining color changes. According to study results, $\Delta E_{001} > 2.25$ was shown in all tested groups after being stored in black tea. This result is consistent with other studies indicating that black tea causes significant discoloration of teeth.[16,20] When whitening mouthrinses's effect on color change were evaluated over time, the whitening mouthrinse groups, excluding the CG, exhibited a clinically noticeable color change effect on the teeth in two different immersion periods (ΔE_{002}, $\Delta E_{003} > 2.25$). Based on this, it should be noted that all of the whitening mouthrinses used in the study reduced tooth stains. However, no significant difference was observed between the groups. Many studies support this outcome.[21,22] In this study, the highest and clinically detectable

Table 2. Median, Minimum and Maximum Color Change (ΔE_{00}) Values by Mouthrinse and Time

Whitening mouthrinse	Duration time of use		
	ΔE_{001} Median (min.-max.)	ΔE_{002} Median (min.-max.)	ΔE_{003} Median (min.-max.)
cTP	4.7 (2.1-11.4)	4.4 (2.6-5.7)	4.2 (2.9-5.9)
cHP	3.1 (2.2-4.7)	3.6 (1.2-5.6)	4.3 (3.1-8.2)
cCP	4.4 (1.4-5.9)	3.9 (1.4-7.5)	3.8 (2.0-5.3)
CG	2.7 (0.7-10.3)	1.7 (1.4-6.8)	1.4 (1.1-5.7)

cTP, mouthrinse containing tetrapotassium pyrophosphate; cHP, mouthrinse containing hydrogen peroxide; cCP, mouthrinse containing charcoal powder; CG, control group (artificial saliva).

Table 3. Descriptive Statistics of Whiteness Index (ΔW_{ID}) Values by Mouthrinse and Time

Whitening mouthrinse	Duration time of use		
	ΔWI_{D1}	ΔWI_{D2}	ΔWI_{D3}
cTP	-6.4 (4.2)^{D}	6.7 (2.9)^{ABC}	11 (3.7)^{AB}
cHP	-8.5 (1.7)^{D}	5.8 (5.0)^{BC}	13.2 (3.5)^{A}
cCP	-9.4 (2.9)^{D}	7.5 (3.5)^{ABC}	10.2 (5)^{ABC}
CG	-8.5 (6.2)^{D}	3.9 (3.4)^{C}	4.3 (3.6)^{BC}

F=2,260. $P = 0.046$ ($P < 0.05$).
^{A,B,C,D}There is no difference between time and mouthrinse interactions with the same letter.
cTP, mouthrinse containing tetrapotassium pyrophosphate; cHP, mouthrinse containing hydrogen peroxide; cCP, mouthrinse containing charcoal powder; CG, control group (artificial saliva).

