



Medical Journal of
Süleyman Demirel University



Medical Journal of Süleyman Demirel University

Süleyman Demirel Üniversitesi Tıp Fakültesi Dergisi

Med J SDU / SDÜ Tıp Fak Derg

The journal is a peer reviewed academic journal and publishes four issues per year in March, June, September, and December.

This journal is indexed by EBSCO, Tr-Dizin.

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Respiratory Symptoms and Quality of Life in First Responders to the 2021 Forest Fires in Turkey: A Cross-Sectional Sri-Based Study

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Cite this article as: Başer T, Saygin M. Respiratory Symptoms and Quality of Life in First Responders to the 2021 Forest Fires in Turkey: A Cross-Sectional Sri-Based Study. Med J SDU 2025;32(4):265–281.

Abstract

Objective

This analytical cross-sectional study aimed to investigate respiratory complaints and their associated quality of life among fire response teams following the major forest fires that occurred in the Mediterranean and Aegean regions of Turkey in August 2021. The study utilized the Severe Respiratory Insufficiency (SRI) questionnaire, a valid tool for illuminating the effects of acute smoke exposure on respiratory health and for identifying key socio-demographic factors that affect quality of life in this at-risk population.

Material and Method

Data for this analytical cross-sectional study were collected using a convenience sampling method from 83 participants who responded to the August 2021 fires. A total of 148 individuals were invited, and 83 were included in the study. The data collection tool included demographic questions and the 49-item SRI questionnaire. Due to the non-normal data distribution, inter-group analyses were performed using the Mann-Whitney U and Kruskal-Wallis H tests, with effect sizes and 95% Confidence Intervals (95% CI) reported. The level of statistical significance was set at ($p < 0.05$).

Results

Analysis revealed that participants in the 18-24 age group reported a higher quality of life compared to other age groups. Conversely, a statistically significant difference ($p < 0.05$) indicated that the 45-65 age group experienced a poorer quality of life when compared to other demographics. Alcohol consumption was found to directly impact quality of life; a significant difference ($p < 0.05$) was observed in quality of life between participants who abstained from alcohol and those who consumed alcohol once a week. Furthermore, individuals without substance addiction exhibited higher scores, indicating better quality of life, with a significant difference ($p < 0.05$) noted when compared to those with substance addiction.

Conclusion

Key factors influencing the respiratory complaints and overall quality of life among individuals directly exposed to forest fires include age, alcohol use, substance addiction, education level, and engagement in sports activities.

Keywords: Air pollution, Forest fire, Respiratory insufficiency, Quality of life

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Received: 21.01.2025 • **Accepted:** 18.10.2025

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Introduction

Air pollution stems from diverse sources, with the Industrial Revolution, technological advancements, and natural events such as fires posing significant threats to public health (1). Beyond its inflammatory impact on the respiratory tract, air pollution also disrupts various other cellular processes (2). While airway epithelial cells typically offer protection against such disruptions, elevated particulate matter concentrations in the air can induce numerous respiratory dysfunctions, even with short-term exposure (3). Forest fires exemplify this scenario, affecting residents in proximity and the personnel—including public officers, private sector employees, and volunteers—involved in firefighting efforts (4).

Forest fires are natural phenomena typically occurring during periods of high ambient temperature, often attributed to both deliberate acts and incompletely understood causes (5). These fires lead to a substantial accumulation of particulate matter in the atmosphere, exhibiting dramatic increases in both the short and long term (6). Consequently, examining forest fires and their associated damage through the lens of air pollution can facilitate the implementation of more effective preventive measures against respiratory ailments (7).

Forest fires commonly release carbon monoxide (CO), carbon dioxide (CO₂), and various organic gases (8). Beyond these noxious gases, human life expectancy is further compromised by airborne particulate matter, its atmospheric persistence, and the systemic absorption of harmful chemicals, exacerbated by changing climatic conditions (9).

Airborne particulate matter constitutes the primary etiological agent for physiological dysfunctions observed during forest fires (10). Following prolonged forest fire events, these airborne particles exhibit extended atmospheric residence times, leading to damage to the epithelial cell barriers of the respiratory tract (11). Concomitantly, pre-existing chronic diseases and lifestyle factors such as alcohol and cigarette consumption exacerbate the detrimental effects of air pollution, thereby diminishing quality of life (12). Consequently, individuals residing in forest-proximate settlements and those engaged in fire suppression activities during and after forest fires are susceptible to irreversible damage to the epithelial cells lining their respiratory tracts (13).

Respiratory morbidities attributable to forest fires represent a critical public health concern warranting

attention from both regional inhabitants and firefighting personnel. Accordingly, the principal objective of this study is to elucidate the physiological and sociodemographic determinants of respiratory complaints associated with forest fires. While existing literature extensively addresses air pollution from industrialization, there is a significant gap in research specifically evaluating the physiological and sociodemographic effects of large-scale, acute smoke exposure from forest fires on the quality of life of direct intervention personnel in the Turkish context. This study addresses this gap by using a validated instrument, the SRI questionnaire, to analyze the determinants of respiratory complaints in this uniquely exposed group.

Based on the detrimental health effects of air pollution observed in antecedent studies, it was hypothesized that individuals directly engaged in forest fire intervention would present with diminished quality of life scores, as quantifiably measured by the SRI questionnaire. Furthermore, key sociodemographic and lifestyle covariates, specifically age, alcohol consumption, substance dependence, educational attainment, and athletic participation, are postulated to be significantly associated with both the severity of respiratory symptomatology and the overall quality of life within this cohort of first responders.

Material and Method

A Working Group and Research Format

The survey instrument utilized in this study was meticulously designed to acquire data pertinent to a cross-sectional investigation, focusing on respiratory morbidities among individuals exposed to forest fire incidents. The questionnaire was administered to participants directly involved in forest fire intervention over a 45-day period. Data collection was conducted online via (<https://forms.office.com/>) during September and October 2021, following the acquisition of informed consent from each participant.

The dependent variable in the study was the total score obtained from the SRI questionnaire, which measures the participants' quality of life related to respiratory complaints. The independent variables consisted of sociodemographic and health factors, including age, gender, education level, professional experience, cigarette use, alcohol consumption, and substance dependence.

Cross-sectional studies provide a valuable methodology for the rapid and simultaneous collection of data in the investigation of regional disease

prevalence, additionally enabling the comparison of diverse findings. Consequently, this study adopted an analytical cross-sectional design, employing a survey-based data collection method. This approach was chosen to investigate the prevalence of respiratory complaints among public officers, private sector personnel, students, and volunteers who participated in the forest fire interventions in Antalya, Isparta, Burdur, and Muğla provinces and their surrounding areas during August 2021, and who subsequently consented to participate in the study. However, due to the cross-sectional nature of the study and the use of univariate statistical methods, the effect of potential confounding variables on the relationship between dependent and independent variables was not controlled for in these analyses.

Participant Selection Procedure

The data for this analytical cross-sectional study were acquired from individuals who had directly participated in forest fire response efforts. Prioritization was given to the inclusion of individuals who worked in shifts, possessed prior experience in forest fire intervention, and had prolonged exposure within the fire zone. Participant inclusion criteria were based on the duration of their presence in the fire zone, documented exposure to noxious gases such as sulfur dioxide (SO₂) and carbon monoxide (CO) emanating from the fire, and previous engagement in forest fire suppression activities. However, a limitation of the current study is the inability to specify in detail quantitative data, such as the precise duration of exposure within the fire zone and specific gas exposure levels, which were integral to the participant selection criteria. Despite meticulous participant selection, the final

sample size was limited to 83 participants out of 148 invited individuals. This limitation was primarily due to factors such as individuals declining survey participation, engagement in short-term shift work, and job transitions (Table 1).

Questions Included in the Survey

The study administered a comprehensive questionnaire comprising 63 items to the 83 participants. This instrument included demographic inquiries and questions derived from the SRI survey, encompassing domains such as respiratory complaints, physical function, symptoms and sleep, social relations, anxiety, psychological well-being, and social functionality.

Severe Respiratory Insufficiency (SRI) Survey

The study utilized questions from the SRI survey, a widely recognized instrument for assessing respiratory failure and potential respiratory complaints. Originating in Germany, the SRI is a self-administered questionnaire suitable for patients or individuals in environments conducive to respiratory complaints. This survey, which has undergone both Turkish translation and transcultural adaptation, comprises 49 items, including those pertaining to respiratory complaints (8 items; It's hard for me to climb stairs, I get short of breath when I eat, I can go out in the evenings, I mostly feel bad, I get breathless even without physical exertion, I get headaches very often, I have many friends and acquaintances, I'm worried that my illness might get worse), physical function (6 items; I can fall asleep easily, I can easily empathize with other people, Sometimes I feel dizzy, I wake up at night with respiratory distress, I'm afraid I'll have shortness of breath at night, I have neck pain very often), symptoms

Table 1 Flow of Participants

Participant Information	Number (n)
Number of Potential Participants	250
Number of Participants Excluded Prior to Survey	102
Number of Participants Excluded Post-Survey	2
Number of Participants Invited	148
Number of Participants Who Consented to Participate	85
Number of Participants Who Declined to Participate	63
Total Included in Analysis	83

and sleep (7 items; I mostly can't leave the house, Housework is difficult for me, I often wake up at night, I can sleep through the night without interruption, I mostly feel short of breath, I feel optimistic about the future, I feel alone), social relations (6 items; I experience shortness of breath when speaking, Guests tire me out, I cough a lot, I frequently have phlegm in my airways, I avoid situations where I might feel embarrassed due to my breathing difficulties, I feel good around my friends/acquaintances), anxiety (5 items; I'm afraid of having a shortness of breath attack, I experience shortness of breath when I move, I'm anxious about the limitations caused by my illness, My relationship with my spouse has deteriorated due to my illness, I can go shopping), psychological well-being (9 items; I can do any activity/hobby I enjoy, I'm mostly restless, My relationships with friends/acquaintances are limited due to my illness, I enjoy life, I can participate in social events, I'm mostly sad, Shortness of breath bothers me in public places I'm mostly angry, I can dress and undress myself), and social functionality (8 items; I'm tired all day long, I feel isolated, I can cope with my illness, My breathing difficulties prevent me from doing my daily tasks, My family is suffering because of my illness, My relationships with other people have been cut off due to my breathing difficulties, My leisure activities are limited, Overall, I'm satisfied with my life). Responses to the SRI survey questions were compared across groups stratified by sociodemographic data, employing appropriate statistical methodologies. (14). Participants' responses to the SRI questionnaire items were assessed on a scale ranging from (-2) to (+2) points, reflecting the degree to which each statement applied to their experience. For each subgroup, responses to the SRI survey questions were scored through recording and the calculation of individual percentage values. Furthermore, the arithmetic mean of these subgroup scores was computed to derive a total score. A higher total score indicated a better quality of life, whereas a lower score signified a poorer quality of life. (15).

The SRI survey is applicable not only to individuals with respiratory failure or existing respiratory complaints but also to healthy individuals exposed to conditions potentially inducing such complaints. This is evidenced by its use in studies investigating potential pulmonary hypertension and subsequent quality of life in patients with Obesity-Hypoventilation Syndrome (OHS) (16). Notably, research also employs the SRI to assess potential respiratory complaints and associated quality of life following ventilator weaning. Consequently, the SRI survey serves as a valuable tool for investigating respiratory complaints and related quality of life in individuals who have

experienced or been exposed to situations with the potential to cause respiratory issues, even in the absence of overt disease (17).

Statistical Analysis

Participants' responses to the sociodemographic and SRI survey questions were scored within the range of [-2, +2], and the internal consistency of the survey was assessed using Cronbach's alpha. The main findings for all quantitative variables were presented as the mean $\pm$ standard deviation, and the effect sizes were reported along with their respective 95% Confidence Intervals (95% CI).

The normality of distribution for groups stratified by sociodemographic data was determined by examining their skewness and kurtosis values. Accordingly, groups exhibiting skewness and kurtosis values outside the [-2, +2] range, indicating a non-normal distribution, were analyzed using the non-parametric Kruskal-Wallis H test. For comparisons between two non-normally distributed groups, the Mann-Whitney U test was employed. Additionally, Dunn's post-hoc test (with Bonferroni correction) was utilized to ascertain significant differences between groups in their survey responses, with the level of statistical significance accepted at $p < 0.05$. However, the use of non-parametric analyses and the sample size ($n=83$) are not suitable for examining multiple variable interactions; therefore, the absence of multivariate regression analyses limits the ability to detail potential simultaneous interactions and causal relationships between variables.

Results

The sociodemographic characteristics of the study participants were assessed across parameters including age, gender, occupation, educational attainment, sports habits, substance addiction, and alcohol consumption. Analysis of age groups revealed that the 35-44 age bracket constituted the largest proportion of participants at 36.14%. Furthermore, 74.70% of individuals engaged in field work were male. Regarding professional distribution, public officers comprised 71.08% of the field workforce, while 36.14% of the total study participants held undergraduate degrees. Demographic analysis concerning sports, smoking, and alcohol habits indicated that 53.01% engaged in sports, 63.86% reported no smoking, and 81.93% abstained from alcohol (Table 2).

The health parameters of the study groups were assessed using survey questions pertaining to chronic diseases, COVID-19 history, and allergies.

Accordingly, 80.72% of the participants reported no chronic disease, while 33.73% had a history of COVID-19. Among groups stratified by allergy status,

81.93% reported no allergies, with allergic rhinitis being the most prevalent specific allergy, affecting 4.82% of participants (Table 3).

Table 2

Sociodemographic Distributions of the Groups Participating in the Study

Sociodemographic Parameters	Variables	n	%
Age	18-24	17	20,48
	25-34	19	22,89
	35-44	30	36,14
	45-65	17	20,48
	65+	0	0,00
Gender	Women	21	25,30
	Men	62	74,70
Jobs	Student	10	12,05
	Public officer	59	71,08
	Private sector personnel	0	0,00
	Contract employee	12	14,46
	Volunteer	2	2,41
Education Level	Unemployed	0	0,00
	Elementary school	2	2,41
	Middle school	4	4,82
	High school	19	22,89
	Associate degree	23	27,71
	Undergraduate	30	36,14
	Postgraduate	5	6,02
Sports	Non-literate	0	0,00
	(+)	44	53,01
	(-)	39	46,99
Substance addiction	Cigarette	30	36,14
	Alcohol	0	0,00
	Various Stimulants	0	0,00
	Non-User	53	63,86
Alcohol use	Non-alcoholic	68	81,93
	Once a week	13	15,66
	1-2 times a week	2	2,41
	3-4 times a week	0	0,00
	5-6 times a week	0	0,00
	Every day	0	0,00

Table 3 Distributions of Health Information of the Groups Participating in the Study

Health Related Parameters	Variables	n	%
Chronic Diseases	Other	8	9,64
	Asthma	2	2,41
	COPD	1	1,20
	Diabetes	0	0,00
	Hypertension	5	6,02
	No Chronic Disease	67	80,72
Covid-19	Yes	28	33,73
	No	55	66,27
Allergy	Other	4	4,82
	Asthma	1	1,20
	Allergic Rhinitis	4	4,82
	Atopic Dermatitis	0	0,00
	Urticaria	3	3,61
	Drug Allergy	3	3,61
	Food Allergy	0	0,00
	Venom Allergy	0	0,00
	Anaphylaxis	0	0,00
	No Allergy	68	81,93

Given the non-normal distribution of the data obtained from the groups, Interquartile Range (IQR) values were calculated (Table 4).

Groups and SRI Scores

Analysis of the SRI and standard deviation (SD) data, presented as percentages of quality of life, revealed a significant inverse correlation between increasing average age and quality of life within age groups exposed to forest fires (Table 5).

A significant association was observed between alcohol consumption and quality of life within the groups stratified by self-reported alcohol use (Table 6).

Additional findings from the study pertained to SRI scores in relation to educational attainment. Specifically, individuals with undergraduate and graduate education who participated in forest fire suppression exhibited a favorable quality of life, as indicated by their SRI scores (Table 7).

The SRI scores for women exposed to forest fires in the field were relatively higher compared to men; however, the overall quality of life for both genders was assessed as poor. Furthermore, the sports group exhibited lower SRI scores than the non-sports group. Regarding substance addiction (smoking), the non-addiction group demonstrated higher SRI scores. Conversely, both groups with and without a history of COVID-19 showed lower SRI scores compared to other demographic stratifications. These findings suggest that participation in sports and the absence of substance addiction significantly influence quality of life by impacting SRI scores (Table 8).

Analysis revealed that the 18-24 age group demonstrated a superior quality of life compared to both the 25-34 and 45-65 age groups, as indicated by their SRI scores. Additionally, the 25-34 and 35-44 age groups exhibited a better quality of life than the 45-65 age group. Participants reporting alcohol consumption 1-2 times per week showed a better quality of life than those who abstained from alcohol. Furthermore, the

Table 4 IQR Analysis by Group

Groups	Q1 - 25th Percentile	Q3 - 75th Percentile	Interquartile Range (IQR)
Age Group 18-24	30.96	81.70	50.73
Age Group 25-34	38.96	80.35	41.39
Age Group 35-44	42.31	74.94	32.63
Age Group 45-65	31.94	71.49	39.55
Non-Alcoholic Group	43.23	73.07	29.84
Alcohol Using Once a Week Group	57.55	76.99	19.44
Alcohol Using 1-2 Times a Week Group	54.86	50.76	-4.09
Elementary School Group	9.45	88.57	79.11
Middle School Group	27.27	87.67	60.40
High School Group	29.04	83.19	54.15
Associate School Group	37.43	76.71	39.28
Undergraduate School Group	38.90	76.07	37.17
Postgraduate School Group	32.49	84.89	52.39
Women Group	36.94	76.58	39.64
Men Group	45,52	80,12	34,60
Sport (+) Group	39.73	79.85	40.11
Spor (-) Group	32.49	75.56	43.07
Substance Addiction (+) Group	32,03	71,36	39,32
Substance Addiction (-) Group	38,97	79,20	40,22
COVID-19 (+) Group	46,34	79,57	33,22
COVID-19 (-) Group	32,49	73,06	40,56

Table 5 Age Groups and SRI Scores

Groups	SRI (%) $\pm$ SD, (CI ₉₅)	n	Cronbach's alpha
Age Group 18-24	60.57 $\pm$ 6.84, (47,10-73,00)	17	0,76
Age Group 25-34	38.68 $\pm$ 12.64, (44,00-69,90)	19	0,78
Age Group 35-44	49.28 $\pm$ 7.79, (48,20-65,60)	30	0,73
Age Group 45-65	27.70 $\pm$ 12.30, (33,90-61,00)	17	0,72

Table 6 Alcohol Groups and SRI Scores

Groups	SRI (%) $\pm$ SD, (CI ₉₅)	n	Cronbach's alpha
Non-Alcoholic Group	44,42 $\pm$ 6,03, (48,60-60,70)	68	0,81
Consumed Alcohol Once a Week Group	61,46 $\pm$ 6.52, (49,80-73,20)	13	0,74
Consumed Alcohol 1-2 Times a Week Group	52,82 $\pm$ 5.17, (0,78-105,00)	2	0,72

Table 7 Education Level Groups and SRI Scores

Groups	SRI (%) $\pm$ SD, (CI ₉₅)	n	Cronbach's alpha
Group Elementary School	31,75 $\pm$ 23.72, (25,30-112,00)	2	0,71
Group Middle School	46,22 $\pm$ 27.83, (26,10-91,40)	4	0,71
Group High School	41,30 $\pm$ 12.19, (43,60-69,80)	19	0,75
Group Associate Degree	34,10 $\pm$ 11.40, (45,00-65,00)	23	0,72
Group Undergraduate	52,71 $\pm$ 6.54, (47,80-66,00)	30	0,74
Group Postgraduate	63,05 $\pm$ 10.84, (32,90-89,80)	5	0,72

Table 8 Other Groups Affecting SRI Scores

Groups	SRI (%) $\pm$ SD, (CI ₉₅)	n	Cronbach's alpha
Women	49,97 $\pm$ 8.66, (47,50-68,10)	21	0,75
Men	42,98 $\pm$ 6.57, (49,20-62,00)	62	0,78
Sport (+)	38,78 $\pm$ 8.50, (48,90-64,10)	44	0,73
Sport (-)	51,48 $\pm$ 5.86, (48,30-63,00)	39	0,73
Substance Addiction (+)	33,36 $\pm$ 10.05, (44,70-62,80)	30	0,84
Substance Addiction (-)	51,19 $\pm$ 5.92, (50,70-64,80)	53	0,82
Covid-19 (+)	49,08 $\pm$ 9.41, (51,70-71,20)	28	0,71
Covid-19 (-)	42,54 $\pm$ 6.48, (46,10-59,50)	55	0,77

group consuming alcohol once a week reported a better quality of life than the group consuming alcohol 1-2 times per week. Regarding educational attainment, the postgraduate group exhibited a superior quality of life compared to individuals with primary, secondary, high school, associate, and undergraduate education.