color change was seen in the cTP group at 12 hours immersion time. In comparison, the cHP group showed the highest color change at 120 hours of immersion time. Whitening mouthrinses usually contain low concentrations of whitening substances including pyrophosphates, peroxides, sodium citrate, sodium hexametaphosphate, and activated charcoal. These agents function by either whitening or removing the stain.[6] With repeating pyrophosphate subunits, sodium hexametaphosphate is a longer-chain pyrophosphate derivative with reduce adsorption of stain-chromogen and whitening potential.[23] cTP is available on the market as a type of mouthrinse that does not contain hydrogen peroxide and was reported to have a whitening impact thanks to chemical agents such as tetrapotassium pyrophosphate. cTP is thought to provide effective whitening because to the presence of tetrapotassium pyrophosphate. The findings of this research are compatible with previous ones.[24,25] Ethanol, added as a solvent in cTP, is an alcohol derivative. Gürdal et al.[26] reported in their research that alcohol in whitening mouthrinses was effective. In the study, the fact that cTP contains alcohol and its pyrophosphate content may have caused its higher whitening effectiveness. cHP is available as a whitening mouthrinse cHP. Hydrogen peroxide is a widely used whitening agent, professionally and as a self-applied agent.[23] The whitening effectiveness of hydrogen peroxide is supported in the literature.[6,23,27] Harorlı and Barutcigil[6] stated that the mouthrinses content, brand, and duration of waiting in the mouthrinse significantly affect color recovery. Karadas and Hatipoglu[21] noted that the whiteness of the enamel-dentin samples they colored in tea solution increased due to being kept in whitening mouthrinses. The immersion time was important for whitening. A study found that chemically induced peroxide containing tooth whitening products accumulate in tooth tissue over time, increasing the total contact time.[28] Conversely, according to the research by Ntovas et al.[22], the effectiveness of mouthrinses decreases after three weeks of use, and there is not always a positive relationship between increasing time and color change. In this study, it is seen that long-term use of cHP causes high color change. Although the long-term values of pyrophosphate-containing mouthrinse decreased, the longterm increased values of hydrogen peroxide-containing mouthrinse may be due to the accumulation of different chemical ingredients on tooth surfaces and the reduction-oxidation mechanism. This study evaluated a new mouthrinse containing activated charcoal as a whitening agent. Activated charcoal is produced by partially oxidizing of various materials as a natural method. Highly porous activated charcoal compounds can exchange ions through nanopores and adhere to tooth enamel and adsorb stains on the tooth surface. It is stated that whitening toothpastes containing activated charcoal have a whitening effect by causing significant changes in tooth color.[9,29] Studies showing the effect of mouthrinses containing activated charcoal on discolored teeth are limited.[30,31] In the research, it was seen that whitening mouthrinse containing activated charcoal caused color change in the teeth after 12-hour and 120-hour immersion times. The whitening effect of mouthrinses containing activated charcoal is suggested to be due to the abrasive nature of the charcoal particles, which are mechanically effective in removing surface stains. Even while color changes upon immersion in various solutions are frequently assessed using the color difference formula, this method by itself does not yield enough information regarding the change in color coordinates. As a result, it is inadequate to compare whiteness values just using the CIEDE2000 calculation (ΔE_{00}). Therefore, in the study, the WI_D (whiteness index) formula, developed specifically for dentistry, was used to evaluate the whiteness degrees of the teeth used and the effect of mouthrinses on the change in whiteness degrees. While the negative results of ΔWI_D values calculated after the coloring process indicate a decrease in the whiteness of the teeth, a high positive index value indicates an increase in the whiteness of the teeth.[32] In this research, significant differences were found in WI_D values after coloring with black tea and immersion in different whitening moutrinses. When the study is examined, the negative values seen in WI_{D1} values, in line with the ΔE_{001} values, show that black tea staining causes a clinically visible degree of darkness in the teeth. However, samples exposed to whitening mouthrinses reached positive values at two different time intervals. This result shows that whitening mouthrinses whitens teeth in short and long-term use. In the study, the highest WI_D value was seen in the cHP group at a 120-hour immersion time. About ΔE_{003}, the high whiteness values can be attributed to the hydrogen peroxide content in the cHP mouthrinse structure and the increase in contact time over time. There are insufficient studies in the literature explaining the relationship between tooth color change and WI_D values and evaluating the materials used in the study or similar materials.

Study Limitations

Compared to clinical investigations, this research has certain limitations because it was planned and carried out *in vitro*. The *in vitro* conditions of study was carried out are different from the oral environment due to the absence of a pellicle layer and the absence of factors such as nutrients and saliva. These factors constitute the limitation of our study. On the other hand, temperature and pH changes can also affect color stability and whiteness values. These limitations are among the factors that are likely to affect the results of our study. Thus, there is a need for more *in situ* and clinical research.

CONCLUSION

The results and recommendations reached within the limits of this study are as follows:

- It was observed that a clinically noticeable color change occurred in all whitening mouthrinses evaluated.

- However, there is no difference in color change between the mouthrinses used.

- There is no significant difference in color change between short- and long-term whitening mouthrinse use.

- It can be said that the use of mouthrinse cHP can provide more effective whitening on stained teeth.

- It was observed that whiteness index values increase significantly as the duration of use of whitening mouthrinses increases.

Within the limitations of this study, it should be taken into account that discoloration may occur as a result of exposure of colored teeth to whitening mouthrinses and that the duration of use of mouthrinses is important for the whitening effect, and potential consumers should be informed about the importance of complying with the recommended application frequency and duration.

Ethics

Ethics Committee Approval: The study was approved by the Erzincan Binali Yıldırım University Non-invasive Clinic Ethics Committee (approval no.: 2023-23/12, date: 28.12.2023) and conducted in accordance with the Helsinki Declaration.

Informed Consent: Written informed consent was obtained from the patients who owned the extracted teeth used in this study.

Footnotes

Author Contributions

Concept - S.G.; Design - S.G.; Supervision - S.G., İ.H.; Resources - S.G., İ.H.; Materials - S.G.; Data Collection and/or Processing - S.G., İ.H.; Analysis and/or Interpretation - S.G., İ.H.; Literature Search - S.G.; Writing - S.G.; Critical Review - S.G., İ.H.

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REFERENCES

1. Joiner A. The bleaching of teeth: a review of the literature. *J Dent*. 2006;34(7):412-419. [CrossRef]
2. Lima FG, Rotta TA, Penso S, Meireles SS, Demarco FF. In vitro evaluation of the whitening effect of mouth rinses containing hydrogen peroxide. *Braz Oral Res*. 2012;26(3):269-274. [CrossRef]
3. Satpathy A, Ravindra S, Porwal A, Das AC, Kumar M, Mukhopadhyay I. Effect of alcohol consumption status and alcohol concentration on oral pain induced by alcohol-containing mouthwash. *J Oral Sci*. 2013;55(2):99-105. [CrossRef]
4. Jaime IM, França FM, Basting RT, Turssi CP, Amaral FL. Efficacy of hydrogen-peroxide-based mouthwash in altering enamel color. *Am J Dent*. 2014;27(1):47-50. [CrossRef]
5. Greenwall L. *Bleaching techniques in restorative dentistry: an illustrated guide*. London: CRC Press; 2001:428. [CrossRef]
6. Harorlı OT, Barutcigil C. Color recovery effect of commercial mouth rinses on a discolored composite. *J Esthet Restor Dent*. 2014;26(4):256-263. [CrossRef]
7. Eimar H, Siciliano R, Abdallah MN, et al. Hydrogen peroxide whitens teeth by oxidizing the organic structure. *J Dent*. 2012;40(Suppl 2):25-33. [CrossRef]
8. Walters PA, Biesbrock AR, Bartizek RD. Benefits of sodium hexametaphosphate-containing chewing gum for extrinsic stain inhibition. *J Dent Hyg*. 2004;78(4):8. [CrossRef]
9. Epple M, Meyer F, Enax J. A critical review of modern concepts for teeth whitening. *Dent J (Basel)*. 2019;7(3):79. [CrossRef]
10. Brooks JK, Bashirelahi N, Reynolds MA. Charcoal and charcoal-based dentifrices: a literature review. *J Am Dent Assoc*. 2017;148(9):661-670. [CrossRef]
11. Gürgan S, Onen A, Köprülü H. In vitro effects of alcohol-containing and alcohol-free mouthrinses on microhardness of some restorative materials. *J Oral Rehabil*. 1997;24(3):244-246. [CrossRef]
12. Kury M, Perches C, da Silva DP, et al. Color change, diffusion of hydrogen peroxide, and enamel morphology after in-office bleaching with violet light or nonthermal atmospheric plasma: an in vitro study. *J Esthet Restor Dent*. 2020;32(1):102-112. [CrossRef]
13. Ghinea R, Pérez MM, Herrera LJ, Rivas MJ, Yebra A, Paravina RD. Color difference thresholds in dental ceramics. *J Dent*. 2010;38(Suppl 2):57-64. [CrossRef]