The undergraduate group also demonstrated a better quality of life than the primary, secondary, high school, and associate degree groups. Women reported a better quality of life than men. Lastly, the non-sporting group displayed a better quality of life than the sporting group (Table 9).

Table 9 Comparison of SRI Scores Across Various Demographic and Lifestyle Groups

Groups	SRI (%)±SD	Statistical Test	p Value	Significantly Different Groups (Post-Hoc Analysis)
Age Groups		Kruskal-Wallis H Test		
18-24	60,57±6.84		0,03	18-24 >25-34
25-34	38,68±12.64		0,02	18-24 >45-65
35-44	49,28±7.79		0,02	25-34>45-65
45-65	27,70±12.30		0,03	35-44>45-65
Alcohol Using Groups		Kruskal-Wallis H Test		
Non-Alcoholic Group	44,42±6.03		0,03	Alcohol Using 1-2 Times a Week Group > Non-Alcoholic Group
Once a Week Group	61,46±6.52		0,04	Alcohol Using Once a Week Group > Alcohol Using 1-2 Times a Week Group
Alcohol Using 1-2 Times a Week Group	52,82±5.17			
Education Level Groups		Kruskal-Wallis H Test		
Elementary School	31,75±23.72		0,03	Postgraduate School > Elementary School
Middle School	46,22±27.83		0,02	Postgraduate School > Middle School
High School	41,30±12.19		0,03	Postgraduate School > High School
Associate Degree	34,10±11.40		0,02	Postgraduate School > Associate Degree
Undergraduate School	52,71±6.54		0,02	Postgraduate School > Undergraduate School
Postgraduate School	63,05±10.84		0,02	Undergraduate School > Elementary School
			0,04	Undergraduate School > Middle School
			0,02	Undergraduate School > High School
			0,03	Undergraduate School > Associate Degree
Sex		Mann-Whitney U Test		
Women	49,97±8.66		0,01	Women > Men
Men	42,98±6.57			
Sport Situation		Mann-Whitney U Test		
Sport (+)	38,78±8.50		0,02	Sport (-) > Sport (+)
Spor (-)	51,48±5.86			
Substance Addiction Groups		Mann-Whitney U Test		
Substance Addiction (+)	33,36±10.05		0,02	Substance Addiction (-) > Substance Addiction (+)
Substance Addiction (-)	51,19±5.92			

Age Groups and SRI Scores

Among the age groups of individuals directly involved in forest fire intervention and affected by associated air pollution, the 18-24 age group exhibited high SRI scores, whereas the 45-65 age group demonstrated low scores. A significant difference in quality of life was observed when comparing the SRI scores across the participating age groups: 45-65 years (SRI: 27.70 ± 12.30), 18-24 years (SRI: 60.57 ± 6.84), 25-34 years (SRI: 38.68 ± 12.64), and 35-44 years (SRI: 49.28 ± 7.79) ($p < 0.05$). Consistent with this, a significant difference in quality of life was also noted when comparing the 25-34 age group with the 18-24 age group ($p < 0.05$) (Figure 1).

Effect of Alcohol Use on SRI Scores

Within the groups stratified by alcohol consumption, a significant difference in quality of life was observed when comparing the non-alcohol use group (SRI: 44.42 ± 6.03) with the group reporting alcohol use 1-2 times per week (SRI: 52.82 ± 5.17) ($p < 0.05$). Furthermore, a significant difference in quality of life was also noted when the group consuming alcohol once a week was compared with the group consuming alcohol 1-2 times per week (SRI: 61.46 ± 6.52) ($p < 0.05$) (Figure 2).

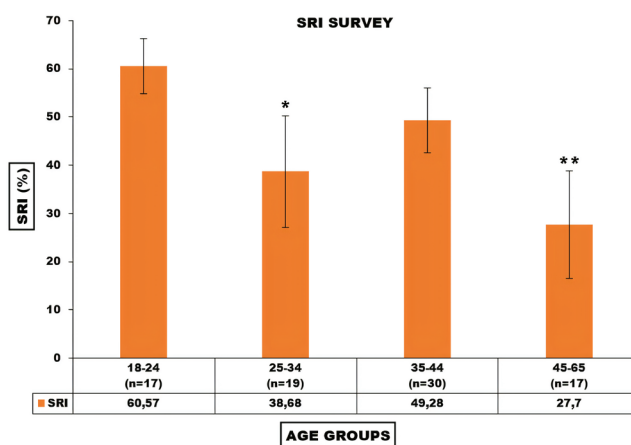


Figure 1

Age Groups and SRI Scores. Each point is expressed as SRI (%) and SD. * $p < 0.05$; compared according to 18-24 age group. ** $p < 0.05$; compared according to 18-24, 25-34 and 35-44 age groups. In the figure means * $p < 0.05$ and ** $p < 0.05$.

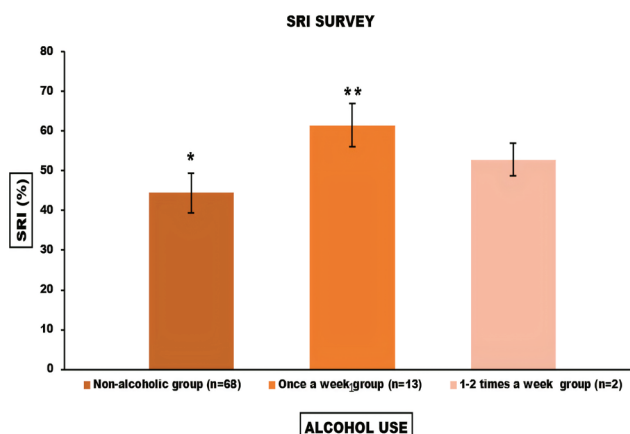


Figure 2

Effect of Alcohol Use on SRI Scores. Each point is expressed as SRI (%) and SD. * $p < 0.05$; compared to the once a week group, ** $p < 0.05$; compared to the 1-2 times a week group. In the figure means * $p < 0.05$ and ** $p < 0.05$.

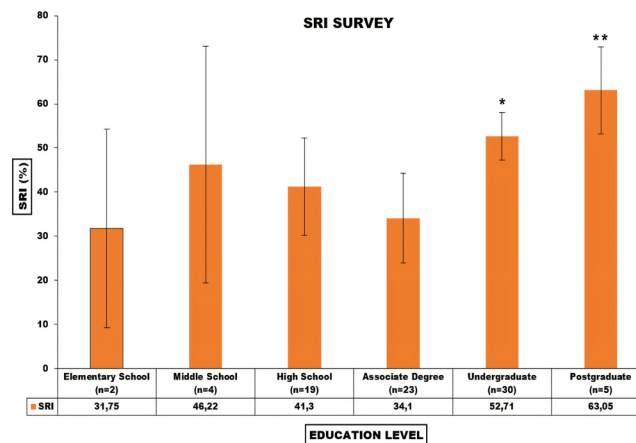


Figure 3

Relationship between Education Level and SRI Scores. Each point is expressed as SRI (%) and SD. * $p < 0.05$; when compared according to elementary school, middle school, high school and associate degree groups. ** $p < 0.05$; when compared according to elementary school, middle school, high school, associate degree and undergraduate groups. In the figure means * $p < 0.05$ and ** $p < 0.05$.

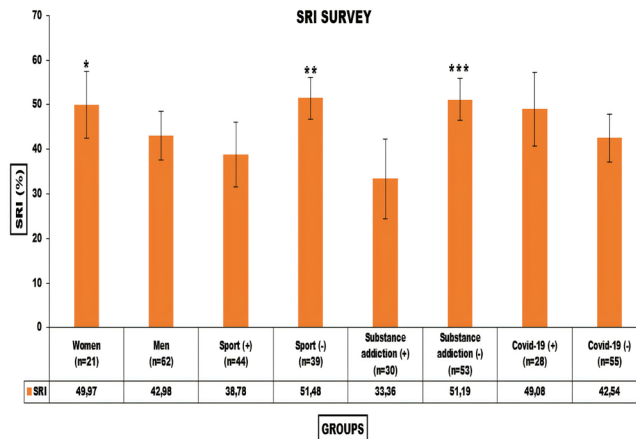


Figure 4

Other Groups Affecting SRI Scores. Each point is expressed as SRI (%) and SD. * $p < 0.05$; compared to the men group, ** $p < 0.05$; compared to the sports group, *** $p < 0.05$; compared to the substance addiction group. In the figure means * $p < 0.05$, ** $p < 0.05$ and *** $p < 0.05$.

Relationship Between Education Level and SRI Scores

Among the groups stratified by educational attainment among individuals directly involved in forest fire intervention, a significant difference in quality of life was observed when the postgraduate group (SRI: 63.05 ± 10.84) was compared with the elementary school group (SRI: 31.75 ± 23.72), middle school group (SRI: 46.22 ± 27.83), high school group (SRI: 41.30 ± 12.19), associate degree group (SRI: 34.10 ± 11.40), and undergraduate group (SRI: 52.71 ± 6.54). ($p < 0.05$) Similarly, a significant difference in quality of life was found when comparing the undergraduate group with the elementary school, middle school, high school, and associate degree groups ($p < 0.05$) (Figure 3).

Other Groups Affecting SRI Scores

A significant difference in quality of life ($p < 0.05$) was observed when comparing the female group (SRI: 49.97 ± 8.66) with the male group (SRI: 42.98 ± 6.57) among study participants. Furthermore, a significant difference ($p < 0.05$) in quality of life, based on SRI scores, was found between the non-sports group (SRI: 51.48 ± 5.86) and the sports group (SRI: 38.78 ± 8.50). Substance addiction (smoking) was identified as another factor influencing quality of life; a significant difference ($p < 0.05$) in quality of life, according to SRI scores, was analyzed between the non-substance addiction group (SRI: 51.19 ± 5.92) and the substance addiction group (SRI: 33.36 ± 10.05) (Figure 4).

Discussion

In the investigation of respiratory complaints attributed to air pollution during forest fires, statistically significant findings emerged from comparisons across age, alcohol consumption, education level, substance addiction (smoking), sports participation, and gender groups. Concurrently, a review by Mermit, SRI scores yielded crucial insights into evaluating the impact of both potential and confirmed respiratory complaints on quality of life. (18). While this assertion is generally accurate, it is crucial to expand the understanding of air pollution beyond industrialization to encompass the impact of uncontrolled natural fires. Statistical analyses by Bert and Stephen further concluded that the persistence of urban air pollution, characterized by ultra-fine particulate matter, induces significant cardiopulmonary toxicity (19). From a holistic perspective, the gases and particulate matter emitted during forest fires are observed to induce cardiopulmonary, immune, and cellular dysfunctions (20). Although this study did not yield direct results concerning cardiopulmonary factors, the data derived from the analysis of age groups, alcohol-consuming groups, and substance-addicted groups corroborate this perspective regarding the effects and indicators of respiratory complaints on quality of life.

Sapkota et al. reported that forest fires intensively release numerous particles, including (CO), (CO₂) and various organic gases, which subsequently accumulate in the atmosphere. In this context, both particle size and chemical composition play crucial roles in their environmental and health impacts. (21). Polan et al. highlight that both the size of particles and their chemical composition are crucial factors influencing the respiratory system. They specifically note that particles smaller than 2.5 micrometers can penetrate the deepest pulmonary tissues, resulting in systemic inflammation (22). Building on this, Karavitis et al. contend that prolonged exposure to air pollution compromises the epithelial cell barriers within the respiratory tract. They further assert that chronic diseases, alcohol consumption, and smoking exacerbate the detrimental effects of air pollution, leading to molecular dysfunctions (23). Interestingly, the study revealed that the SRI score of the non-alcoholic group was lower than that of the other alcohol-consuming groups. This unexpected observation may stem from various unmeasured or confounding factors within the non-alcoholic group. Potential influences include pre-existing health conditions like allergies or asthma, socioeconomic disparities, environmental exposures such as passive cigarette smoke, nutritional deficiencies, obesity, or

undiagnosed cardiovascular and renal diseases, all of which could have adversely impacted their SRI scores. In contrast, the SRI scores for the group with substance addiction were consistently low, aligning with existing literature.

Kelly et al. (2011) reported a significant association between air pollution exposure and the prevalence of respiratory diseases, including asthma and chronic bronchitis (24). The findings indicate no statistically significant difference in health impacts between long-term exposure to ambient air pollution and inhalation of particulate matter and harmful gases emitted during extensive forest fires. Furthermore, Nakane demonstrated, through statistically supported research, that specific particulate matter concentrations (ppm values) in the atmosphere are implicated in the etiology of pulmonary diseases, subsequently contributing to the development of other chronic conditions (25). The development of chronic respiratory diseases is influenced by both environmental factors and lifestyle choices. While a direct correlation between educational attainment, sports participation, and respiratory health has yet to be thoroughly explored in the existing literature, observations indicate a higher incidence of respiratory issues among individuals involved in forest fire intervention and those residing in forested areas. This study's findings suggest that higher educational levels positively correlate with an improved quality of life for individuals experiencing actual or potential respiratory complaints. Notably, the most compelling results emerged from the comparative analysis between participants engaged in regular physical activity and their sedentary counterparts.

A notable finding from the cross-sectional study, which utilized the SRI scale, was the elevated SRI score observed in the non-sporting groups. Snedden et al.'s study demonstrated that physical activity and sports positively influence quality of life (26). Consequently, the sports group's low SRI score, comprising individuals directly involved in forest fire intervention, appears inconsistent with the findings of this study. This discrepancy can be elucidated from two perspectives: firstly, the principle of reverse causality, as highlighted in the meta-analysis by Kim et al. (27). Thus, individuals with pre-existing low quality of life, or those whose quality of life has diminished due to health issues, might initiate exercise to improve their circumstances or alleviate symptoms. Thus, sports or physical activities could be seen not as a cause of reduced quality of life, but rather as a consequence or a coping mechanism. Furthermore, in their review of compulsive exercise, Lichtenstein et al. reported that

this condition contributes to injuries and impairments in social relationships and overall life, even though they did not classify it as a psychological disorder (28). Sports programs tailored for professionals may contribute to the development of compulsive exercise, and engaging in excessive or inappropriate types of physical activity can result in injuries or fatigue, consequently diminishing quality of life.

Individual genetic predispositions may influence susceptibility to air pollution. Specifically, Liao et al. highlighted that polymorphisms in genes regulating inflammatory responses could account for the varying severity of respiratory complaints among individuals (29). In this cross-sectional study conducted in the Mediterranean and Aegean regions, the observed respiratory complaints attributable to genetic factors might stem from ancestral exposure to past forest fires. The elevated SRI scores found in the non-athletic, non-alcoholic, and COVID-19 survivor groups suggest a potential association with this phenomenon. Therefore, pharmacogenetic studies could facilitate the development of personalized protective strategies for at-risk populations.

Significant differences observed across age, alcohol, and substance abuse groups indicate a potential role for psychological factors. In support of this, Öztekin and Örkü concluded that significant negative human and natural events impacting society can precipitate the emergence of psychosocial stressors, including post-traumatic stress disorder (PTSD), anxiety, and depression (30). Conversely, Caulfield indicated that from a respiratory physiology perspective, anxiety and stress can exacerbate respiratory complaints by augmenting bronchoconstriction or inflammatory responses (31). The findings from age, alcohol, and substance abuse groups, particularly among those directly involved in forest fire intervention and exposed to air pollution, corroborate these assertions. Notably, with advancing age, psychological factors become more prominent, correlating with a low SRI score. Similarly, the literature supports the observation of low SRI scores in individuals with substance abuse. Conversely, within alcohol groups, the low SRI scores among non-alcohol users imply the presence of other potential metabolic diseases and suggest a substantial role for environmental factors.

Turkoglu examined respiratory system diseases in children and adolescents from a psychological perspective, reporting significant age-group differences (32). Numerous studies have explored the relationship between psychology and respiration, a perspective further supported by the significant

differences observed among this study's age, alcohol use, and substance addiction groups. While limited research currently addresses the impact of global warming and its projected climate changes on the respiratory system, Çimen et al.'s literature review highlighted that global warming and subsequent adverse climatic conditions exacerbate air pollution, leading to various respiratory system diseases, particularly upper respiratory tract infections (33). Large forest fires, frequently occurring in densely forested regions and often during specific seasons, can significantly exacerbate global warming and, consequently, climate change. This creates conditions conducive to the development of respiratory system diseases and various socio-environmental illnesses, such as 'metropolitan bronchitis,' which is characterized by respiratory symptoms.

Moore et al. demonstrated that pathogenic bioaerosols and other biological agents, alongside chemical particles, constitute components of air pollution during forest fires (34). A review by Deng et al. indicates that pathogenic bioaerosols may be a primary cause of respiratory tract infections and allergic reactions, potentially exacerbating respiratory complaints (35). Research exploring the intricate relationship among air pollution, pathogenic bioaerosols, and respiratory tract infections provides crucial insights into the etiology of respiratory complaints. Thus, pathogenic aerosols likely represent a significant factor contributing to the statistically significant differences observed between the groups in this study. Given these findings, it's crucial to acknowledge that the interactions between pathogens in forest fire smoke and the resulting immune responses in the respiratory tract warrant further investigation.

Study Limitations

Individuals participating in the study were exclusively composed of teams that intervened in the 2021 forest fires in Turkey's Mediterranean and Aegean regions (Antalya, Muğla, Isparta, Burdur and surrounding areas). Fire types, intervention strategies, climatic conditions, and the socio-cultural structure of the participants may differ from region to region. The findings obtained cannot be directly generalized to first responder teams across the country or in other geographies.

The sample size (n=83) of the study is small. Consequently, there is a risk of failing to detect relationships or differences that actually exist but have a small effect size. Furthermore, a small sample size reduces the precision of the findings obtained.

Participants were selected using a convenience sampling method. This is a significant factor that limits the extent to which the results can represent the wider population. The findings are specific only to the group included in the study, and generalization of the findings to broader populations requires cautious interpretation.

Since this study has a cross-sectional design, its ability to determine the cause-and-effect direction of the relationships between variables is limited. As all data were collected at a single point in time, it cannot be clarified whether the observed relationships are due to the intervention experience or to an underlying health status. This only expresses a correlation, and more comprehensive studies are needed to understand which variable is the cause and which is the result.

As an observational study, not all confounding factors could be controlled. Unmeasured or unknown confounders that were not included in our study model, but which may be related to both respiratory complaints and quality of life, could have influenced the study findings.

Despite these limitations, the conducted study provides pioneering evidence examining the relationship between respiratory symptoms and quality of life at a cross-sectional level in forest fire intervention teams. The absence of multivariate regression analyses limits the interpretations and the findings obtained have been primarily treated as group comparisons.

In addition to the limitations discussed above, the cross-sectional and self-report survey nature of the data introduces further methodological constraints that must be carefully considered when interpreting the findings. Specifically, the retrospective nature of the survey data increases the risk of recall bias, as participants may not accurately remember their past exposures and symptoms. Furthermore, the reliance on self-report to assess health behaviors and outcomes introduces social desirability bias. This means participants may tend to underreport undesirable behaviors or overreport favorably viewed conditions to align with perceived social norms. To mitigate this risk, the survey was administered on a completely anonymous and voluntary basis. Despite these collective limitations, the data obtained provide important insight into the participants' experiences and symptoms.

Conclusion

This cross-sectional and analytical study preliminarily investigated the relationship between quality of

life, linked to respiratory complaints, and socio-demographic and lifestyle factors in a small (n=83) and convenience sample group of individuals who responded to the 2021 Mediterranean and Aegean Forest fires.