14. Berger SB, Coelho AS, Oliveira VA, Cavalli V, Giannini M. Enamel susceptibility to red wine staining after 35% hydrogen peroxide bleaching. *J Appl oral Sci*. 2008;16(3):201-204. [CrossRef]
15. Attin T, Manolakis A, Buchalla W, Hannig C. Influence of tea on intrinsic colour of previously bleached enamel. *J Oral Rehabil*. 2003;30(5):488-494. [CrossRef]
16. Naser Alavi F, Salari A, Farzi Z. Effects of three different whitening mouth rinses on the color recovery of stained teeth. *J Dentomaxillofacial*. 2023;12(2):7-15. [CrossRef]
17. Del Rio D, Stewart AJ, Mullen W, et al. HPLC-MSn analysis of phenolic compounds and purine alkaloids in green and black tea. *J Agric Food Chem*. 2004;52(10):2807-2815. [CrossRef]
18. Barutcigil Ç, Barutcigil K, Özarslan MM, Dündar A, Yilmaz B. Color of bulk-fill composite resin restorative materials. *J Esthet Restor Dent*. 2018;30(2):3-8. [CrossRef]
19. Barutçugil Ç, Bilgili D, Barutcigil K, Dündar A, Büyükkaplan UŞ, Yilmaz B. Discoloration and translucency changes of CAD-CAM materials after exposure to beverages. *J Prosthet Dent*. 2019;122(3):325-331. [CrossRef]
20. Peterson J, Dwyer J, Bhagwat S, et al. Major flavonoids in dry tea. *J Food Compos Anal*. 2005;18(6):487-501. [CrossRef]
21. Karadas M, Hatipoglu O. Efficacy of mouthwashes containing hydrogen peroxide on tooth whitening. *Sci World J*. 2015;2015:961403. [CrossRef]
22. Ntovas P, Masouras K, Lagouvardos P. Efficacy of non-hydrogen peroxide mouthrinses on tooth whitening: an in vitro study. *J Esthet Restor Dent*. 2021;33(7):1059-1065. [CrossRef]
23. Joiner A. Whitening toothpastes: a review of the literature. *J Dent*. 2010;38:17-24. [CrossRef]
24. Bilgili Can D, Özarslan M. Effect of whitening mouthwash on color change of discolored bulk-fill composite resins. *Cumhur Dental Journal*. 2022;25(Suppl):108-113. [CrossRef]
25. Mutlu ŞN, Tunçdemir MT. Renklendirilmiş kompozit rezinin renk değişimine ve yüzey pürüzlülüğüne beyazlatıcı ağız gargarasının etkisi. *Selcuk Dental Journal*. 2020;7(3):435-439. [CrossRef]
26. Gürdal P, Akdeniz BG, Hakan Şen B. The effects of mouthrinses on microhardness and colour stability of aesthetic restorative materials. *J Oral Rehabil*. 2002;29(9):895-901. [CrossRef]
27. Tredwin CJ, Naik S, Lewis NJ, Scully C. Hydrogen peroxide tooth-whitening (bleaching) products: review of adverse effects and safety issues. *Br Dent J*. 2006;200(7):371-376. [CrossRef]
28. Serraglio CR, Zanella L, Dalla-Vecchia KB, Rodrigues-Junior SA. Efficacy and safety of over-the-counter whitening strips as compared to home-whitening with 10 % carbamide peroxide gel--systematic review of RCTs and metanalysis. *Clin Oral Investig*. 2016;20(1):1-14. [CrossRef]

29. Ghajari MF, Shamsaei M, Basandeh K, Galouyak MS. Abrasiveness and whitening effect of charcoal-containing whitening toothpastes in permanent teeth. *Dent Res J (Isfahan)*. 2021;18.51. [CrossRef]

30. Dionysopoulos D, Papageorgiou S, Malletzidou L, Gerasimidou O, Tolidis K. Effect of novel charcoal-containing whitening toothpaste and mouthwash on color change and surface morphology of enamel. *J Conserv Dent*. 2020;23(6):624-631. [CrossRef]

31. Özarslan M, Bilgili Can D. Effect of whitening mouthwashes on hybrid ceramic with different surface treatments. *Eastem J Med*. 2022;27(4):566-572. [CrossRef]

32. Pérez MM, Pecho OE, Ghinea RI, Pulgar R, Della Bona A. Recent advances in color and whiteness evaluations in dentistry. *Curr Dent*. 2019;1(1):23-29. [CrossRef]

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Review

The Use of Metyrosine in the Treatment of Pheochromocytoma and Paraganglioma Patients: A Review of the Literature

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ABSTRACT

Metyrosine (α-methyl-parathyrosine) functions as an inhibitor of tyrosine hydroxylase, thereby impeding the conversion of tyrosine to 3,4-dihydroxyphenylalanine. This reaction represents the rate-limiting step in the synthesis of catecholamines. This review examines the mechanisms of metyrosine action and its application for treatment purposes. The published literature was collated from a range of scientific databases, including PubMed, SciFinder, ScienceDirect, Wiley Online Library, Google Scholar and Web of Science. The use of metyrosine has been demonstrated to reduce catecholamine biosynthesis in patients with catecholamine-secreting pheochromocytoma and paraganglioma. The safety and efficacy of metyrosine in the treatment of pheochromocytoma and paraganglioma is substantiated by empirical evidence from studies demonstrating its general tolerability and clinical practice use. Metyrosine has been shown to potentially mitigate the occurrence of surgical complications by enhancing intraoperative hemodynamics. Studies have demonstrated that the administration of metyrosine prior to pheochromocytoma and paraganglioma surgery reduces the risk of hypertensive crisis and severe hypertension, as well as intraoperative haemodynamic variability. It is imperative that further research is conducted to elucidate the pharmacokinetics, intricate molecular mechanisms, and safety profile of methyrone. To this end, the utilization of meticulously designed randomized clinical trials is crucial.

Keywords: Metyrosine, pheochromocytoma, paraganglioma

INTRODUCTION

Mechanism of Action and Uses of Metyrosine

The tyrosine hydroxylase inhibitor metyrosine (α-methyl-parathyrosine) has been shown to inhibit the conversion of tyrosine to 3,4-dihydroxyphenylalanine, which is the rate-limiting step in the synthesis of catecholamines. Methyrosine, a pharmaceutical agent, exerts its biological effects by attenuating the synthesis of catecholamines, a class of hormones, by selectively inhibiting the activity of tyrosine hydroxylase, an enzyme that plays a pivotal role in the aforementioned biosynthetic pathway (Figure 1). In patients with catecholamine secreting diseases such as pheochromocytoma and paraganglioma, daily administration of 1,000-4,000 mg of metyrosine reduces catecholamine biosynthesis by 80%. In catecholamine secreting patients such as pheochromocytoma and paraganglioma, a gradual improvement in urinary catecholamine levels is observed as the metyrosine dose is adjusted up to 1,500 mg daily. Administration of a dose of metyrosine higher than 1,500 mg daily continues to reduce the level of catecholamine, although at a proportionally lower level of urinary catecholamine excretion. The highest level of catecholamine reduction is seen especially within three days. Within four days following the discontinuation of metyrosine

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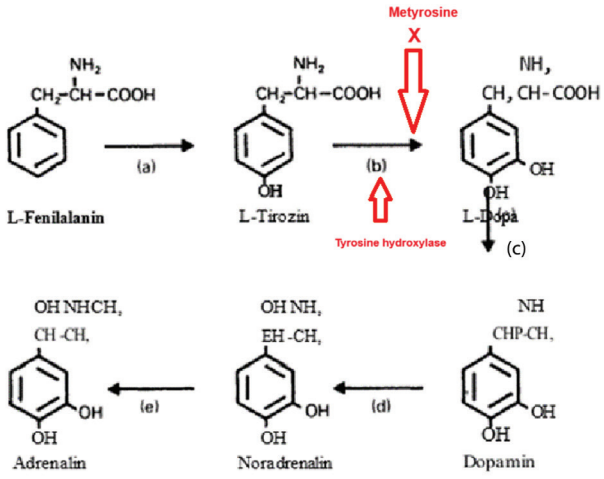

Figure 1. Biosynthetic pathway of catecholamines and enzymes involved.

(a) *L-phenylalanine hydroxylase;* ***(b)*** *L-tyrosine hydroxylase;* ***(c)*** *aromatic L-amino acid decarboxylase;* ***(d)*** *dopamine-β-hydroxylase;* ***(e)*** *phenylethanolamine N-methyl transferase.*

administration, catecholamine and its metabolites in urine concentrations return to pretreatment levels.[1]

The Use of Metyrosine in Pheochromocytoma and Paraganlioma

Pheochromocytomas and paragangliomas are neuroendocrine tumors that derive from chromaffin cells. These cells are located within the adrenal medulla, as well as the paraganglia within the nervous systems that are sympathetic and parasympathetic, respectively.[2] Pheochromocytomas and paragangliomas are tumors that synthesize catecholamines. Symptoms associated with these tumors include paroxysmal hypertension, tachycardia, sweating, episodic headaches, and constipation. Surgical resection has been identified as the primary treatment for these tumors. However, it has been demonstrated that the preoperative administration of medical treatment can effectively prevent intraoperative and postoperative events.[3,4]