Forest fires release numerous toxic gases and particles, significantly degrading air quality. Following these events, individuals residing near affected regions and personnel from public, private, and non-governmental organizations (NGOs) involved in fire suppression efforts frequently experience severe respiratory diseases, which diminish their quality of life. The harmful effects of air pollution from forest fires on various organs can manifest years later, leading to chronic and fatal conditions like cancer, chronic obstructive pulmonary disease (COPD), and asthma. To mitigate these potential damages, it is crucial to address the serious consequences of forest fires within the framework of preventive health services. Accordingly, educational initiatives should be systematically integrated into the programs of public, private sector, and NGO institutions.

The escalating global warming inevitably leads to climate changes that can cause respiratory system diseases. Regional large forest fires and the subsequent adverse weather conditions represent a significant component of these climate changes, potentially leading to numerous respiratory complaints, especially when compounded by factors like age, alcohol, and substance addiction. Furthermore, existing respiratory pathologies exacerbated by forest fires are worsened by factors such as alcohol and cigarette use, which can further reduce the respiratory rate. Consequently, the detrimental effects of air pollution from forest fires on life expectancy and quality should be considered within this broader context.

Given the rise in air pollution, extensive research is being conducted on preventive health services. This study specifically demonstrates that forest fires inflict irreversible damage to the respiratory tract. Therefore, forest fires warrant consideration as a crucial component of preventive health strategies.

In this study, 'exposure to forest fires' and 'air pollution caused by forest fires' specifically denote smoke exposure. A key limitation was the inability to directly measure smoke concentrations. Nevertheless, significant findings were derived using parameters such as presence in the fire zone and exposure to fire-emitted gases. Future research should aim to quantify smoke exposure using biomarkers and/or air quality sensors.

As a result, individuals actively involved in forest fire suppression will inevitably experience respiratory complaints, which will adversely impact their quality of life. The quality of life indicators, as determined by SRI scores and linked to potential or confirmed respiratory issues, are directly influenced by factors including age, alcohol use, substance addiction, sports participation, and education level. Therefore, this study underscores the necessity for a more detailed examination of air pollution events like forest fires on human health and the various factors influencing respiratory physiology.

The intensive release of chemical and biological particles from forest fires directly impacts respiratory function and, consequently, quality of life. To enhance the quality of life and enable early identification of existing or potential health issues in individuals directly involved in forest fire response, routine health screening procedures are essential. These screenings should specifically include pulmonary function tests, evaluation of cardiovascular parameters, and the development of health policies addressing the potential for post-traumatic stress disorder. Beyond periodic health screenings as part of preventive health services, establishing peer support groups with a focus on sociological aspects is crucial. Such initiatives can alleviate emotional burdens through the solidarity of individuals who have undergone similar experiences.

Developing psychological and sociological preventive health services should precede forest fire events. It's crucial to utilize personal protective equipment (PPE) specifically designed for forest fires or other extraordinary blazes involving the dispersion of chemical-biological particles. This PPE must include high-temperature-resistant, ergonomic masks offering superior gas and particle filtration. Furthermore, a fresh air breathing apparatus for use during a fire should be supplied with adequate spares, and its periodic maintenance must be conducted without interruption. Regular drills on both maintenance procedures and the proper use of this breathing apparatus are also essential.

Direct intervention in forest fires presents numerous risks. Thus, beyond personal protective equipment, technological devices capable of monitoring body temperature and heart rate should be supplied, and these physiological parameters meticulously tracked throughout fire suppression operations.

In any emergency, meticulous work planning and systematic organization are paramount. To mitigate direct exposure to toxic gases and particles, optimal

working hours, shifts, and rest periods must be established. Work scheduling should prioritize flexibility and be people-oriented, thereby avoiding prolonged and continuous shifts.

Approaches incorporating psychological and sociological support alongside the provision of physical equipment are not merely practical measures; they also significantly enhance the quality of life by positively influencing the SRI scores of field personnel directly involved in fire suppression.

The findings obtained from this study, due to the nature of its cross-sectional design, only demonstrate a correlation, and the ability to establish a causal relationship between variables is limited.

Analyses indicate that participants in the 45-65 age group have a statistically lower quality of life score related to respiratory complaints compared to the 18-24 age group. This suggests an association highlighting the potential for advanced age to be more negatively affected following fire exposure.

Individuals who reported substance addiction have significantly lower quality of life scores compared to those who did not. This finding is consistent with existing literature, suggesting that substance use exacerbates the potential negative effects of fire exposure.

A higher level of education was found to be associated with a better quality of life.

The finding that those who do not participate in sports have higher SRI scores than those who do, and that some groups who use alcohol report higher scores than non-users, must be interpreted cautiously due to methodological limitations such as reverse causality, social desirability bias, or unaddressed confounding factors.

In conclusion, this study suggests that factors such as age and substance use have a potential impact on respiratory complaints and quality of life for fire response teams in Turkey's Mediterranean and Aegean regions. It is recommended that these preliminary data be used to guide the planning of regional and post-exposure intervention programs.

Future studies should employ larger and randomly selected samples. Self-reported data should be supported by objective biological and physiological measurements, and the effect of confounding factors should be controlled through multivariate analyses.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Ethical Approval

The study in question was carried out with the decision numbered 10 and dated 10.11.2021 of the Suleyman Demirel University Health Sciences Ethics Committee. The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki of the World Medical Association (WMA).

Consent to Participate and Publish

Consent to participate was obtained from all participants.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of Data and Materials

Datasets generated and/or analyzed during the current study will be made available by the corresponding author upon request from the editor or reviewers.

Artificial Intelligence Statement

The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables or their corresponding captions.

Authors Contributions

TB: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Visualization; Writing-original draft; Writing- review & editing.

MS: Validation; Writing-original draft; Formal analysis; Critics

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Comparative Study of Proximal Femoral Nailing in Trochanteric and Subtrochanteric Fractures with or Without Cerclage Cable Augmentation

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Cite this article as: Karapinar SE, Dincer R, Ceylan D. Comparative Study of Proximal Femoral Nailing in Trochanteric and Subtrochanteric Fractures with or Without Cerclage Cable Augmentation. Med J SDU 2025;32(4):283-290.

Abstract

Objective

This study aimed to examine the effect of the use of proximal femoral nail (PFN) and cable cerclage on the radiological and functional results and correlation with complications such as non-union and malunion, in cases of trochanteric and subtrochanteric femur fractures.

Material and Method

The study included patients treated with PFN and/or cable cerclage because of closed, isolated spiral/oblique subtrochanteric and trochanteric fractures with a minimum follow-up period of 1 year. Patients were excluded if they had a pathological fracture, open fracture, any additional fracture, or if the epiphyseal line was open. The fractures were classified according to the AO/OTA classification. Bone union was evaluated on anteroposterior and lateral/oblique radiographs taken at postoperative 2, 4, 6, and 12 months. Functional evaluation was made according to the lower extremity functional scale and visual analog scale.

Results

The time to union was a mean of 20 weeks (range, 16-28 weeks) for patients treated with PFN + cable and a mean of 17 weeks (range, 17-32 weeks) for the group treated with PFN alone. In the lower extremity functional evaluation scale, the mean score was 74

(range, 74-80) and the percentage was calculated as 93% (88-100%) in the study group, and the mean score was 55 (range, 20-74) and 56% (35-93%) in the control group. According to the Baumgartner et al criteria for radiological reduction quality evaluation, 33 patients were reported as good, 17 patients as acceptable, and 8 patients as poor. Radiological and clinical union was obtained within 6 months in 45 patients. Delayed union was determined in 1 patient in the study group and in 3 patients in the control group. Although the PFN-only group showed slightly faster union, this may reflect differences in age distribution or fracture complexity rather than treatment superiority. (Figure 1 shows a representative postoperative X-ray of a PFN with cerclage).

Conclusion

The results of this study demonstrated that the use of PFN and cable cerclage is a reliable method in the treatment of trochanteric and subtrochanteric fractures, which increases fixation stability, allows early mobilisation and weight-bearing, and may provide improved functional outcomes. Surgical success and patient functionality will be increased with the additional use of cable cerclage in patients with a free unstable fracture where an acceptable closed reduction cannot be made.

Keywords: Cable; cerclage; pfn; trochanteric fracture; subtrochanteric fracture.

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Received: 12.04.2025 • **Accepted:** 10.09.2025

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Introduction

In proximal femur trochanteric fractures, the fracture line generally extends from the trochanter major to the minor. In reverse oblique fractures, it extends from distal to medial (1). The subtrochanteric femur is defined as 5cm distal to the proximal and mid-third junction or inferior to the trochanter minor (2). Subtrochanteric femur fractures show a bimodal distribution. They develop as a result of high-energy trauma in young individuals, and in the elderly, even low-energy trauma can lead to fracture (3). This is the body region exposed to the highest tension and compressive forces and has limited blood circulation (4). Deformation occurs with the effect of adherent muscles in the procurvatum, abduction, and external rotation positions (5).

Intertrochanteric fractures form as a result of direct or indirect forces. Compression of the region of cancellous structures is caused by the effect of sudden forces applied to the trochanter major and minor, resulting from the direct or indirect effect of forces applied along the femur axis (6). Intertrochanteric fractures are seen more in individuals aged ≥ 65 years (6). Several series have reported that they are seen at rates of 2-8-fold more in females than males. The reasons that they are seen more in females include greater exposure to metabolic bone disease, the pelvic structure is wider and the femoral neck-shaft angle is smaller, and longer life expectancy (7).

In the treatment of patients with femur trochanteric region fractures, the main aim is to regain the pre-fracture living standard, avoid being bedridden with early mobilisation, and minimise complications that could occur after the fracture. There is a question of instability in hip fractures, which are fractures of the trochanter minor, those where the fracture line is reverse oblique, those with varus angulation and a vertical fracture line, when there is displacement evident on lateral radiographs, and in fractures with 4 fragments extending to the subtrochanteric region (8). The main aim in trochanteric region fractures is to obtain anatomic reduction and apply rigid fixation that can be maintained. Implant failure and the development of associated non-union can lead to serious problems of shortness and deformity. However, a standard treatment method remains a matter of debate.

Better reduction is obtained with open reduction. However, fracture hematoma evacuation causes extensive soft tissue and periosteal stripping, and this hurts union (9). In intramedullary fixation, reduction is generally obtained indirectly, and the biology

of the soft tissue is damaged less than in open reduction. Moreover, among the fixation materials, it is accepted as the most advantageous treatment method biomechanically (9, 10). Sometimes it may not be possible to obtain an acceptable reduction with an indirect method, and therefore, open reduction is required. To increase the stability of fixation after this reduction, the application of cerclage or cable has been widely used in recent years (11). This cerclage, or the number of cables and placement, depends to a great extent on the fracture configuration and the surgeon operating. Increased complexity of fracture patterns and the need for anatomic reduction have caused an increase in their use (12). Although the use is not as frequent as it is thought to hurt trochanteric region vascularity, recent studies have shown that the application of cerclage does not impair microvascular circulation (13, 14).

Fixation is required, which allows weight-bearing and early mobilisation, and which will have the least effect on the postoperative biological healing process. Therefore, this study aimed to evaluate the potential effect of applying cable cerclage in addition to intramedullary nailing, not only in subtrochanteric femur fractures but also in unstable trochanteric region fractures.

Material and Method

The study included 65 patients with a closed isolated spiral /oblique subtrochanteric or trochanteric femur fracture applied with fixation using PFN or PFN plus cable cerclage between January 2014 and August 2020, and had a minimum 1-year follow-up period. Approval for the study was granted by the Ethics Committee (Decision No:293, dated:10.09.2021). All the study participants provided a signed informed consent form. Patients were excluded if they had a pathological fracture, open fracture, any additional fracture, or if the epiphyseal line was open. Of the 65 patients who met the defined criteria, mortality occurred in 3 patients during follow-up, and 4 could not be contacted, so the evaluation was made of 58 patients who completed regular follow-up and attended the final follow-up examination.

The fractures were classified according to the AO/OTA classification system (15). Bone union was evaluated on anteroposterior and lateral/oblique radiographs taken at postoperative 2, 4, 6, and 12 months. The presence of callus tissue in 3 of the 4 cortices in the fracture line was evaluated as union. Cases not showing union in the 6th month were recorded as non-union, and those with incomplete

union as delayed union. Reduction quality (shortness, angulation, rotation) was evaluated according to the modified Baumgartner et al criteria (good, acceptable, and poor, based on cortical displacement <4mm and angulation <10°) (16, 17). Functional evaluation was made according to the lower extremity functional scale, and visual analog scale (VAS) (18, 19). To eliminate any conflicting results, all the patients were evaluated by two different surgeons. Complications such as infection, shortness, deformity, or reoperation observed during follow-up were recorded. Cases with implant failure and implant extraction were reported.

Surgical Technique and Postoperative Protocol

All the operations were performed on a radiolucent table with the patient in the lateral decubitus position. Regional anaesthesia was administered to 37 patients and general anaesthesia to 21. First-generation cephalosporin at a dose of 1gr was administered preoperatively to all patients. By making controlled traction under fluoroscopy, an image in the anteroposterior plane was obtained. After confirmation with fluoroscopy of the region where the cable was to be applied from the lateral of the fracture line, a 5cm incision was made. The fracture was reduced with the mini-open method. While reducing the fracture with a reduction clamp, fixation was applied with one or more cables. Then the proximal femoral nail (PFN) was placed, checking that the tip-apex distance was sufficient with fluoroscopy. A thick K-wire was advanced to the column over the proximal guide. The anteroposterior position of the K-wire was checked with fluoroscopy. While maintaining the temporary fixation position with the K-wire, lateral fluoroscopic images were obtained in internal and external rotation by moving the hip into 90° flexion and 45° abduction. The version of the K-wire was confirmed. Compression was applied by placing lag screws in the femoral neck. All the distal locking screws were locked statically (Figure 1).

Statistical Analysis

Data obtained in the study were analyzed statistically using IBM SPSS version. 25.0 software (SPSS Inc., Chicago, IL, USA). Conformity of the data to normal distribution was assessed with the Kolmogorov-Smirnov test. Descriptive statistics were stated as mean±standard deviation (SD), median, minimum, and maximum values for continuous variables, and as number (n) and percentage (%) for categorical variables. In the analyses of the data, the Chi-square test, Mann-Whitney U-test, Kruskal-Wallis test, and Spearman correlation analysis were used. A value of $p < 0.05$ was considered statistically significant.

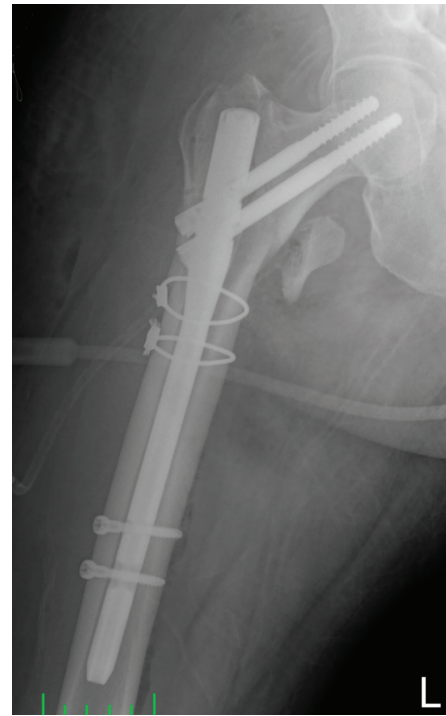


Figure 1

Sample postoperative X-ray image of a patient treated with PFN and cerclage cable.

Results

Evaluation was made of 58 patients, comprising 30 females and 28 males. PFN+cable cerclage was applied to 33 patients and PFN alone to 25 patients as a control group. The hip fracture was right-sided in 32 patients and left-sided in 26. The etiology of the fracture was a traffic accident in 20 patients and a fall from height in 38. According to the AO/OTA fracture classification, 13 fractures were 31-A.1, 11 fractures were 31-A.2, and 34 fractures were 31-A.3. The fracture pattern was determined as oblique in 28 patients and spiral fracture in 30 patients (Table 1).

The operation duration was 90 mins (range, 50-120 mins) in the PFN+cable group and 70 mins (range, 35-100 mins) in the control group. The intraoperative duration of fluoroscopy use was a mean of 96 secs (range, 34-321 secs) in the PFN+cable group and 100 secs (range, 40-150 secs) in the control group. The mean follow-up period was 33 months (range, 12-80 months) for all the patients.

The time to union was a mean of 20 weeks (range, 16-28 weeks) for patients treated with PFN + cable and a mean of 17 weeks (range, 17-32 weeks) for the group applied with PFN alone. In the lower extremity

Table 1 Demographic data of patients.

	Cable-cerklage group (n=33)	Control group (n=25)	p score
Age	49 ± 17	62 ± 11	<0.001
Sex			
F	17	13	0.671
M	16	12	
Side			
R	18	14	0.412
L	15	11	
Etiology			
Motor accident	13	7	0.366
Falling from high	20	18	
Type of fracture			
Spiral	19	11	0.306
Oblique	14	14	
AO Class. (%)			
31A1.1	-		
31A1.2	2 (6.1%)	4 (16%)	
31A1.3	2 (6.1%)	5 (20%)	
31A2.1	-	1 (4%)	
31A2.2	1 (3%)	2 (8%)	
31A2.3	-	7 (28%)	
31A3.1	15 (45.6%)	1 (4%)	
31A3.2	-	-	
31A3.3	13 (39.2%)	5 (20%)	

Abbreviations: F:female, M:male, R:right, L:left.

Table 2 Radiological and Clinical data of the patients

	Cable-cerklage group (n=33) Med. (min-max)	Control group (n=25) Med.(min-max)	p score
Union time (w)	20 (16-28)	17 (17-32)	0.048*
Surgery Time (min.)	90 (50-120)	70 (35-100)	< 0.001*
Fluoroscopy time (sec.)	96 (34-321)	100 (40-150)	0.626
Tip-apex distance(mm)	16 (12-24)	23 (17-28)	< 0.001*
Shortness (mm, mean)	0.9	3.4	< 0.001*
Coronal angulation (x°)	0.6 (-3, 4)	0.9 (-6, 10)	0.729
Sagittal angulation (x°)	0.4 (-4,4)	1.4 (-4,7)	0.261
VAS (med/min-max)	0.8 (0-4)	4 (2-7)	< 0.001*
LEFS	74 (74-80)	55 (20-74)	<0.001*
LEFS %	93 (88-100)	56 (35-93)	<0.001*

Abbreviations: w:week, min:minute, sec: second, VAS: visual analog score, LEFS: Lower Extremity functionale scale.

Table 3 Baumgaertner reduction quality criteria

Reduction quality	Cable-cerklage group (n=33)	Control group (n=25)
Good	28	5
Acceptable	5	12
Poor	0	8

Table 4 Complication data of patients who underwent cable cerclage and control group

Complication	Cable-cerklage group (n=33)	Control group (n=25)
Serous discharge	1	3
Superficial infection	2	2
Delayed union	1	3
Failure	-	4
Re-operation	-	5

functional evaluation scale, the mean score was 74 (range, 74-80) and the percentage was calculated as 93% (88-100%) in the study group, and the mean score was 55 (range, 20-74) and 56% (35-93%) in the control group. The tip-apex distance was measured radiologically as 16mm (range, 12-24mm) in the PFN+cable group and 23mm (range, 17-28mm) in the control group. Shortness developed in 24 patients, evaluated a mean of 0.9mm in the study group and a mean of 3.4mm in the control group. Coronal angulation was measured radiologically as mean 0.6° (-3° to 4°) in the study group and as 0.9° (-6° to 10°) in the control group, and sagittal angulation as mean 0.4° (-4° to 4°) in the study group and as 1.4° (-4° to 7°) in the control group (Table 2). Although the PFN-only group showed slightly faster union, this may reflect differences in age distribution or fracture complexity rather than treatment superiority.

According to the Baumgartner et al criteria for radiological reduction quality evaluation, 33 patients were reported as good, 17 patients as acceptable, and 8 patients as poor (Table 3). (Figure 1 shows a representative postoperative X-ray of a PFN with cerclage).

Radiological and clinical union was obtained within 6 months in 45 patients. Superficial infection was

observed in 4 patients with serous discharge continuing after the operation, which recovered with antibiotic treatment in 3 patients. In one of these 4 patients, one patient required reoperation due to superficial infection. Delayed union was determined in 1 patient in the study group and in 3 patients in the control group. There was no implant failure, and reoperation was not required in any of the PFN+cable group, and in the control group, implant failure developed in 4 patients, and reoperation was required in 5 (Table 4).

Discussion

The results of this study demonstrated that the application of cable cerclage with open reduction provided ideal reduction appropriate to normal anatomy. This technique is generally difficult to achieve using closed reduction alone. In cases of closed reduction, when an acceptable reduction cannot be obtained, reliance on fracture hematoma does not make a positive contribution to union. Good reduction not only facilitates the nailing procedure but can also be considered to make the whole reduction more stable, because the majority of weight-bearing forces are transferred through aligned bone fragments.

Trochanteric and subtrochanteric spiral/oblique fractures are difficult fractures for treatment and

rehabilitation. Open and closed methods are used in treatment. Open reduction and internal fixation provide better visualisation of the fracture line, and anatomic reduction is obtained. Wide surgical exposure causes soft tissue damage, periosteal stripping, and fracture hematoma evacuation. The biological environment required for fracture healing is damaged. Although excellent bone union is obtained with the use of a plate as fixation material, it has been reported that the mechanical performance of plates is lower than that of intramedullary fixation materials (20). Intramedullary fixation methods are biomechanically superior in trochanteric and subtrochanteric fractures, but the disadvantage of the method is indirect reduction of the fracture.

The effect of deforming muscle forces can cause incorrect selection of trochanteric entry and malreduction of the fracture. Therefore, better reduction can be provided minimally invasively with reduction clamps and cable cerclage in fracture types where it is required (21). The results of the current study show that the cable cerclage method provided an anatomic reduction or close to an anatomic reduction. Generally, this technique is not possible with closed reduction alone.

In a study by Boopalan et al, it was reported that, as intramedullary nailing showed a supportive function in intertrochanteric fractures, there was a limited effect of the instability created by an unstable lateral femoral cortex. However, in fractures where the lateral femoral cortex has been displaced during the injury, it is not clear whether or not the supportive function provided by intramedullary nailing contributes to stability and union. Therefore, there is no clear guideline for additional treatment of displaced and free lateral femoral cortex fragments. The findings of recent studies in the literature have shown that, in contrast to what has been assumed, the application of cable cerclage does not have any harmful effect, such as lateral thigh pain or delayed bone union (22, 23).

Recommendations can be found in orthopaedic literature related to the addition of minimally invasive cable cerclage to subtrochanteric fractures with a similar effect to reverse intertrochanteric fractures (24). The application of cable cerclage has been advocated in interventions for failed closed reduction. With the help of a clamp, reduction combinations are used in spiral and oblique fractures (3). It has been reported that following cable cerclage use, the reoperation rates and reduction quality are better, and there is a smaller amount of fracture displacement (25).

When weight-bearing is permitted early in the postoperative period, it is important that weight transfer is obtained with aligned bone fragments to protect the reduction and to reduce complication rates. In a biomechanical study, additional cable cerclage was reported to provide significant posteromedial support and to reduce the risk of osteosynthetic failure in complex fractures (10). In the current study, reoperation because of mechanical problems was not required for any patient treated with cable cerclage. Moreover, the application of cable cerclage reduced lateral femoral cortex displacement and was seen to provide good posteromedial support. In contrast to expectations, fewer complications were seen in the patient group with cable cerclage applied with a minimally invasive method compared to the control group.

There is a belief that non-union emerges as a result of impaired blood support and bone vascularity associated with the use of cable cerclage (11). This is associated with excessive dissection of periosteal and soft tissue. If minimally invasive techniques are applied, the disruption in soft tissue and bone vascularity is reduced (26). In an animal model without fracture, vascular support was seen to be preserved following the use of cable cerclage (27). The results of the current study showed that there was no negative effect of the use of cable cerclage. In all the cases treated with cable cerclage, full bone union was obtained, and no difference was determined between the cable cerclage group and the control group with respect to the time to bone union.

In a study by Codesido et al, the mean time to union in patients applied with cerclage was reported as 4.35 ± 1.75 months, complications were seen in 1 (3.3%) patient, and reduction success was good in 29 (96.7%) patients, acceptable in 1 (3.3%), and poor in none (28). Gong et al reported a mean time to union of 20 weeks (range, 16-24 weeks) with no major complications such as non-union, malunion, or implant breakage. The neck-shaft angle was restored up to 5° , and translation reduced from 2.05cm to 0.15cm (29). In a study of 20 patients who underwent cerclage, Hoskins et al did not observe any major complications, and while major complications were reported in 9.7% of a group of 135 patients, it was stated that this rate would be 11.4% when cerclage was not applied (30). In the current study, the time to union was a mean of 20 weeks (range, 16-28 weeks) for patients treated with PFN + cable and a mean of 17 weeks (range, 17-32 weeks) for the group treated with PFN alone. In the lower extremity functional evaluation scale, the mean score was 74 (range, 74-80) and the percentage

was calculated as 93% (88-100%) in the study group, and the mean score was 55 (range, 20-74) and 56% (35-93%) in the control group. According to the Baumgartner et al criteria for radiological reduction quality evaluation, 33 patients were reported as good, 17 patients as acceptable, and 8 patients as poor. The mean VAS scores were recorded as 1 (range, 0-4) in the study group and 4 (range, 2-7) in the control group.

Limitations of this study were that it was retrospective in design, the number of patients was relatively low, and, because of an optimal fracture classification system, some fracture types were labelled according to the closest fracture type. There is a need for further prospective, randomised controlled, multicentre studies to compare different fixation materials in the same fracture patterns in homogenous age ranges.

Conclusion

The results of this study demonstrated that the use of PFN and cable cerclage is a reliable method in the treatment of trochanteric and subtrochanteric fractures, which increases fixation stability, allows early mobilisation and weight-bearing, and may provide improved functional outcomes. Surgical success and patient functionality will be increased with the additional use of cable cerclage in patients with a free unstable fracture where an acceptable closed reduction cannot be made.

Acknowledgment

I would like to thank Dr. Umut Can Duvarci for his assistance in data collection.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Ethical Approval

Approval for the study was granted by the Ethics Committee (Decision No:293, dated:10.09.2021-Suleyman Demirel University). The study was conducted in accordance with the principles set forth in the Declaration of Helsinki.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of Data and Materials

Data availability: Data available on request from the authors. Data sets generated and/or analyzed during the current study can be requested from the authors' e-mail addresses.

Artificial Intelligence Statement

No artificial intelligence (AI) tools were used in this article.

Authors Contributions

SEK: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Visualization; Writing-original draft.

RD: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Visualization; Writing-original draft; Writing-review & editing.

DC: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Visualization; Writing-original draft; Writing-review & editing.

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The Relationship Between Urinary Incontinence and Motor Symptoms in Patients with Stroke

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Cite this article as: Yaşar P, Duray M, Kutluhan S, Yürekli VA. The Relationship Between Urinary Incontinence and Motor Symptoms in Patients with Stroke. Med J SDU 2025;32(4):291-298.

Abstract

Objective

This study aims to evaluate the relationship between post-stroke urinary incontinence and the severity of spasticity, balance, and gait performance.

Material and Method

This cross-sectional study was conducted with 46 patients with stroke. The Modified Rankin Scale (MRS) was used to determine the functional status of the participants. A 24-hour pad test was performed to assess urinary incontinence, and the Danish Prostate Symptom Score (DANN-PSS) was utilized to evaluate urinary function. Spasticity, as one of the motor symptoms, was assessed using the Modified Ashworth Scale (MAS), while balance and gait were evaluated through the Tinetti Balance and Gait Assessment.

Results

The mean age of patients with urinary incontinence

was significantly higher than that of those without incontinence ($p<0.05$). When comparing balance and gait performance between groups, the balance scores of the incontinent group were found to be significantly lower ($p<0.05$), whereas no significant difference was observed in gait scores ($p>0.05$). According to the Tinetti test results, both the balance and total scores were significantly lower in the group with urinary incontinence ($p<0.05$).

Conclusion

While urinary incontinence in post-stroke patients was not associated with spasticity, it was negatively associated with balance and, to a lesser extent, walking performance. These findings suggest that UI may contribute to functional dependence by indirectly affecting motor functions.

Keywords: Stroke, urinary incontinence, spasticity, balance, gait.

Introduction

Urinary incontinence (UI) is defined by the International Continence Society as the involuntary loss of urine that can be objectively demonstrated (1). UI is one of

the most common and severe complications observed following stroke (2). It has been found that more than 80 % of stroke survivors experience at least one abnormal urinary symptom, and approximately 43.5 % report urinary incontinence at three months

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Received: 19.06.2025 • **Accepted:** 04.09.2025

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poststroke (3). Post-stroke UI may arise from both direct factors, such as damaged neural pathways, and indirect factors, such as motor, sensory, and cognitive impairments (4). It is known that UI after stroke hinders patients from performing physical functions like dressing and mobility, resulting in limitations in activities of daily living, delayed functional recovery, balance impairments, and an increased risk of falls (5,6). Consequently, patients with UI become more dependent on others and experience a decline in quality of life (7).

In patients with stroke, UI may be directly associated with the site of the cerebral lesion or may result from secondary motor symptoms such as difficulty in reaching the toilet (8). Additionally, increased tone in the lower extremities and external sphincter following stroke is presumed to exacerbate voiding dysfunction and incontinence (9). Prior studies have highlighted a relationship between urinary problems and lower extremity spasticity in stroke survivors, indicating that those with both spasticity and UI demonstrate lower levels of independence in daily activities (10,11).

The main factors affecting independence in daily life after stroke are motor problems such as increased tone, balance and walking disorders (12). Spasticity, defined as a motor disorder characterized by a velocity-dependent increase in muscle tone resulting from excessive stimulation of the stretch reflex (13), reaches its maximum level in the 1-3 month period after stroke and causes disorders such as muscle shortening and soft tissue contractures in the long term (9,14,15). Spasticity in the lower extremities most frequently presents with adduction at the hips, extension at the knees, and inversion at the ankles (16). Balance and gait disorders are observed in stroke patients as a result of increased tone, motor control deficiencies and muscle weakness (11). The physical disability that spasticity causes limits people's ability to perform basic activities such as self-care and ambulation (15,17).

Changes in muscle tone, loss of strength, and gait and balance disorders following stroke are among the primary factors influencing recovery and functional independence (18). Early identification and management of risk factors that may cause functional loss in stroke survivors are crucial (19). Motor symptoms such as tone abnormalities, balance, and gait dysfunctions, when accompanied by urinary symptoms, may negatively affect patients' ability to carry out daily activities and maintain independent living (15). Post-stroke UI also impacts the duration of treatment, patient participation in treatment and

motivation during the rehabilitation process. Lower limb motor impairment has been suggested as a potential cause of UI in stroke patients (20). The literature indicates that post-stroke UI adversely affects functionality, including activity performance and mobility (21).

Evaluating UI and motor symptoms in stroke rehabilitation may help guide treatment approaches and improve functional outcomes of stroke survivors. This study aims to investigate the relationship between post-stroke UI and spasticity, balance, and gait functions.

Material and Method

This study was designed as a cross-sectional clinical investigation and included patients in the chronic stage of stroke who applied to the Neurology Outpatient Clinic of Süleyman Demirel University Research and Practice Hospital between September 2023 and February 2024. Ethical approval was obtained from the Clinical Research Ethics Committee of the Faculty of Medicine, Süleyman Demirel University (Date: 16.11.2021, Protocol No: 72867572-050.01.04-320), and the study was registered on ClinicalTrials.gov (NCT06333119). Inclusion criteria were as follows: aged between 20–65 years, history of a single stroke at least three months prior, Modified Rankin Scale (MRS) score between 0–2, ability to stand and walk independently or with a walking aid, and proficiency in speaking and understanding Turkish. Patients with speech disorders impairing intelligibility, comorbid neurological conditions, orthopedic or cardiovascular disorders that could affect balance, pregnancy, or visual/hearing impairments were excluded (Figure 1).

While calculating the sample size of the study, the effect size was calculated according to the 24-hour pad test results in the stroke patient group in the study by Arkan et al. (22), a one-tailed power analysis was performed using G*Power 3.1.9.2 (Universität Kiel, Germany). With an effect size (d) of 0.438, 90% power, and a type I error rate of 0.05, the required sample size was determined as n = 46.

Patients who voluntarily agreed to participate in the study signed an informed consent form, their demographic information was recorded, and functional level was determined using the Modified Rankin Scale (MRS). Participants scoring 0–2 on the MRS underwent a 24-hour pad test for UI assessment. Patients who were objectively identified as having incontinence based on pad test results were included in the group with UI. The Danish Prostate Symptom Score (DANN-PSS)

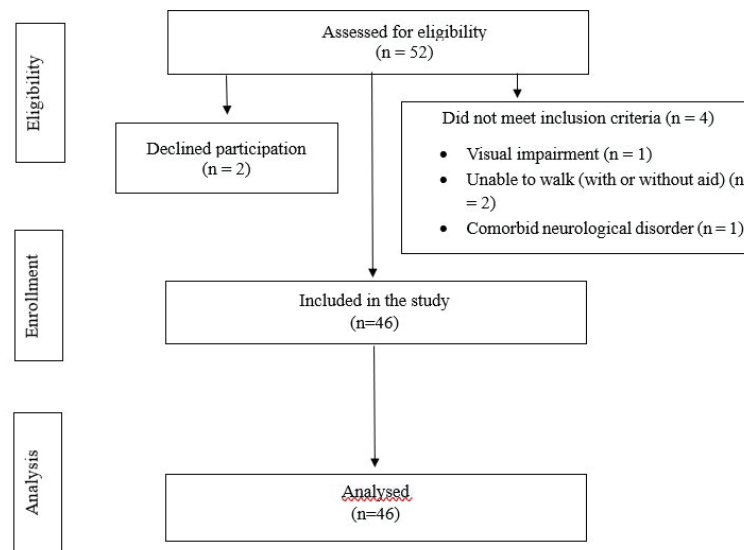


Figure 1
Flow chart

questionnaire was used to assess bladder storage and urinary function. Spasticity of hip musculature was assessed using the Modified Ashworth Scale (MAS), while balance and gait functions were evaluated via the Tinetti Balance and Gait Assessment.

Modified Rankin Scale (MRS): Used to assess functional status, ranging from 0 (no symptoms) to 6 (death) (23). Scores ≥ 4 indicate severe functional impairment. Only patients with MRS scores of 0–2 were included in this study (0: No symptoms; 1: No significant disability despite symptoms; able to carry out all usual duties and activities; 2: Slight disability; unable to carry out all previous activities but able to look after own affairs without assistance; 3: Moderate disability; requires some help but able to walk without assistance; 4: Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance; 5: Severe disability; bedridden, incontinent, and requires constant nursing care and attention; 6: Dead).

24-Hour Pad Test: Participants collected all pads used in the last 24 hours in an airtight bag and brought a clean identical pad for comparison. The used pad weight was calculated by subtracting the expected weight (number of used pads $\times$ clean pad weight) from the total collected weight. Incontinence severity was categorized as: Mild: 1.3–19 g; Moderate: 20–74 g; Severe: ≥ 75 g (24).

Danish Prostate Symptom Score (DANN-PSS): A 12-item questionnaire applicable to both sexes, evaluating

urinary complaints and associated discomfort. Each question is scored between 0–3 points depending on the complaint and the discomfort felt due to this complaint. Each question has complaint and discomfort scores, these values are multiplied by each other to calculate the total score (the highest score is 9). If the complaint is serious but there is no discomfort, the total score is zero. Final score is the product of complaint and discomfort scores, with a total possible score ranging from 0–108. Turkish validity and reliability were established in 2017 (25).

Modified Ashworth Scale (MAS): A reliable scale for assessing spasticity, scored from 0 to 4 [0: No increase in tone; 1: Slight increase at end of range; 1+: Slight increase through $<50\%$ of range; 2: Marked increase through most of the range; 3: Considerable increase, passive movement difficult; 4: Affected joint(s) rigid] (11).

Tinetti Balance and Gait Assessment: Consists of 16 items: 9 for balance and 7 for gait. Total score interpretation: ≤ 18 : High fall risk; 19–24: Moderate fall risk; ≥ 25 : Low fall risk (26). Turkish validation was conducted by Ağırca in 2009 (27).

Statistical Analysis

All statistical analyses were performed using SPSS 24.0 (IBM Corporation, Armonk, NY, USA). Normality of data was evaluated using the Kolmogorov-Smirnov test, with $p < 0.05$ considered statistically significant. Continuous variables are presented as mean $\pm$ standard deviation, and categorical variables

as counts and percentages. Due to non-normal distribution, Mann-Whitney U test was used for group comparisons and Spearman's correlation analysis to evaluate relationships among variables.

Results

Out of 52 women evaluated for eligibility, four did not meet the inclusion criteria and two declined participation, resulting in a final sample of 46 participants. The duration of stroke in the group with UI was 25.25 ± 28.01 years, while the duration of stroke in the group without UI was 22.63 ± 24.91 years. The mean age of participants with urinary incontinence (UI) was 64.00 ± 12.92 years, significantly higher than the

53.73 ± 13.74 years observed in those without UI ($p < 0.05$; Table 1).

When grouped according to UI status, participants without UI demonstrated significantly higher balance scores and total scores on the Tinetti test compared to those with UI ($p < 0.05$; Table 2).

Table 3 presents the correlations between UI and motor symptoms. There is a low negative correlation between UI and balance and gait in the group with UI ($r = -0.312^*$, $p = 0.035$). Similarly, a weak negative correlation was found between UI severity and the total Tinetti score ($r = -0.329^*$, $p = 0.026$).

Table 1 Demographic characteristics of participants with and without UI

	Group with UI (n=16) Mean $\pm$ Sd	Group without UI (n=30) Mean $\pm$ Sd	p
Age	64.00 $\pm$ 12.92	53.73 $\pm$ 13.74	0.013
BMI	27.87 $\pm$ 2.75	27.90 $\pm$ 3.74	0.75
Stroke duration	25.25 $\pm$ 28.01	22.63 $\pm$ 24.91	0.75
	Group with UI n (%)	Group without UI n (%)	p*
Dominant side			
Right	16 (100)	27 (90)	0.542
Left	0	3 (10)	
Affected side			
Right	8 (50)	10 (33.3)	0.347
Left	8 (50)	20 (66.6)	
Gender			
Female	8 (50)	10 (33.3)	0.347
Male	8 (50)	20 (66.6)	
Education			
Primary school	11 (68.8)	16 (53.3)	0.321
Secondary school	2 (12.5)	4 (13.3)	
High school	2 (12.5)	5 (16.6)	
University graduate	0	5 (16.6)	
Postgraduate	1 (6.3)	0	
Marital status			
Married	12 (75)	24 (80)	0.665
Widowed	3 (18.8)	3 (10)	
Single	1 (6.3)	3 (10)	
MRS			
0	6 (37.5)	20 (66.6)	0.146
1	6 (37.5)	7 (23.3)	
2	4 (25)	3 (10)	

UI: Urinary Incontinence, MRS: Modified Rankin Scale, n: number, p*: Chi-square test, p: T-test, SD: Standard Deviation.

Table 2 Comparison of balance, gait and hip spasticity between with UI and without UI groups

	Group with UI n:16	Group without UI n:30	p
Tinetti balance test	12.75±3.37	13.86±3.07	0.09
Tinetti gait test	8.81±2.50	10.06±2.25	0.058
Tinetti total score	21.56±5.58	23.93±4.96	0.044
Right add. spasticity	0.37±0.88	0.06±0.25	0.191
Left add. spasticity	0.12±0.50	0.23±0.62	0.526
Right Hip Extensor Spasticity	0.06±0.25	0.06±0.25	0.958
Left Hip Extensor Spasticity	0.00±0.00	0.13±0.43	0.103

UI: Urinary Incontinence, add: adductor muscle, p<0.05. Mann Whitney U test.