Metyrosine, which improves intraoperative hemodynamics, may reduce the incidence of surgical complications.[5,6] Observations have revealed that administration of metyrosine has the potential to mitigate the occurrence of hypertension and hypertensive crises in patients undergoing surgery for pheochromocytoma and paraganglioma. In addition, it was found to reduce intraoperative hemodynamic variability. In a study by Wachtel et al.[4]142 patients with pheochromocytoma and paraganglioma treated with metyrosine and phenoxybenzamine were compared with 32 patients treated with phenoxybenzamine alone. The data from the study showed that intraoperative haemodynamic variability was significantly reduced in patients treated with metyrosine.[5] The incidence of an arrhythmia was significantly lower in those treated with metyrosine than in those treated with phenoxybenzamine.[5]

Steinsapir et al.[6] conducted a comparative analysis of two cohorts of pheochromocytoma patients: one study (n=20) received metyrosine and alpha-adrenergic blockade, while the other (n=6) used phenoxybenzamine. The metyrosine-treated group showed a reduction in the use of intraoperative vasopressors (5% vs. 50%) and a reduction in the need for phentolamine for intraoperative hypertension management (19% vs. 33%) compared with the phenoxybenzamine-only group. In a study comparing outcomes in patients with pheochromocytoma, In the study by Sand et al.[7], 17 patients with pheochromocytoma were treated with metyrosine with phenoxybenzamine (n=14) or metyrosine alone (n=3). The results showed that intraoperative systolic pressure exceeded 180 mmHg in 27% of the group in which metyrosine and phenoxybenzamine were used in treatment, while this rate was higher in 67% of the group in which metyrosine alone was used in treatment.

In supplementary studies, the use of metyrosine has been shown to alleviate symptoms caused by catecholamine excess. Naruse et al.[8] studied 13 patients, including eight patients with metastatic disease, who received chronic medical treatment for pheochromocytoma and paraganglioma. Patients were treated for approximately 125 days using an average dose of 1,028 mg of metyrosine per day. In 25% of the patients, urinary catecholamine levels decreased by more than 50%. The results were favorable with 61.5% of the patients showing a decrease in symptoms related to catecholamine elevation and a tendency to improve.

Effects That can be Observed When Using Metyrosine

Metyrosine is generally well tolerated and no side effects have been observed in patients. Drowsiness and fatigue are the most common side effects observed. The potential for sedation improvement resulting from continued use of metyrosine is a plausible hypothesis; however, it is important to consider that elevated doses of metyrosine have the potential to induce protracted sedation.[9] A variety of adverse effects have been observed, including diarrhea, tremor, anxiety, depression, and weight gain. The metyrosine package insert states that diarrhea and psychiatric effects such as anxiety, depression or hallucinations may occur in up to 10% of patients.[10] Metyrosine is excreted by the kidneys without being metabolized.[11] Caution should be exercised in patients with chronic kidney disease due to renal elimination. At high doses (2 g per day and above), crystal formation in the urine may be observed. If crystal formation is observed, the dose of metyrosine should be reduced in general.[9] Methyrosine may cause extrapyramidal symptoms by causing

MAIN POINTS

- Metyrosine, as a tyrosine hydroxylase inhibitor, effectively reduces catecholamine biosynthesis in pheochromocytoma and paraganglioma patients.
- Clinical evidence demonstrates that metyrosine is generally safe and well tolerated, although adverse effects such as sedation or extrapyramidal symptoms may occur.
- Metyrosine may be considered in patients unresponsive to alpha-adrenergic blockade or at high risk for catecholamine release due to tumor size or location.

a decrease in dopamine levels. The package insert states that up to 10% of patients may experience symptoms ranging from drooling or speech difficulties to overt parkinsonism.[9] The symptoms observed were generally mild. It is usually seen as stiff posture or unsteady gait. Symptoms were severe in three patients, and one patient was treated with intravenous abortive agents because the symptoms did not improve.[12] Extrapyramidal symptoms may worsen in patients taking other drugs that inhibit dopamine activity, such as metoclopramide and antipsychotics.[9] High risk in patients taking serotonin reuptake inhibitors and other antidepressants due to inhibition of dopamine in the central nervous system.[13] Patients using these drugs should be monitored for extrapyramidal side effects and should be informed that these symptoms may occur. The utilization of metyrosine during pregnancy is classified as category C, indicating that its application is permissible only if the anticipated benefits to the mother exceed the potential risks to the fetus.[9] Since it is not known whether metyrosine is excreted in breast milk, it is not recommended for use during breastfeeding.[9]