Table 3 Correlation between urinary incontinence severity and motor function in participants with UI

		Right hip add.	Left hip add.	Right hip ext.	Left hip ext.	Tinetti balance	Tinetti gait	Tinetti total
DANN-PSS	r p	0.264 0.077	-0.153 0.310	0.260 0.081	-0.063 0.675	-0.229 0.125	-0.112 0.460	-0.200 0.182
Pad test	r p	0.188 0.211	-0.112 0.460	0.043 0.777	-0.187 0.212	-0.312* 0.035	-0.304* 0.040	-0.329* 0.026
Right hip add.	r p	1.000 .	-0.122 0.421	0.743** 0.000	-0.092 0.543	-0.0422** 0.004	-0.195 0.194	-0.367 0.012
Left hip add.	r p	-0.122 0.421	1.000 .	-0.092 0.542	0.774** 0.000	-0.308* 0.038	-0.329* 0.025	-0.315* 0.033
Right hip ext.	r p	0.743** 0.000	-0.092 0.542	1.000 .	-0.070 0.645	-0.355* 0.016	-0.213 0.155	-0.334* 0.023
Left hip ext.	r p	-0.092 0.543	0.774** 0.000	-0.070 0.645	1.000 .	-0.354* 0.016	-0.386** 0.008	-0.371* 0.011
Tinetti balance	r p	-0.0422** 0.004	-0.308* 0.038	-0.355* 0.016	-0.354* 0.016	1.000 .	0.772** 0.000	0.928** 0.000
Tinetti gait	r p	-0.195 0.194	-0.329* 0.025	-0.213 0.155	-0.386** 0.008	0.772** 0.000	1.000 .	0.939** 0.000
Tinetti total	r p	-0.367 0.012	-0.315* 0.033	-0.334* 0.023	-0.371* 0.011	0.928** 0.000	0.939** 0.000	1.000 .

Add: Adductor muscles, ext: extensor muscles, DANN-PSS: Danish Prostate Symptom Score, **: Spearman correlation analysis.

Discussion

This study examined the relationship between UI and motor symptoms in patients who had experienced a stroke. Findings revealed significantly lower balance and gait abilities among patients with UI. These results support the hypothesis that fear of leakage and urgency

associated with UI may lead to hurried movements, thereby contributing to balance disturbances. Furthermore, disruptions in normal gait patterns and shortened stride lengths due to UI concerns may compromise walking ability. No significant relationship was found between UI and spasticity.

While the exact cause of UI in stroke patients remains unclear, both neurological and functional impairments may contribute (8). Wang et al. (2024) reported that UI is 40% more prevalent in post-stroke women than in men, potentially due to anatomical differences, childbirth history, and obesity (2,28). In addition, when the relationship between the lesion side and UI is examined, it has been stated in the literature that the UI rate is higher in patients with left brain involvement. In our study, no gender or lesion-side differences were noted between groups, likely due to the limited number of participants with UI.

Although spasticity tends to increase with age within the first year post-stroke, prior research suggests no consistent relationship with age, gender, or lesion side (15). In our study, there was no significant relationship between spasticity and UI. Pizzi et al. (2014) found that incontinence was more common in older patients, indicating a potential age-related decline in continence mechanisms (29). Our findings also reflect higher mean age among participants with UI. This may be considered as a result of the increased risk of UI with age.

After a stroke, both motor functions and the autonomic nervous system are affected. Abnormal contractions reflected in the pelvic region with lower extremity spasticity can increase pressure on the bladder, make it difficult to control bladder emptying, and lead to UI (30). Previous studies have linked increased lower limb spasticity with greater severity of urinary dysfunction and lower quality of life (9). Combined spasticity and UI have been associated with reduced independence in daily activities (10). Similarly, in multiple sclerosis, UI and spasticity are known to negatively affect quality of life and functional abilities (31,32). While one of our hypotheses posited a relationship between post-stroke UI and increased tone in hip adductors, no such link was identified. However, patients with UI demonstrated worse outcomes in balance and gait.

While trunk control and balance problems are common in stroke patients, UI is also known to be common in these patients. UI may negatively affect postural stability and balance by increasing the compensatory activity of the trunk and pelvic floor muscles (33). It is reported that balance skills may be weak in women with stress UI and that advanced age may further negatively affect this condition. Similarly, the higher mean age of the group with UI in our study suggests that the weakness in balance skills may be partly due to the age factor. It was also observed that balance skills were better in patients with lower UI severity. This suggests that decreasing physical activity levels

due to concerns about experiencing incontinence may have negative effects on balance over time. Therefore, it should be kept in mind that UI may affect not only pelvic floor health but also balance and physical functions.

Effective functional movement and postural control require coordinated muscular effort across the ankles, knees, hips, and trunk (34). Increased spasticity negatively affects lower limb function (14,15). Khiabani et al. (2017) found that patients with higher spasticity had poorer frontal plane balance control (35). Consistent with this, our findings suggest that spasticity in the hip adductors may impair balance by altering lower extremity alignment and center of gravity.

This study has certain limitations. Notably, the uneven distribution of participants between groups is a methodological constraint that may impact the reliability and generalizability of the findings. Additionally, the relatively small sample size limits the extrapolation of results to broader populations. Future studies with larger, preferably multicenter samples are warranted to enhance the scientific validity and clinical relevance of the findings.

This study aimed to explore the relationship between post-stroke urinary incontinence and motor symptoms. UI in post-stroke patients was not significantly associated with spasticity but was negatively associated with balance and, to a lesser extent, gait performance. Furthermore, patients with UI were older, a factor that may exacerbate balance impairments. These results suggest that UI may indirectly negatively impact motor function and contribute to functional dependence. Consequently, UI should be addressed as a multifactorial problem in stroke rehabilitation programs, with a particular focus on improving postural control and walking ability.

Clinical Implications

Post-stroke urinary incontinence (UI) should be routinely screened as it may negatively affect balance and gait, even in the absence of a relationship with spasticity.

Rehabilitation programs should integrate continence care with balance and gait training to reduce fall risk and functional dependence.

Incorporating pelvic floor muscle training, postural control exercises, and mobility strategies into stroke rehabilitation may improve participation, motivation, and functional recovery.

Addressing UI as a multifactorial condition provides a more holistic rehabilitation approach and may enhance quality of life and independence in stroke survivors.

Conflict of Interest Statement

The authors declare no conflicts of interest.

Ethical Approval

Ethical approval was obtained from the Clinical Research Ethics Committee of the Faculty of Medicine, Süleyman Demirel University (Date: 16.11.2021, Protocol No: 72867572-050.01.04-320). Informed consent forms were obtained from the participants in accordance with the principles of the Declaration of Helsinki.

Consent to Participate and Publish

Following the provision of detailed information regarding the study, written informed consent was obtained from all participants.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Availability of Data and Materials

Data can be requested from the authors.

Artificial Intelligence Statement

The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

Authors Contributions

PY: Conceptualization; Formal analysis; Investigation; Visualization; Writing-review & editing.

MD: Conceptualization; Formal analysis; Methodology; Writing-original draft. Supervision; Writing-review & editing.

SK: Data curation.

VAY: Data curation.

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Dual Role of Cannabidiol in Mitigating Apoptosis and Inflammation in Cardiovascular Complications of Lung Ischemia-Reperfusion

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Cite this article as: Aşci H, Çamlıca T, İmeci OB, Özmen Ö. Dual Role of Cannabidiol in Mitigating Apoptosis and Inflammation in Cardiovascular Complications of Lung Ischemia-Reperfusion. Med J SDU 2025;32(4):299-307.

Abstract

Objective

Lung ischemia-reperfusion (I/R) injury is a critical complication in thoracic surgeries and lung transplantation, leading to oxidative stress, inflammation, and apoptosis. Secondary cardiac damage often occurs due to the systemic inflammatory response, highlighting the need for protective interventions. Cannabidiol (CBD), known for its anti-inflammatory, antioxidant, and anti-apoptotic properties, may mitigate this damage through modulation of apoptotic (B-cell lymphoma 2 [Bcl-2], Bcl2-associated X protein [Bax] and inflammatory (interleukin 10 [IL-10]) markers.

Material and Method

This study involved forty male Wistar albino rats divided into four groups: Control, Lung I/R induced cardiac injury (LICI), LICI treated with CBD (LICI+CBD), and CBD-only. Lung I/R was induced by clamping the left lung hilus for 60 minutes, followed by 60 minutes of reperfusion. The cardiac and aortic tissues were collected post-intervention, and histopathological as well as immunohistochemical analyses were conducted to assess the expression levels of Bax, Bcl-2, and IL-10.

Results

Histopathological findings revealed significant tissue damage in the LICI group, including increased hyperemia, hemorrhage, mononuclear cell infiltration, and necrosis compared to the control. CBD treatment markedly reduced these pathological markers. Immunohistochemical analysis showed a significant increase in pro-apoptotic Bax and a decrease in anti-apoptotic Bcl-2 and IL-10 in the LICI group. Conversely, the LICI+CBD group demonstrated reduced Bax levels and elevated Bcl-2 and IL-10 expression, indicating CBD's role in reducing apoptosis and inflammation.

Conclusion

CBD exhibits cardioprotective effects in lung I/R-induced cardiac injury by decreasing Bax-driven apoptosis, maintaining Bcl-2 levels, and upregulating IL-10 expression. These findings suggest CBD as a promising therapeutic agent for reducing secondary cardiac injury in lung I/R scenarios, though further studies are warranted to confirm its efficacy in clinical settings.

Keywords: Cannabidiol, lung ischemia-reperfusion injury, cardioprotection, apoptosis, inflammation.

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Received: 26.05.2025 • **Accepted:** 24.09.2025

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Introduction

Lung ischemia-reperfusion (I/R) injury is a serious complication observed during various clinical procedures, such as lung transplantation, cardiopulmonary bypass, and certain thoracic surgeries. It involves a period of restricted blood flow (ischemia), followed by the restoration of blood flow (reperfusion). Although reperfusion is essential for tissue survival, it paradoxically exacerbates cellular damage through oxidative stress, inflammation, and apoptosis. The heart is one of the key organs affected by lung I/R injury, suffering secondary damage from systemic inflammation and oxidative stress (1,2). This phenomenon, known as remote organ injury, underscores the importance of understanding and mitigating the cardiovascular effects associated with lung I/R injury.

Apoptosis, or programmed cell death, is a significant factor in the progression of I/R-related myocardial damage. The balance between pro-apoptotic and anti-apoptotic proteins determines the extent of cell survival or death following I/R. Bcl2-associated X protein (Bax), a well-known pro-apoptotic protein, promotes mitochondrial membrane permeabilization, leading to cell death, while B-cell lymphoma gene 2 (Bcl-2) is an anti-apoptotic protein that counters these effects by inhibiting Bax activity and stabilizing the mitochondrial membrane. The Bax/Bcl-2 ratio is a critical indicator of apoptosis, with higher ratios favoring cell death and lower ratios supporting cell survival (3,4). Therefore, targeting the regulation of these proteins is a promising strategy to mitigate myocardial injury secondary to lung I/R.

In addition to the apoptotic pathway, inflammation plays a central role in lung I/R-induced cardiac injury. Anti-inflammatory cytokines, such as interleukin-10 (IL-10), help suppress pro-inflammatory cytokine production and reduce tissue damage during reperfusion. IL-10's protective effects have been demonstrated in various models of I/R injury, where it limits the extent of myocardial and pulmonary damage by reducing oxidative stress and neutrophil infiltration (5). Therefore, increasing IL-10 expression represents a potential therapeutic strategy to counteract the inflammatory damage associated with lung I/R.

Cannabidiol (CBD), a non-psychoactive compound derived from *Cannabis sativa*, has attracted attention for its broad-spectrum therapeutic properties, particularly its anti-inflammatory, antioxidant, and anti-apoptotic effects. Recent studies have demonstrated the ability of CBD to reduce oxidative stress, modulate apoptotic pathways, and enhance anti-inflammatory cytokine

production in various models of tissue injury, including myocardial and pulmonary damage (6). However, its protective effects against cardiac injury secondary to lung I/R have not been fully elucidated. This study aims to investigate the cardioprotective effects of CBD by examining its impact on key molecular markers such as Bax, Bcl-2, and IL-10, which are crucial in modulating apoptosis and inflammation during lung I/R-induced cardiac damage (7).

By focusing on the balance between apoptotic and anti-apoptotic pathways (Bax/Bcl-2) and the regulation of anti-inflammatory responses (IL-10), this research seeks to explore how CBD may offer a protective effect against secondary cardiac injury following lung I/R. Understanding these mechanisms could provide valuable insights into the development of novel therapeutic strategies for managing lung I/R injury and its associated cardiovascular complications.

Material and Method

Reagents

CBD was obtained from the Natural Products Application and Research Centre of a university. The source of the CBD was the extract of *Cannabis sativa* L. (Cannabaceae). CBD content was >99.9, and the tetrahydrocannabinol content was < 0.01. Limits of residual alcohol and heavy metals comply with the USP and EU pharmacopeias. Ketamine (Keta-Control, Doğa İlaç, Turkey) and Xylazine (Xylazinbio 2%, Bioveta, Czech Republic) were used to induce sedation and anesthesia applications.

Experimental Design

In the experiment, forty adults male Wistar albino rats weighing 350–400 g were kept at 21–22 °C and 60% ± 5% humidity. They were fed commercial feed ad libitum and had a 12-hour light 12-hour dark cycle and were divided into 4 groups (each containing ten rats) after they were obtained. Groups as:

Control Group: Rats received 0.5-1 ml saline intraperitoneally (i.p). After 30 minutes, a thoracotomy was performed, but lung ischemia was not created. The hilus was visualized.

LICI Group: Rats were administered 0.5-1 ml saline i.p. After 30 minutes, a non-traumatic vascular clamp was placed on the hilus following the left thoracotomy, and 60 minutes of ischemia and 60 minutes of reperfusion were applied (8).

LICI+CBD Group: Rats received 5 mg/kg CBD i.p. (9). Following the left thoracotomy, a non-traumatic

vascular clamp was placed on the hilus, and 60 minutes of ischemia and 60 minutes of reperfusion were applied.

CBD Group: Rats received 5 mg/kg CBD i.p. After 30 minutes, a thoracotomy was performed, but the lung ischemia model was not created.

Surgical Procedure

After 12 hours of fasting, the thorax area was shaved, and the left thoracotomy was performed under i.p. Ketamine (90 mg/kg) / Xylazine (8-10 mg/kg) anesthesia. After the left lung hilus was identified by visualizing the trachea, it was clamped with a nontraumatic vascular clamp (in LICI and LICI+CBD groups) for 60 min, and reperfusion was performed for 60 min. Animals were sacrificed after collecting blood from the inferior vena cava through an abdominal incision for surgical exsanguination. Then the heart and aorta tissues were removed, fixed in formaldehyde for subsequent histopathological and immunohistochemical analysis.

Histopathological Analysis

During the necropsy, samples of the heart and aorta were taken, and they were preserved in a 10% buffered formalin solution. Before the tissues were embedded in paraffin wax, a standard tissue processing method was carried out using a fully automated tissue processing apparatus (Leica ASP300S, Wetzlar, Germany). Sections of the paraffin blocks were prepared at a thickness of 5µm using a fully automatic rotary microtome (Leica RM2155 Leica Microsystems, Wetzlar, Germany). Hematoxylin-eosin (HE) and coverslips were used to stain the sections, which were then seen under a light microscope.

The evaluated parameters (hyperemia, hemorrhage, mononuclear cell infiltration, and necrosis) were pre-determined based on established ischemia-reperfusion injury scoring systems. Each parameter was semi-

quantitatively graded on a scale of 0–3 (0 = absent, 1 = mild, 2 = moderate, 3 = severe) by a blinded pathologist, modified by Asci et al. 2022 (Table 1).

Immunohistochemical Examination

For immunohistochemical analysis, three sections were cut from the paraffin blocks and placed on slides covered in poly-L-lysine. Sections were then stained immunohistochemically using the streptavidin-biotin procedure, as directed by the manufacturer, to assess the expression of Bax, Bcl-2, and IL-10. Primary antibodies for Bax (Anti-Bax antibody [E63] (ab32503)), Bcl-2 (Anti-Bcl-2 antibody (ab194583)), and IL-10 (Anti-IL-10 antibody [JES5-2A5] (ab189392)) (Abcam, Cambridge, UK) were used for this aim. Primary antibodies were used at a 1/100 dilution and were bought from Abcam in Cambridge, UK. Streptavidin-alkaline phosphatase conjugate and a biotinylated secondary antibody were used for immunohistochemistry on the sections after they had been incubated with the primary antibodies for 60 minutes. The rabbit-specific HRP/DAB Detection IHC Kit (ab64261) from Abcam in Cambridge, UK was used as a secondary antibody. Diaminobenzidine (DAB) was used as the chromogen. Instead of using primary antibodies, an antigen dilution solution was used for the negative controls. On blinded samples, a trained pathologist from a different university performed each evaluation.

For each antibody, slices were examined independently for immunohistochemical examination. Using a grading score that ranged from 0 to 3, semiquantitative analysis was carried out to assess the strength of the immunohistochemical reactivity of cells with markers. In this case, (0-) denotes negativity; (1) focal weak staining; (2) diffuse weak staining; and (3) diffuse marked staining. In each part, ten distinct locations were inspected under 40X objective magnification for evaluation. Utilizing the Database Manual Cell Sens Life Science Imaging Software System (Olympus

Table 1 Stages used in histopathological and immunohistochemical evaluation.

HEART		AORTA	
0	No change	0	No change
1	Mild (only one area)	1	1–2 desquamated cells
2	Moderate (2-3 area)	2	3–4 desquamated cells
3	Severe (more than 4 areas)	3	5 or more desquamated

At 40x magnification

Co., Tokyo, Japan), morphometric analysis and microphotography were carried out. After being saved, the outcomes were statistically examined. The immunohistochemical expression of Bax, Bcl-2, and IL-10 was predominantly cytoplasmic.

Statistical Analysis

For the statistical analysis of histopathological scores and the number of immunohistochemically positive cells, the GraphPad Prism 10.1 software was utilized. Initially, the Shapiro-Wilk method was employed to assess the normality of the data distribution. One-way ANOVA was employed as a means of comparing the groups since the data showed a normal distribution ($p > 0.05$). The pairwise differences between the groups were obtained using the post hoc Tukey test. The significance threshold was set at $p < 0.05$, and the findings are shown as means $\pm$ standard deviation.

Results

Histopathological Examination

The control and CBD groups showed normal tissue histology at the histological analysis of the heart and aorta sections. When comparing the control group to the LICI group, the LICI group exhibited significantly elevated levels of hyperemia ($p \leq 0.001$), hemorrhage ($p \leq 0.001$), mononuclear cell infiltration (MNCI) ($p \leq 0.05$), and necrosis ($p \leq 0.01$). In the LICI+CBD group, CBD treatment reduced the pathological results; compared to the LICI group, hyperemia ($p \leq 0.01$) and hemorrhage ($p \leq 0.001$) levels significantly decreased. There wasn't a significant difference between these groups' MNCI and necrosis levels. In the CBD group, hyperemia

($p \leq 0.001$), hemorrhage ($p \leq 0.001$), and necrosis ($p \leq 0.01$) levels were found to be significantly lower compared to the damage group, while MNCI levels weren't significant. The results of this investigation showed hyperemia, hemorrhage, MNCI, and necrosis were seen in the LICI group. These pathological findings were significantly reduced in LICI+CBD and CBD treatment groups (Figs. 1 and 2).

Immunohistochemically Examination

Bax, Bcl-2, and IL-10 expressions were examined by immunohistochemistry, and the results indicated that the control and CBD groups had significant Bcl-2 and IL-10 expressions but very little or no Bax expression. The LICI group exhibited significantly elevated levels of Bax (Heart: $p \leq 0.001$, Aorta: $p \leq 0.01$), and significantly decreased levels of Bcl-2 (Heart: $p \leq 0.05$, Aorta: $p \leq 0.01$) and IL-10 (Heart: $p \leq 0.001$, Aorta: $p \leq 0.05$) expressions in the aortic endothelium and myocardium. In the LICI+CBD groups, compared to the LICI groups, Bax levels significantly decreased (Heart: $p \leq 0.001$, Aorta: $p \leq 0.01$), while IL-10 levels were observed to increase significantly (Heart: $p \leq 0.01$, Aorta: $p \leq 0.05$). There was no significant difference between the Bcl-2 levels of these groups. In the CBD group, Bax levels were found to be significantly lower compared to the damage group ($p \leq 0.001$ for both tissues), while Bcl-2 (Heart: $p \leq 0.05$, Aorta: $p \leq 0.01$) and IL-10 (Heart: $p \leq 0.001$, Aorta: $p \leq 0.01$) levels were significantly higher. These findings demonstrate that CBD can reduce heart and aortic damage caused by LICI (Figs. 3-6). Immunohistochemical expression of Bax, Bcl-2, and IL-10 was predominantly cytoplasmic.

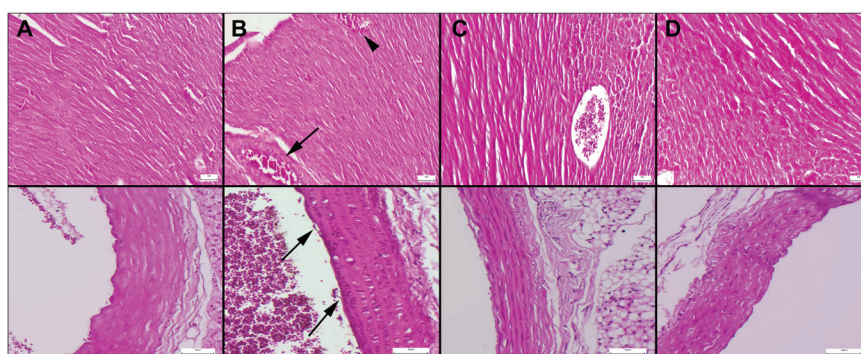


Figure 1

Representative histopathological figures of hearts (upper row) and aorta (below row) sections between the groups. (A) Normal tissue architecture in the control group. (B) Marked hyperemia (arrow) and hemorrhage (arrowhead) in the myocardium and endothelial sloughing in the aortas (arrows) in the LICI group. (C) Decreased pathological findings in the LICI+CBD group (D). Normal in the myocardium and aortic histology in the CBD group, HE, scale bars=50µm.

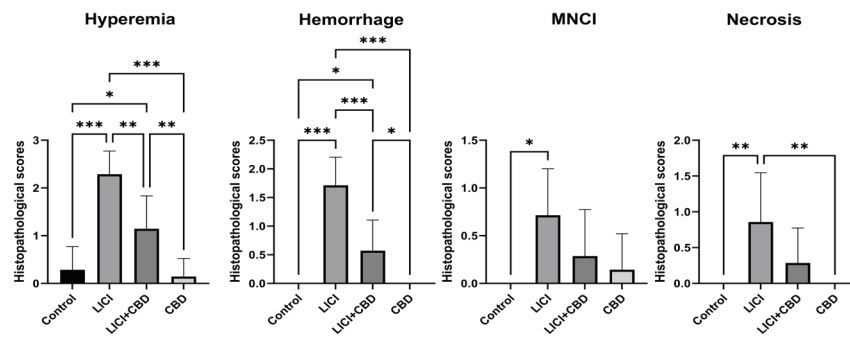


Figure 2

Histopathological appearance of the heart and aorta among the groups.

Values are presented as the mean $\pm$ SD. Group comparisons of histopathological scores were conducted using a one-way ANOVA, followed by Tukey's test. MNCI: Mononuclear cell infiltration, LICI: Lung ischemia-reperfusion induced cardiac injury, CBD: Cannabidiol. * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$

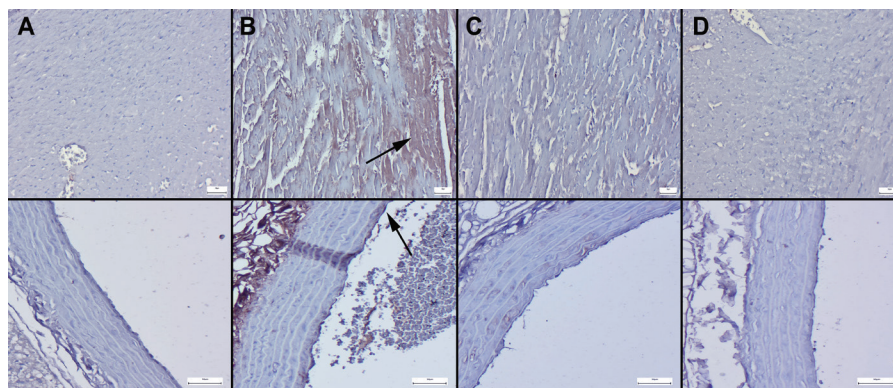


Figure 3

Bax immunohistochemistry findings of hearts (upper row) and aortas (lower row) between the groups. (A) Negative expression in the control group. (B) The marked increase in expression in myocardial and endothelial cells (arrows) in the LICI group. (C) Decreased expression in the LICI+CBD group. (D) Negative expression in both myocardial cells and endothelial cells in the CBD group, Streptavidin biotin peroxidase method, scale bars=50 μ m.

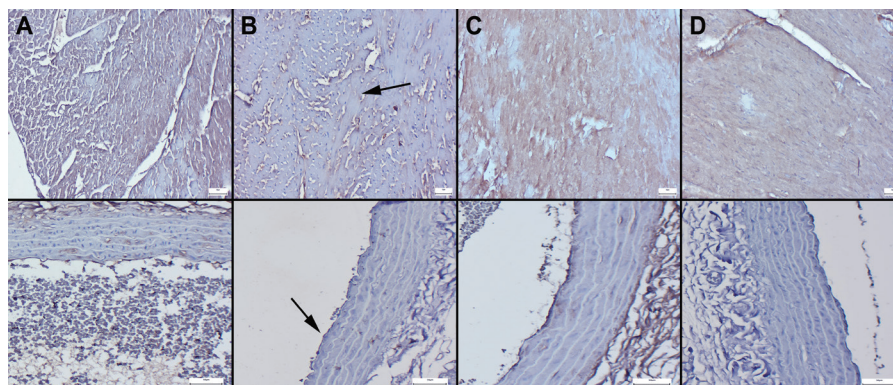


Figure 4

Bcl-2 expression of hearts (upper row) and aortas (lower row) between the groups. (A) Significant expression in the control group. (B) The marked decrease in expressions in both myocardium and endothelial cells (arrows) of the aortas in the LICI group. (C) Increased expressions in the LICI+CBD group. (D) Marked expression in myocardial and endothelial cells in the CBD group, Streptavidin biotin peroxidase method, scale bars=50 μ m.

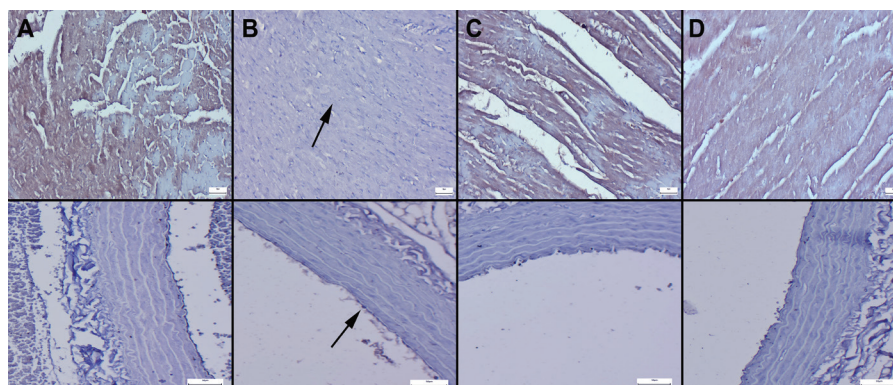


Figure 5

IL-10 immunoexpression of the heart (upper row) and aorta (lower row) between the groups. (A) Marked expression in the control group. (B) Negative expression in both myocardium and endothelial cells (arrows) in the LICI group. (C) Increased expression in the LICI+CBD group. (D) Marked expression in myocardial and endothelial cells in the CBD group, Streptavidin biotin peroxidase method, scale bars=50µm.

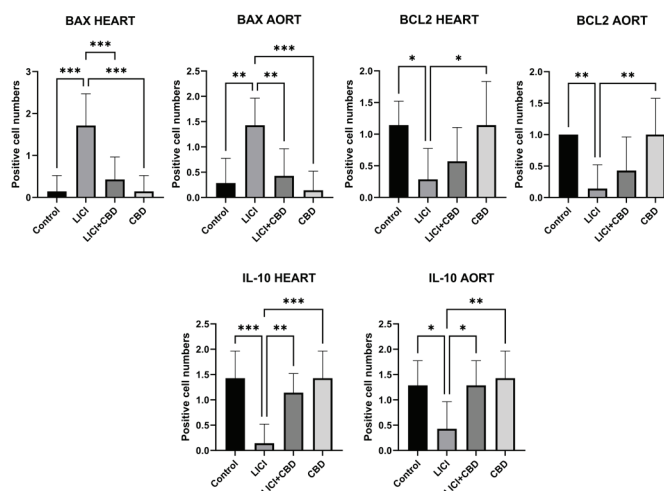


Figure 6

Graphs showing the immunohistochemical appearance of Bax, Bcl-2, and IL-10 expressions between the groups

Values are presented as the mean $\pm$ SD. Group comparisons of immunohistochemical analyses were conducted using a one-way ANOVA, followed by Tukey's test. LICI: Lung ischemia-reperfusion induced cardiac injury, CBD: Cannabidiol, Bax: Bcl-2 associated X protein, Bcl-2: B-cell lymphoma 2, IL-10: Interleukin-10. * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$

Discussion

This study investigates the molecular mechanisms by which CBD may reduce cardiac injury secondary to lung I/R, specifically through its effects on key apoptotic and inflammatory markers: Bax, Bcl-2, and IL-10. Each of these markers plays a distinct but interconnected role in the cellular response to ischemic injury, where oxidative stress and inflammation often lead to significant tissue damage (11).

Bax and Bcl-2 belong to the Bcl-2 protein family, which tightly regulates the mitochondrial pathway of apoptosis. Bax is a pro-apoptotic protein that, when activated, translocates to the mitochondria, promoting the release of cytochrome c, triggering caspase activation and subsequent cell death. In contrast, Bcl-2 functions as an anti-apoptotic protein, preserving mitochondrial membrane integrity and preventing cytochrome c release (12). The balance between

these two proteins, often quantified as the Bax/Bcl-2 ratio, is critical for determining cell fate in response to stressors like I/R injury (13,14).

In this study, lung I/R significantly increased Bax expression in cardiac and aortic tissues while decreasing Bcl-2 expression in the LICI group. This shift, resulting in a higher Bax/Bcl-2 ratio, indicates heightened susceptibility to apoptosis, with myocardial and aortic cells more prone to programmed cell death (15). However, in groups treated with CBD (LICI+CBD and CBD-only), Bax expression decreased significantly while Bcl-2 levels were preserved or elevated. This shift towards a lower Bax/Bcl-2 ratio suggests that CBD's cardioprotective effect may be partly due to its ability to reduce mitochondrial-mediated apoptosis (16,17). By lowering the Bax/Bcl-2 ratio, CBD likely stabilizes mitochondrial membranes, thus reducing cytochrome c release and subsequent activation of caspases that execute cell death.

IL-10 is a potent anti-inflammatory cytokine known for its ability to suppress the expression of pro-inflammatory cytokines, including tumor necrosis factor alpha (TNF- α) and interleukin 6 (IL-6), which are heavily implicated in I/R-related tissue damage. IL-10 achieves this by inhibiting nuclear factor-kappa B signaling, a critical pathway that mediates inflammatory responses following I/R injury (18). Cao et al. have shown that increased IL-10 expression is associated with reduced neutrophil infiltration, lower levels of reactive oxygen species, and mitigated oxidative damage, contributing to improved tissue recovery (19).

In this study, the LICI group exhibited a marked reduction in IL-10 expression, correlating with heightened inflammatory response and significant cardiac and aortic tissue damage. This drop in IL-10 levels aligns with increased inflammatory markers observed in other I/R models, emphasizing IL-10's role in protecting tissues against reperfusion-associated oxidative stress (20). However, treatment with CBD reversed this trend: IL-10 levels significantly increased in both the LICI+CBD and CBD-only groups, suggesting that CBD may exert its anti-inflammatory effects by upregulating IL-10 expression (20,21). This aligns with recent research showing CBD's potential to elevate IL-10 levels and modulate other cytokines in I/R injury and various inflammatory diseases (8, 21, 22).

The concurrent regulation of apoptotic and anti-inflammatory pathways by CBD highlights its therapeutic potential in complex injuries like I/R. In

lung I/R, which often triggers secondary damage in organs like the heart, targeting multiple pathways becomes crucial. CBD's dual action-suppressing Bax-driven apoptosis while promoting Bcl-2-mediated cell survival and enhancing IL-10 levels positions it as a versatile therapeutic agent (23). This multifaceted mechanism of action not only preserves cell viability by reducing apoptosis but also dampens the inflammatory response, thereby addressing the primary mechanisms underlying I/R-induced tissue damage. This synergistic effect may have significant implications for the management of lung I/R injury, as well as other conditions involving similar ischemic and inflammatory profiles.

Our results align with Cao and Yang's study, demonstrating CBD's anti-apoptotic and anti-inflammatory effects in other models of I/R injury. For instance, studies on myocardial and hepatic I/R injuries report that CBD reduces infarct size and improves tissue recovery, primarily through modulation of Bax, Bcl-2, and IL-10 pathways (24,25). A study by Xiong et al. shows that CBD can enhance cardiac and hepatic cell survival, reduce apoptosis, and lower inflammatory cytokine levels, highlighting its broad-spectrum protective effects across various tissues (25).

This study has several limitations that should be considered. First, while animal models are invaluable for studying disease mechanisms and potential treatments, differences in physiology and immune response between animals and humans may limit the generalizability of these findings to clinical settings. The specific response to CBD, including pharmacokinetics and bioavailability, can vary across species, and thus, human trials are necessary to confirm these results. Second, the study utilized a relatively short reperfusion time, which may not capture the full extent of CBD's long-term protective effects on cardiac and aortic tissues. Extending the reperfusion duration in future studies could provide a more comprehensive understanding of CBD's therapeutic efficacy over time. Finally, this study focused on a select group of molecular markers, Bax, Bcl-2, and IL-10, while other pathways, such as oxidative stress markers (e.g., MDA, thiol, antioxidant enzymes) and pro-inflammatory cytokines (e.g., TNF- α), were not included. Future studies that integrate these additional markers could yield a more holistic view of CBD's protective mechanisms in lung I/R-induced cardiac injury.

Conclusion

Our findings contribute to the growing body of evidence that CBD offers protective effects in lung I/R-

induced cardiac injury by regulating critical apoptotic and inflammatory pathways. By simultaneously reducing pro-apoptotic Bax expression, maintaining anti-apoptotic Bcl-2 levels, and upregulating anti-inflammatory IL-10, CBD emerges as a promising therapeutic approach to mitigate secondary cardiac damage in I/R scenarios. Future research, especially human clinical trials and studies incorporating additional inflammatory and oxidative markers, is necessary to fully elucidate CBD's therapeutic potential in managing ischemic injuries and their systemic impacts.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Ethical Approval

The protocols for Animal Research have been followed for this study: Reporting in Vivo Experiments (ARRIVE) 2.0 at all experiment stages. Permission was obtained from the university's local animal experimentation ethics committee (The number:508). In addition, this research received funding from the Scientific Research Projects Coordination Unit of a Suleyman Demirel University (grant number: TSG-2024-9515).

Funding

This research received funding from the Scientific Research Projects Coordination Unit of Suleyman Demirel University (grant number: TSG-2024-9515).

Availability of Data and Materials

Data available on request from the authors.

Artificial Intelligence Statement

No artificial intelligence (AI) tools were used in this article.

Authors Contributions

HA: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Visualization; Writing-original draft.

TC: Formal analysis; Investigation; Validation; Writing-original draft; Visualization

OBI: Formal analysis; Investigation; Validation; Visualization; Writing-original draft.

OO: Data curation; Formal analysis; Writing- review & editing.

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Evaluation of Oral Health Literacy Level and Oral Health-Related Quality of Life in Patients Admitted to a University Hospital

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Cite this article as: Arslangiray O, Önsüz MF, Ünsal A, Er O, Yanik EA, Karaca EO, Basu CE, Avci E, Talantbekova F, Sarper R, Dinç E, Elma İB, Aşasin D, İbadova Z, İsayev M. Evaluation of Oral Health Literacy Level and Oral Health-Related Quality of Life in Patients Admitted to a University Hospital. Med J SDU 2025;32(4):309-317.

Abstract

Objective

Oral health literacy (OHL) plays a crucial role in improving individuals' quality of life by promoting preventive oral and dental health behaviors and raising awareness. This study aimed to investigate the association between OHL levels and oral health-related quality of life (OHRQoL) among adults attending a university hospital.

Material and Method

A total of 423 participants and their relatives aged 18 and over, who attended Eskişehir Osmangazi University Health Practice and Research Hospital between May- July 2024, were included in this cross-sectional investigation. Data were collected using a questionnaire form that included questions about participants' sociodemographic characteristics, oral and dental health behaviors, the Health Literacy Dental Scale-Short Form (HeLD-14), and the Oral Health Impact Profile (OHIP-14). Statistical analyses were performed using descriptive statistics, the Mann-Whitney U test, the Kruskal-Wallis test, Spearman's correlation, and multivariate linear regression analysis, with a significance threshold set at $p < 0.05$.

Results

The mean scores for HeLD-14 and OHIP-14 among the participants were 43.59 ± 11.45 and 11.30 ± 9.8 , respectively. Multivariate linear regression analysis revealed that living in the urban center, having health insurance, reporting good oral health status, and engaging in regular tooth brushing at least once daily and using dental floss were significantly associated with higher OHL levels. A weak negative correlation was observed between HeLD-14 and OHIP-14 scores, indicating that better OHL was associated with an improved OHRQoL.

Conclusion

The study determined that the participants' OHL levels were moderate. Higher OHL levels are associated with more positive health behaviors and better OHRQoL. To improve OHL in the community, it is recommended to raise awareness about oral and dental health through primary healthcare facilities and social media, and to disseminate educational programs using brochures, videos, infographics, and other educational materials.

Keywords: Oral health literacy, Oral health, Quality of life, Oral health behaviors, Cross-sectional.

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Received: 17.06.2025 • **Accepted:** 10.09.2025

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Introduction

The World Health Organization (WHO) defines health not merely as the absence of disease or infirmity, but as a state of complete physical, mental, and social well-being. (1) Oral and dental health, a fundamental component of overall health, constitutes a critical factor directly influencing individuals' general health and quality of life. Preventable oral pathologies, including dental caries, periodontal diseases, and tooth loss, are still among the most prevalent health issues worldwide. (2). The main reasons for this situation include socioeconomic disparities, insufficient knowledge regarding oral health, limited access to dental care services, and inadequate health literacy (3).

Health literacy refers to individuals' ability to access, understand, evaluate, and effectively use health information and healthcare services to maintain and improve their health (4). Oral health literacy (OHL), a fundamental subcomponent of health literacy, is defined as individuals' ability to access, process, and effectively utilize the necessary information and services to make correct decisions regarding their oral and dental health (5). Factors such as educational attainment, socioeconomic status, language skills, cultural and environmental characteristics, and access to healthcare services are key determinants that significantly influence individuals' OHL levels. (6). Low oral health literacy (OHL) has been linked to a higher susceptibility to preventable oral conditions such as periodontal disease, dental caries, and oral cancers. These conditions are further associated with negative quality-of-life outcomes, including nutritional deficiencies, social isolation, and reduced self-esteem (7,8).