CONCLUSION

The use of metyrosine is safe in pheochromocytoma and paraganglioma patients before surgical or interventional procedures. In some patients, this procedure has been observed to improve intraoperative hemodynamics and reduce the occurrence of symptoms that are caused by catecholamine elevation. For patients with hypertension who do not respond to alpha-adrenergic blockade, adding metyrosine to their treatment is a viable option. In cases of patient non-compliance with regard to alpha-adrenergic blockade or high risk for catecholamine release due to factors such as tumor size and/or location, and who require intervention that may accelerate catecholamine release, it may be recommended to add metyrosine to treatment.

Author Contributions

Concept Design: O.K.Ç., H.S., Data Collection or Processing M.B., O.K.Ç., Literature Review: G.H., M.B, O.K.Ç, H.S., Writing, Reviewing and Editing O.K.Ç, H.S.

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REFERENCES

1. Fang F, Ding L, He Q, Liu M. Preoperative Management of Pheochromocytoma and Paraganglioma. *Front Endocrinol (Lausanne)*. 2020;11:586795. [CrossRef]
2. Kimura N, Takayanagi R, Takizawa N, et al. Pathological grading for predicting metastasis in phaeochromocytoma and paraganglioma. *Endocr Relat Cancer*. 2014;21(3):405-414. [CrossRef]
3. Lenders JW, Duh QY, Eisenhofer G, et al. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2014;99(6):1915-1942. Erratum in: *J Clin Endocrinol Metab*. 2023;108(5):e200. [CrossRef]
4. Wachtel H, Kennedy EH, Zaheer S, et al. Preoperative Metyrosine Improves Cardiovascular Outcomes for Patients Undergoing Surgery for Pheochromocytoma and Paraganglioma. *Ann Surg Oncol*. 2015;22(Suppl 3):646-654. [CrossRef]
5. Ohmachi Y, Yamamoto M, Inaba Y, et al. The combination of doxazosin and metyrosine as a preoperative treatment for pheochromocytomas and paragangliomas. *Endocrine*. 2024;84(2):694-703. [CrossRef]
6. Steinsapir J, Carr AA, Prisant LM, Bransome ED Jr. Metyrosine and pheochromocytoma. *Arch Intern Med*. 1997;157(8):901-906.
7. Sand J, Salmi J, Saaristo J, Auvinen O. Preoperative treatment and survival of patients with pheochromocytomas. *Ann Chir Gynaecol*. 1997;86(3):230-232. [CrossRef]
8. Naruse M, Satoh F, Tanabe A, et al. Efficacy and safety of metyrosine in pheochromocytoma/paraganglioma: a multi-center trial in Japan. *Endocr J*. 2018;65(3):359-371. [CrossRef]
9. Gruber LM, Jasim S, Ducharme-Smith A, Weingarten T, Young WF, Bancos I. The role for metyrosine in the treatment of patients with pheochromocytoma and paraganglioma. *J Clin Endocrinol Metab*. 2021;106(6):e2393-e2401. [CrossRef]
10. Hamidi O, Young WF Jr, Iñiguez-Ariza NM, et al. Malignant pheochromocytoma and paraganglioma: 272 patients over 55 years. *J Clin Endocrinol Metab*. 2017;102(9):3296-3305. [CrossRef]
11. Takekoshi K, Satoh F, Tanabe A, et al. Correlation between urinary fractionated metanephrines in 24-hour and spot urine samples for evaluating the therapeutic effect of metyrosine: a subanalysis of a multicenter, open-label phase I/II study. *Endocr J*. 2019;66(12):1063-1072. [CrossRef]
12. Fishbein L, Orlowski R, Cohen D. Pheochromocytoma/paraganglioma: review of perioperative management of blood pressure and update on genetic mutations associated with pheochromocytoma. *J Clin Hypertens (Greenwich)*. 2013;15(6):428-434. [CrossRef]
13. Madhusoodanan S, Alexeenko L, Sanders R, Brenner R. Extrapyramidal symptoms associated with antidepressants--a review of the literature and an analysis of spontaneous reports. *Ann Clin Psychiatry*. 2010;22(3):148-156. [CrossRef]