Oral health-related quality of life (OHRQoL), an integral component of overall quality of life, is a multidimensional concept that reflects individuals' satisfaction with their oral health during essential daily activities such as nutrition, communication, sleep, and social interaction (9). Studies reported that individuals with higher levels of OHL demonstrate greater adoption of preventive health behaviors, experience fewer oral health problems, and consequently enjoy better OHRQoL (10,11). Assessing the impact of individuals' OHL levels on both general and oral health-related quality of life is of significant importance. However, there is a critical lack of local studies and comprehensive data in Turkey on how OHL levels affect these outcomes. (12,13). In addition, there are no studies in Türkiye that evaluate both OHL and OHRQoL together in patients and their relatives.

This study aimed to determine the OHL levels of

patients and their relatives aged 18 years and older who attended a university hospital, to examine associated factors, and to evaluate their OHRQoL.

Material and Method

This cross-sectional study was conducted on patients and their relatives aged 18 and older attending an Eskişehir Osmangazi University (ESOGU) Health Practice and Research Hospital between May 5 and July 28, 2024.

The minimum number of patients and their relatives to be reached in this study was calculated as 384 people using Epi Info™ version 7.2.6.0 (frequency of adequate oral health literacy level 50%, margin of error 5%, and confidence interval 95%). Although the study was not conducted in a dental hospital, OHL and OHRQoL are integral components of general health and are therefore relevant to a broad spectrum of the population. Including both patients and their relatives in a general university hospital setting ensured a heterogeneous and valuable sample, enabling the evaluation of these constructs from a comprehensive public health perspective.

During the data collection period, patients and their relatives who applied to the hospital were interviewed in the waiting rooms of the outpatient clinics and informed about the study's objectives and procedures. A total of 423 people who agreed to participate in the study constituted the study group. The pre-prepared questionnaire forms were filled in by the patients and their relatives under observation; this process took approximately 10-15 minutes.

In this study, data were collected using a questionnaire that was developed based on a comprehensive review of the literature (12-14). The questionnaire included questions regarding participants' sociodemographic characteristics (age, gender, educational and employment status, and the presence of chronic diseases), some variables potentially associated with oral and dental health literacy (nutritional habits, self-reported oral health status, oral and dental care routines, and the presence of oral and dental complaints), the Health Literacy in Dental Scale–Short Form (HeLD-14) and the questions from the Oral Health Impact Profile-Short Form (OHIP-14).

In our study, participants' OHL levels were assessed using the HeLD-14 scale. The original scale was developed by Jones et al. in 2013 and consisted of 29 items rated on a five-point Likert-type scale (15). In 2014, Jones et al. developed a short form of the scale

consisting of 14 questions (16). The Turkish version of the scale, including its validity and reliability analyses, was adapted by Aydin et al. in 2023 (12). HeLD-14 consists of 14 items, each scored on a five-point Likert scale: "0" (unable to do), "1" (very difficult), "2" (with some difficulty), "3" (with little difficulty), and "4" (without any difficulty) points. Total scale score ranges from 0 to 56; as the scores increase, the level of oral health literacy increases.

Patients' and their relatives' OHRQoL was assessed using the OHIP-14 scale. The original scale was developed by Slade et al. in 1994 and consisted of 49 items rated on a five-point Likert scale. The 49-item version of the scale was revised into a 14-item short form by the same researchers in 1997 (17, 18). The Turkish version of the scale, including its validity and reliability analyses, was adapted by Mumcu et al. in 2006 (19). OHIP-14 consists of 14 items with a five-point Likert-type scale, where the responses are scored as "0" (never), "1" (hardly ever), "2" (occasionally), "3" (fairly often), and "4" (very often). The scale total score ranges from 0 to 56; as the scores increase, OHRQoL decreases.

In this study, participants who reported daily consumption of one or more cigarettes were classified as "smokers". Those who consumed five or more sugar cubes (or five teaspoons of granulated sugar) daily were categorized as "yes". Participants' oral health status was categorized by self-perceptions into three groups: "good", "fair", and "poor". In this study, individuals engaged in any form of income-generating employment were classified as "working". Additionally, family income status was assessed based on self-perceptions and categorized as "good", "moderate", and "poor".

The data obtained were analyzed using IBM SPSS Statistics (version 24). Descriptive statistics, including

frequency, percentage, mean, and standard deviation values, were used for analyses. The Kolmogorov-Smirnov test was used to assess the normality of measurable data. As the data did not follow a normal distribution, non-parametric tests (Mann-Whitney U and Kruskal-Wallis) and Spearman's rho for correlation analysis were employed. Multivariate Linear Regression Analysis was also performed. A p-value of ≤ 0.05 was considered statistically significant. The internal consistency of the scales was assessed using Cronbach's alpha. HeLD-14 and OHIP-14 were evaluated separately.

Reliability Analysis

The internal consistency of the scales was evaluated using Cronbach's alpha. HeLD-14 demonstrated a Cronbach's alpha coefficient of 0.89, indicating high reliability. Similarly, OHIP-14 yielded a Cronbach's alpha coefficient of 0.91, confirming strong internal consistency. Item-total correlation analysis revealed that one item in each scale (HeLD-14 item 6 and OHIP-14 item 5) showed relatively low correlations with the total score. However, exclusion of these items resulted in only marginal increases in the alpha values (from 0.89 to 0.91 for HeLD-14, and from 0.91 to 0.93 for OHIP-14). Therefore, both scales were retained in their original form for subsequent analyses.

Results

Among the study group, 237 (56.0%) were female and 186 (44.0%) were male. Participants' ages ranged from 18 to 75 years (mean age=41.49±15.18; median 41.0). The study population's HeLD-14 scores spanned 0-56, with a mean of 43.59±11.45 (median 46.0). Table 1 presents the distribution of HeLD-14 scores according to some sociodemographic characteristics in the study group.

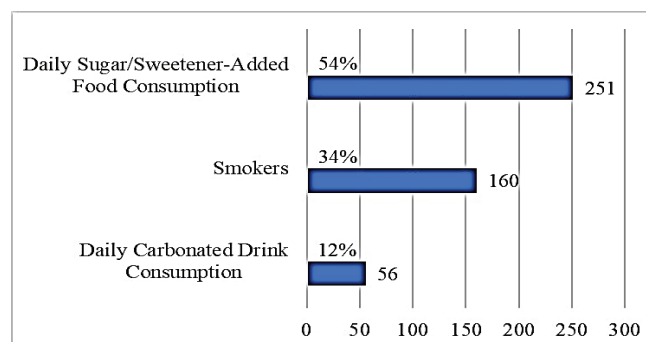


Figure 1

The distribution of oral health-related risky behaviors in the study group.
*Numbers are calculated based on the answers given, not on individuals.

Among the patients and their relatives, 56 individuals (12%) reported daily consumption of carbonated or acidic beverages, 251 individuals (54%) consumed sugar- or sweetener-added foods daily basis, and 160 individuals (34%) were smokers. Figure 1 presents the distribution of oral health-related risky behaviors in the study group.

Participants' OHIP-14 scale scores varied from 0 to 54, with an average score of 11.30 ± 9.8 (median: 9.0). Analysis revealed a weak negative correlation between scores on the HeLD-14 and OHIP-14 scales among

patients and their relatives ($r = -0.263$; $p = 0.001$). Figure 2 presents a scatterplot of the HeLD-14 and OHIP-14 scale scores for the study group.

The findings indicated that participants who defined their dental health status as "good", who reported no dental caries, who maintained toothbrushing at least once daily, who used dental floss, and who attended regular dental check-ups demonstrated higher levels of OHL. Table 2 presents the distribution of HeLD-14 scale scores according to some oral health-related behaviors in the study group.

Table 1

The distribution of HeLD-14 scale scores according to some sociodemographic characteristics in the study group

Sociodemographic Characteristics	n (%)	HeLD-14 Scale Score Median (min-max values)	Test Statistic (z/KW)*; p value
Gender			
Female	237 (56.0)	47.0 (0.0-56.0)	2.044; 0.041
Male	186 (44.0)	44.5 (0.0-56.0)	
Age Group			
≤ 40	210 (49.6)	48.0 (0.0-56.0)	2.598; 0.009
>41	213 (50.4)	45.0 (1.0-56.0)	
Education Status			
High school and below	182 (43.0)	43.5 (0.0-56.0)	4.808;< 0.001
University	241 (57.0)	48.0 (1.0-56.0)	
Employment Status			
Yes	182 (43.0)	48.0 (0.0-56.0)	2.159; 0.031
No	241 (57.0)	46.0 (1.0-56.0)	
Family Income Status			
Poor	138 (32.6)	46.0 (1.0-56.0)	2.870; 0.238
Moderate	83 (19.6)	46.0 (11.0-56.0)	
Good	202 (47.8)	47.0 (0.0-56.0)	
Place of Residence			
Province	301 (71.2)	48.0 (0.0-56.0)	24.016;< 0.001
District	90 (21.3)	44.5 (0.0-56.0)	
Village	32 (7.6)	38.5 (4.0-55.0)	
Presence of Health Insurance			
Yes	379 (89.6)	47.0 (0.0-56.0)	2.094; 0.036
No	44 (10.4)	42.5 (0.0-56.0)	
Total	423 (100.0)	(0.0-56.0)	-

(z/KW)*: z=Mann-Whitney U test statistic; KW=Kruskal-Wallis test statistic

Table 2

The distribution of HeLD-14 scale scores according to some oral health-related behaviors in the study group.

Some Oral Health-Related Behaviors	n (%)	HeLD-14 Scale Score Median (min-max values)	Test Statistic (z/KW)*; p-value
Oral Health Status			
Poor	67 (15.8)	37.0 (0.0-56.0)	49.390;< 0.001
Moderate	167 (39.5)	45.0 (0.0-56.0)	
Good	189 (44.7)	49.0 (15.0-56.0)	
Presence of Carious Tooth			
Yes	203 (48.0)	45.0 (0.0-56.0)	3.265;< 0.001
No	220 (52.0)	48.0 (0.0-56.0)	
Frequency of Tooth Brushing			
Never	29 (6.9)	39.0 (0.0-56.0)	28.332;< 0.001
At least once a week	78 (18.4)	41.0 (0.0-56.0)	
At least once a day	316 (74.7)	48.0 (1.0-56.0)	
Dental Floss Use Status			
No	301 (71.2)	45.0 (0.0-56.0)	5.092;< 0.001
Yes	122 (28.8)	50.0 (4.0-56.0)	
Dentist Examination Status			
Never	33 (7.8)	40.0 (0.0-56.0)	7.514; 0.023
When there is a complaint	283 (66.9)	46.0 (0.0-56.0)	
Regularly	107 (25.3)	48.0 (1.0-56.0)	
Total	423 (100.0)	(0.0-56.0)	-

(z/KW)*: z=Mann-Whitney U test statistic; KW=Kruskal-Wallis test statistic

Table 3

Multivariate Linear Regression Analysis (Enter Method) of variables associated with OHL level in the study group

Variables	HeLD-14 Scale Score				
	Unstandardized β	SE	p	Standardized β	95% CI
Gender	0.015	0.018	0.413	0.039	-0,020; 0.049
Age	0.017	0.018	0.354	0.046	-0.019; 0.052
Education Status	0.025	0.019	0.182	0.067	-0.012; 0.061
Active Employment Status	0.004	0.019	0.848	0.010	-0.034; 0.041
Place of Residence	0.036	0.014	0.013	0.120	0.007; 0.064
Presence of Health Insurance	0.069	0.029	0.016	0.114	0.011; 0.127
Oral Health Status	0.049	0.014	<0.001	0.192	0.021; 0.076
Presence of Caries in Teeth	0.056	0.018	0.059	0.152	0.021; 0.091
Frequency of Tooth Brushing	0.041	0.016	0.010	0.131	0.010; 0.072
Use of Dental Floss	0.039	0.019	0.042	0.096	0.001; 0.076
Dentist Examination Status	0.001	0.016	0.928	0.004	-0.029; 0.032
R ²	0.184				0.001
F	7.651				

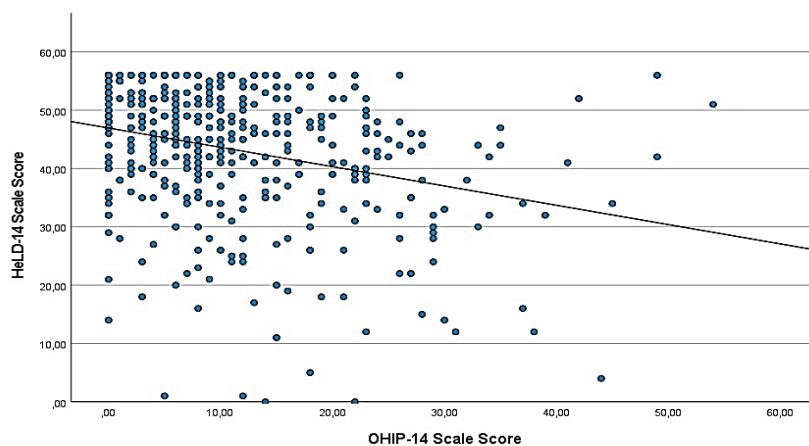


Figure 2

The scatterplot shows the correlation between HeLD-14 and OHIP-14 scores for the study group.

Table 3 presents the results of the multivariate linear regression analysis performed with variables found to be associated with OHL level in the analyses (gender, age, educational and employment status, place of residence, presence of health insurance, self-rated oral health status, presence of dental caries, tooth-brushing frequency, dental floss usage, and frequency of dental visit).

Discussion

A critical determinant of general health and quality of life, oral health is a multidimensional concept that includes not only the presence of teeth but also the absence of pain and infection, as well as the functionality and social well-being of an individual. In this context, WHO has emphasized the need to integrate targets related to the prevention of oral and dental diseases and the enhancement of OHRQoL into its global objectives established for the prevention of non-communicable diseases (2). OHRQoL is an important health indicator that evaluates the physical, psychological, and social impacts of individuals' oral and dental health on their daily lives. Improving individuals' OHL levels is essential for the adoption of preventive and protective oral health behaviors and for enhancing OHRQoL (20).

Findings from this study indicate that the OHL level of participants was moderate. However, some studies have reported low OHL levels among participants (7,8). Educational and socioeconomic conditions, cultural and linguistic characteristics, and access to healthcare services are primary factors influencing health literacy. Differences in these factors across populations lead to variations in both general health and OHL levels.

With advancing age, older adults experience a decline in cognitive functions and face limitations in understanding and utilizing digital resources, which can reduce their ability to access, interpret, and apply current health information (3). This decline can lead to a reduction in health literacy levels concerning both general and oral health (21). In the present study, OHL was found to be higher among participants aged 40 and below. However, this difference was not observed following further analysis. Murakami et al reported that participants under 45 years of age had higher OHL levels (22). In a study conducted by McCarlie et al. among patients attending a university dental hospital in America, it was also found that OHL levels decreased with advancing age (23). Some studies have reported no significant association between age and OHL (24,25). The differences reported in these findings may be due to variations in the sociodemographic characteristics of societies, such as education level and access to health services, as well as differences in cultural norms.

Gender is one of the key sociodemographic variables associated with OHL. It is well known that hormonal changes during menstruation, pregnancy, and menopause in women can lead to a higher prevalence of certain oral diseases, such as gingivitis, periodontitis, and xerostomia (26). This situation may enhance women's awareness and preventive behaviors regarding oral health, potentially increasing their OHL levels. Furthermore, factors such as women's generally greater sensitivity towards health issues and the higher priority of aesthetic concerns may also contribute to the expectation of higher OHL levels in women (27). Our study found that the level of OHL was higher in women than in men. Further analysis showed

that this difference disappeared. Studies conducted in India and Iran have also reported that women have higher OHL levels than men (11,27). In various studies, no significant difference in OHL between men and women has been reported (20,28). In contrast, the study by Lee et al. reported that men have higher OHL levels (29). The discrepancies in findings across various studies may be attributed to factors such as differences in the measurement tools employed, the sociocultural characteristics of the participants, and variations in access to healthcare services.

Place of residence is a determining factor affecting individuals' health behaviors, access to services, and health literacy levels. In rural areas, healthcare provision is often more limited compared to urban regions. Restricted access to healthcare services due to geographical conditions, inadequate oral health education, and constrained access to digital health resources are among the reasons reported for lower OHL levels among rural residents (30). The results of this study indicated that individuals living in the urban center had higher levels of OHL. Various studies have also reported that OHL levels are lower among rural residents (31,32).

The presence of health insurance increases individuals' health literacy levels by facilitating their access to and use of healthcare services and enabling them to obtain accurate health information from healthcare institutions (33). In our study, it was found that those with health insurance had higher levels of OHL compared to those without insurance. Studies conducted in Sweden and the United States have also reported that participants with health insurance or coverage had higher OHL (33,34).

In this study, participants with "good" oral health were found to have higher levels of OHL. Similar results have been reported in studies conducted in China by An et al. and Iran by Naghibi-Sistani et al. (35,36). Individuals with higher levels of OHL are more likely to demonstrate positive health behaviors such as regular toothbrushing, flossing, attending regular dental check-ups, adherence to recommended interventions or treatments, and maintaining a healthy diet, which consequently is expected to result in "better" oral health outcomes.

Tooth brushing and flossing are effective methods for preventing plaque formation and dental caries; it has been reported that such oral and dental care practices are more common among individuals with higher levels of OHL (37). In our study, it was found that participants who brushed their teeth at least once daily and used

dental floss exhibited higher levels of OHL (for both, $p < 0.05$). The study by Joshi et al. also reported that individuals with a regular daily toothbrushing habit exhibited higher levels of OHL (38). Similarly, Yan et al., in their research conducted in China, found that individuals who regularly used dental floss had higher levels of OHL (39).

OHL is a concept that refers to individuals' capacity to access, understand, evaluate, and utilize information related to oral health in their daily lives. As OHL increases, individuals are more likely to adopt positive oral health behaviors such as preventive oral and dental care habits, regular dental check-ups, and adherence to recommended treatments, while harmful habits, including tobacco use or excessive sugar consumption, may decrease. Consequently, OHRQoL is expected to improve. In this study, it was observed that as the level of OHL increased, OHRQoL also improved. Various studies have also reported that as OHL increases, individuals' OHRQoL improves accordingly (7,20,29).

Limitations

Due to its cross-sectional nature, this study can not determine a cause-and-effect relationship between OHL and OHRQoL. Furthermore, as the study was conducted with patients and their relatives who presented to a single university hospital, the generalizability of the findings to other populations or regions may be limited. As the data were collected through self-report, the possibility of social desirability and recall bias cannot be ruled out.

Conclusion and Recommendations

In our study, the participants' level of OHL can be described as moderate. Higher levels of OHL were observed among individuals residing in the urban center, those with health insurance, those with good oral health status, those who regularly brushed their teeth at least once daily, and those with a habit of using dental floss. Additionally, as OHL increased, OHRQoL also improved. In our study, individuals with higher levels of OHL were found to exhibit more favorable oral health behaviors and to report better OHRQoL. These findings suggest that interventions aimed at improving OHL in the community may not only enhance oral and dental health but also contribute to strengthening general health perceptions and overall quality of life. However, being a single-center, cross-sectional study based on self-reported data, the results should be interpreted with caution, as generalizability is limited and potential biases such as social desirability and recall cannot be entirely excluded.

Based on the findings of this study, we propose the following recommendations:

Implement targeted oral health literacy interventions. Practical oral care training and education on preventive methods should be delivered by experienced healthcare professionals in public education centers, primary healthcare facilities, and dental hospitals, with a focus on younger individuals through school-based curricula and campus oral health clubs.

Address the needs of vulnerable populations. Mobile dental clinics and outreach education for rural and uninsured populations, along with age-friendly educational materials for older adults, can help overcome access barriers and improve OHL in at-risk groups.

Utilize modern communication channels. Informative videos, infographics, and consistent oral health messages should be disseminated through official social media accounts of health institutions and national television channels to enhance public awareness.

Advocate for policy-level changes. National oral health strategies should be expanded to include the monitoring of OHL indicators, and insurance coverage should be broadened to encourage regular dental visits, thereby supporting sustainable improvements.

Conduct further large-scale research. To fully understand the relationship between OHL and OHRQoL, future studies should include a wider range of age groups, geographic regions, and educational levels.

Conflict of Interest Statement

There is no financial conflict of interest with any organization, institution, or person related to our article and there is no conflict of interest between the authors.

Ethical Approval

Approval for the conduct of this study was obtained from the Eskişehir Osmangazi University (ESOGU) Non-Interventional Clinical Research Ethics Committee (dated May 2, 2024; approval no: E-25403353-050.99-2400082849), and the necessary written permissions were also obtained from the hospital's chief physician. The study was conducted in accordance with the principles set forth in the Declaration of Helsinki.

Funding

This research received no specific grant from any

funding agency in the public, commercial, or not-for-profit sectors.

Availability of Data and Materials

The data is available upon reasonable requests from the Corresponding Author.

Artificial Intelligence Statement

The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

Authors Contributions

OA: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Visualization; Writing-original draft., Writing-review & editing,

MFO: Conceptualization; Formal analysis; Investigation; Validation; Supervision,

AU: Conceptualization; Formal analysis; Investigation; Validation; Supervision,

OE: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation,

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Evaluation of Ceftazidime-Avibactam Susceptibility in Carbapenem-Resistant Gram-Negative Bacteria

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Cite this article as: Ayvalık Rüzgarkesen T, Şekercioğlu Y, Erol MT, Bilir G, Sesli Çetin E, Şirin MC. Evaluation of Ceftazidime-Avibactam Susceptibility in Carbapenem-Resistant Gram-Negative Bacteria. Med J SDU 2025;32(4):319-326.

Abstract

Objective

Resistance to carbapenem antibiotics, commonly preferred to treat infections caused by multidrug-resistant (MDR) Gram-negative bacteria, is gradually increasing. Ceftazidime-avibactam (CZA) is a novel beta-lactam/beta-lactamase inhibitor combination, proposed as an alternative treatment option for severe infections caused by carbapenem-resistant Gram-negative bacteria. This study aimed to determine the susceptibility of carbapenem-resistant *Klebsiella pneumoniae* (CR-KP), carbapenem-resistant *Escherichia coli* (CR-EC), and carbapenem-resistant *Pseudomonas aeruginosa* (CR-PA) isolates to CZA using the Kirby-Bauer disk diffusion method (DDM) and the BD Phoenix automated system, and to compare the results.

Material and Method

A total of 320 strains (209 CR-KP, 53 CR-EC, and 58 CR-PA) resistant to at least one carbapenem (ertapenem, imipenem, and meropenem), collected between August 2021 and August 2023, were included in the study. CZA susceptibility testing was performed using the DDM and the CPO detect panel of the BD Phoenix automated system (Becton Dickinson, USA). Results were interpreted in accordance with the European Committee on Antimicrobial Susceptibility Testing (EUCAST) standards.

Results

While CZA susceptibility rates determined by the automated system were 74.1% for CR-KP, 64.5% for CR-EC, and 90.9% for CR-PA, the DDM method yielded susceptibility rates of 87.8% for CR-KP, 94.4% for CR-EC, and 81.3% for CR-PA. Categorical agreement was observed in 86.9% of 115 isolates tested by both methods. Although not statistically significant, a declining trend in CZA susceptibility was observed over the years with both methods.

Conclusion

CZA susceptibility rates among carbapenem-resistant Gram-negative isolates in our hospital were consistent with current global data. Determining accurate CZA susceptibility results is important for guiding effective treatment strategies against infections caused by carbapenem-resistant bacteria. The observed discrepancies in susceptibility results between the DDM and the automated system, particularly across different species, underscore the need for further species-specific studies to identify the most reliable testing methodology for CZA susceptibility.

Keywords: ceftazidime-avibactam, antibiotic susceptibility test, automated system, disk diffusion method

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Received: 22.07.2025 • **Accepted:** 08.10.2025

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Introduction

The increasing antimicrobial resistance in Gram-negative bacteria leads to multidrug-resistant (MDR) bacterial infections, limits treatment options, and thus contributes to higher morbidity and mortality (1). Resistance to carbapenem antibiotics, which are among the important alternatives in the treatment of infections caused by MDR Gram-negative bacteria, is also increasing and spreading rapidly (2). Options such as aminoglycosides, fosfomycin, and colistin are preferred for treating infections caused by carbapenem-resistant Gram-negative bacteria (3). Due to the limited benefits of these antibiotics, finding alternative antibacterials for treating infections caused by carbapenem-resistant bacteria has become a priority (4). Ceftazidime-avibactam (CZA) is a β -lactam/ β -lactamase inhibitor combination effective against Ambler class A, C, and D carbapenemases, but inactive against class B. It was approved by the United States Food and Drug Administration (FDA) for the treatment of Gram-negative bacterial infections with limited treatment options. These include complex intra-abdominal and urinary tract infections, as well as hospital-acquired pneumonia caused by carbapenem-resistant Enterobacterales (CRE) and hard-to-treat resistant *Pseudomonas aeruginosa* strains (3). Although CZA is a relatively new antibiotic, there are reports of resistance to CZA, and this issue requires close attention (5). Assessment of CZA susceptibility is important to determine and monitor the effectiveness of the antibiotic and to detect possible resistance during treatment (6). Various susceptibility testing methods, such as broth microdilution (BMD), broth disk elution, the Kirby-Bauer disk diffusion method (DDM), gradient strip test, and an automated system, can be used to determine CZA susceptibility. (7). While the minimum inhibitory concentration (MIC) value of CZA for the tested isolate can be determined with the CPO detect panel of the BD Phoenix automated system (Becton Dickinson, USA), the inhibition zone diameter, which shows the inhibition of bacterial growth in the presence of the CZA disk, can be determined with DDM (8). This study aimed to determine the susceptibility of carbapenem-resistant *Klebsiella pneumoniae* (CR-KP), carbapenem-resistant *Escherichia coli* (CR-EC), and carbapenem-resistant *P. aeruginosa* (CR-PA) strains, isolated from various clinical samples, to CZA using the DDM and the BD Phoenix automated system, and to compare the results of both methods.

Material and Method

Clinical samples submitted to the Medical Microbiology

Laboratory from various clinics between August 2021 and August 2023 were routinely cultured on 5% sheep blood agar (RTA, Turkey), eosin methylene blue agar (RTA, Turkey), and, when required, chocolate agar (RTA, Turkey). All cultures were incubated at $35\pm 2^{\circ}\text{C}$ for 24-48 hours. Blood cultures were incubated in an automated blood culture system (BacT/ALERT 3D, bioMérieux, France), and upon detection of a growth signal, subcultures were performed and incubated under the same conditions. Bacterial identification and antimicrobial susceptibility testing of strains isolated from the culture and evaluated as causative agents were performed using the BD Phoenix automated system (Becton Dickinson, USA). Isolates identified as *K. pneumoniae*, *E. coli*, and *P. aeruginosa* and determined to be resistant to at least one carbapenem antibiotic (ertapenem, imipenem, and meropenem) were included in the study. Susceptibility to CZA was determined using the DDM and/or the CPO detect panel of the BD Phoenix automated system. For DDM, a 0.5 McFarland standard suspension was prepared from fresh colonies and spread evenly on Mueller-Hinton agar (MHA) (RTA, Turkey) plates. A CZA disk (10/4 μg , Bioanalyse, Turkey) was placed on an MHA plate within 15 minutes and left to incubate in the incubator at $35\pm 2^{\circ}\text{C}$. Inhibition zone diameters were read from the back of the plate against a dark background illuminated with reflected light after 18-24 hours of incubation. Simultaneously, the BD Phoenix automated system was loaded with the CPO panel, and results were obtained after 18-24 hours. The results obtained by both methods were interpreted in accordance with the current European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines (9-11). *E. coli* ATCC 25922 was used as the quality control strain for CZA susceptibility testing. Repeated isolations of the same species from different specimens of the same patient were excluded from the study. The data obtained in the study were analyzed using the IBM SPSS Statistics 31.0 program. Pearson's chi-square test was applied to compare CZA susceptibility rates between 2021-2022 and 2022-2023, and a p-value <0.05 was considered statistically significant. Cohen's Kappa (κ) analysis was performed to assess the degree of agreement between the two methods.

Results

A total of 320 carbapenem-resistant isolates, including 209 CR-KP, 53 CR-EC, and 58 CR-PA, were included in the study. Among these, 161 were obtained from the intensive care unit, 82 from the internal medicine ward, 47 from the surgical ward, and 30 from outpatient clinics. The most frequent specimen types were urine,

endotracheal aspirate, and blood. The distribution of isolates by sample type is shown in Table 1.

A total of 199 isolates, including 135 CR-KP, 31 CR-EC, and 33 CR-PA, were tested with the automated system, and a total of 236 isolates, including 157 CR-KP, 36 CR-EC, and 43 CR-PA, were tested with

DDM, while 115 of the isolates (83 CR-KP, 14 CR-EC, and 18 CR-PA) were tested with both DDM and the automated system.

Of the 199 isolates tested for CZA susceptibility by the automated system, 150 (75.4%) were found to be susceptible and 49 (24.6%) were found to be resistant.

Table 1

Distribution of isolates tested for ceftazidime-avibactam susceptibility according to sample types (n)

Sample type	CR-KP	CR-EC	CR-PA	Total
Urine	101	27	13	141
ETA	38	2	22	62
Blood	33	8	9	50
Sputum	14	4	6	24
Abscess	9	5	1	15
Wound	5	2	2	9
Tissue	2	-	4	6
Bile	3	2	-	5
Thoracentesis fluid	2	2	1	5
Catheter	2	1	-	3
Total	209	53	58	320

ETA: Endotracheal aspirate, CR-KP: Carbapenem-resistant *K. pneumoniae*, CR-EC: Carbapenem-resistant *E. coli*, CR-PA: Carbapenem-resistant *P. aeruginosa*

Table 2

Ceftazidime-avibactam susceptibility rates of carbapenem-resistant isolates by bacterial species, testing method, and study year [number of CZA susceptible isolates/number of tested isolates (%)]

Date	Bacterial Species	BD Phoenix	Disk Diffusion Method
2021-2022	CR-KP	59/77 (76.6)	36/40 (90)
	CR-EC	12/18 (66.7)	7/7 (100)
	CR-PA	14/14 (100)	5/6 (83.3)
	Total	85/109 (77.9)	48/53 (90.6)
2022-2023	CR-KP	41/58 (70.7)	102/117 (81.2)
	CR-EC	8/13 (61.5)	27/29 (93.1)
	CR-PA	16/19 (84.2)	30/37 (81.1)
	Total	65/90 (72.2)	159/183 (86.8)
Total	CR-KP	100/135 (74.1)	138/157 (87.8)
	CR-EC	20/31 (64.5)	34/36 (94.4)
	CR-PA	30/33 (90.9)	35/43 (81.3)
	Total	150/199 (75.3)	207/236 (87.7)

S: Susceptible, CR-KP: Carbapenem-resistant *K. pneumoniae*, CR-EC: Carbapenem-resistant *E. coli*, CR-PA: Carbapenem-resistant *P. aeruginosa*

Table 3

Comparison of the CZA susceptibility test results obtained by the disk diffusion method and the BD Phoenix automated system according to bacterial species [n (%)]

Bacterial Strains			Methods		
CR-KP	Disk Diffusion Method		BD Phoenix		
			S	R	Total
		S	61 (73.4)	10 (12.1)	71 (85.5)
		R	1 (1.2)	11 (13.3)	12 (14.5)
		Total	62 (74.6)	21 (25.4)	83 (100)
CR-EC	Disk Diffusion Method		BD Phoenix		
			S	R	Total
		S	10 (71.4)	3 (21.5)	13 (92.9)
		R	0 (0)	1 (7.1)	1 (7.1)
		Total	10 (71.4)	4 (28.6)	14 (100)
CR-PA	Disk Diffusion Method		BD Phoenix		
			S	R	Total
		S	16 (88.8)	0 (0)	16 (88.8)
		R	1 (5.6)	1 (5.6)	2 (1.2)
		Total	17 (94.4)	1 (5.6)	18 (100)
All strains	Disk Diffusion Method		BD Phoenix		
			S	R	Total
		S	87 (75.6)	13 (11.3)	100 (86.9)
		R	2 (1.8)	13 (11.3)	15 (13.1)
		Total	89 (77.4)	26 (22.6)	115 (100)

CR-KP: Carbapenem-resistant *K. pneumoniae*,

CR-EC: Carbapenem-resistant *E. coli*, CR-PA: Carbapenem-resistant *P. aeruginosa*

While the CZA susceptibility rate was determined as 77.9% by the automated system between 2021 and 2022, 72.2% of the isolates tested between 2022 and 2023 were found to be susceptible to CZA. Of the 236 isolates tested for CZA susceptibility by DDM, 207 (87.7%) were found to be susceptible and 29 (12.3%) were found to be resistant. While the CZA susceptibility rate determined by DDM was 90.6% between 2021-

2022, 86.8% of the isolates tested by DDM between 2022-2023 were found as susceptible to CZA (Table 2).

When the susceptibility test results were evaluated considering the bacterial species, CZA susceptibility rate was found to be 74.1% for CR-KP, 64.5% for CR-EC, and 90.9% for CR-PA using the automated

system, while it was 87.8% for CR-KP, 94.4% for CR-EC, and 81.3% for CR-PA using DDM. Ceftazidime-avibactam susceptibility rates of carbapenem-resistant isolates according to bacterial species, testing method, and study year are given in Table 2. While a decrease in susceptibility rates was observed over the years with both methods, there was no statistically significant difference between CZA susceptibility rates determined by BD Phoenix ($p=0.35$) and DDM ($p=0.47$) between 2021-2022 and 2022-2023 (Table 2).

Of the 115 isolates that were tested using both methods, the CZA susceptibility rate was detected as 77.4% by the automated system and 86.9% by DDM, while 75.6% of the isolates were detected as susceptible by both methods. The overall categorical agreement rate of the CZA susceptibility test results obtained by the DDM and automated system was 86.9% (100/115). On the other hand, when bacterial species were taken into account, categorical agreement rates were 86.7% (72/83) for CR-KP, 78.6% (11/14) for CR-EC, and 94.4% (17/18) for CR-PA (Table 3). While moderate agreement was observed between the DDM and automated system results for all isolates ($\kappa=0.56$), substantial agreement for CR-PA ($\kappa=0.64$), moderate agreement for CR-KP ($\kappa=0.59$), and fair agreement for CR-EC ($\kappa=0.32$) was observed. Among the isolates with discordant test results, 9 were urine, 4 were endotracheal aspirates, and 2 were blood isolates. These included 11 CR-KP, 3 CR-EC, and 1 CR-PA isolates.

Discussion

Infections caused by MDR gram-negative bacteria are a significant cause of morbidity and mortality. Due to high resistance rates to existing antibiotics, new antibiotics are essential for effective treatment (12, 13). Determining the susceptibility of CZA, approved specifically for treating resistant infections, is crucial for managing and controlling these challenging pathogens (5). This study investigated the susceptibility of CR-KP, CR-EC, and CR-PA isolates to CZA, which is a prominent option in the treatment of serious infections caused by these isolates. Moreover, annual variations in susceptibility rates and the outcomes of different testing methods were compared. It was observed that the CZA susceptibility rates determined by both the automated system (from 77.9% to 72.2%) and DDM (from 90.6% to 86.8%) for all isolate types decreased in 2022-2023 compared to 2021-2022. Although a statistically significant difference was not observed between the two periods, the observed trend toward decreased susceptibility to CZA may indicate an early warning sign of emerging resistance.

Several international programs have been conducted to determine CZA susceptibility and perform surveillance. These studies are important for evaluating the global situation, analyzing potential resistance problems, and developing appropriate solutions. According to the International Network for Optimal Resistance Monitoring (INFORM) Surveillance Program, CZA susceptibility was found to be 88.3% for CR-KP, 76.2% for CR-EC, and 81.5% for CR-PA. CZA susceptibility in isolates included in this surveillance program from Turkey was reported as 89.5% for CR-KP and 85.7% for CR-EC (14, 15). According to the Antimicrobial Testing Leadership and Surveillance (ATLAS) data network, CZA susceptibility was 52.1% for CR-KP, 8.8% for CR-EC, and 41.1% for CR-PA. In this data network, the susceptibility rate for isolates originating from Turkey was found to be 85.8% for CR-KP, 75% for CR-EC, and 46.67% for CR-PA (16). Additionally, although the CZA susceptibility determined by both the DDM and the automated system in our study was higher than the ATLAS data overall, the results for isolates from our country in the ATLAS program were similar to those in our study.

Among the methods used to determine CZA susceptibility, BMD is considered the gold standard; however, it is costly and requires specialized laboratory equipment. The DDM is practical and cost-effective. Automated systems are practical for routine laboratory use and help minimize operator errors; however, inaccurate results may still occur (17). For these reasons, numerous studies have been conducted to determine CZA susceptibility using different methods. In studies conducted in Turkey between 2022 and 2024 involving CR-KP, CR-EC, and CR-PA isolates, varying susceptibility rates were reported using the DDM, ranging from 64% to 85% for CR-KP, 44% to 100% for CR-EC, and 24% to 83% for CR-PA (18-24). In our study, CZA susceptibility determined by the DDM was 87.9% for CR-KP, 94.4% for CR-EC, and 81.4% for CR-PA. These rates are comparable to those reported by Cetinkol et al., Koca et al., and Bilgin et al., and notably higher than those reported by Oztas et al., Arici et al., Akbas et al., and Yakut et al. (18-24). In our study, CZA susceptibility determined by DDM was similar to that reported in the INFORM study for all isolates, while susceptibility determined by the automated system was lower for CR-KP and CR-EC and higher for CR-PA compared to INFORM. Arici et al. attributed the lower susceptibility observed in their study to a higher prevalence of extensively drug-resistant (XDR) isolates in their study whereas Akbas et al. suggested that the reduced susceptibility in their setting might be associated with the presence of specific resistance genes (22, 23). The higher CZA

susceptibility rates determined in our study compared to previous reports may be attributed to the lower proportion of MDR isolates. Additionally, the lower prevalence of isolates harboring carbapenemase genes associated with intrinsic resistance to CZA may also have contributed to this finding.

Using the CPO test panel of the BD Phoenix 100 automated system, Ugurlu et al. reported CZA susceptibility rates of 97.6% for CR-KP and 50% for CR-EC (25). Mermutluoglu et al. reported rates of 57% and 66% for CR-KP and CR-EC, respectively, while Albichr et al. documented a CZA susceptibility rate of 31.1% for CR-PA (26, 27). In our study, the CZA susceptibility rates determined by the automated system were 74.1% for CR-KP, 64.5% for CR-EC, and 90.9% for CR-PA. In comparison to the findings of Mermutluoglu et al., in our study CZA susceptibility rate for CR-KP isolates was higher, while the CR-EC result was similar. Compared to Albichr et al., our CR-PA result was higher. Albichr et al. reported that 60% of the isolates in their study contained Ambler class B carbapenemase, and therefore their CZA susceptibility for CR-PA isolates remained low (26). Hosbul et al. determined the susceptibility of CZA using BMD as 92.7% for CR-KP and 100% for CR-PA (28, 29). These rates were higher than those we observed with both methods in all isolates. In the study conducted at our hospital by Kole et al. between 2018 and 2020, CZA susceptibility among CR-KP isolates, as determined by the BMD method, was reported to be 91.4% (30). In our study conducted between 2021 and 2023, CZA susceptibility among CR-KP isolates was found to be 74.1% using the automated system and 87.9% using DDM, indicating a decrease in CZA susceptibility rates in our hospital over the years. This decrease may be associated with the increased use of CZA, which can contribute to the development of resistance. Additionally, this difference in susceptibility rates compared to those reported by Kole et al. may also be attributed to the use of different testing methods to determine CZA susceptibility. The inability to perform BMD testing in our study represents a limitation that may have influenced the comparability of the results.

Numerous studies have been conducted to compare different methods for determining CZA susceptibility and to evaluate their accuracy in order to identify the most appropriate, cost-effective, and practical option. Shields et al. reported a categorical agreement of 76% between DDM and BMD among CRE isolates, while emphasizing that 28% of CZA susceptible CRE isolates were misclassified as resistant by DDM. The cause remained unclear, possibly related to the antibiotic disks used or the distribution of the

antibiotic on the agar. Based on these findings, the authors concluded that BMD could overestimate CZA resistance and emphasized the need for further studies to evaluate the suitability of DDM for routine clinical use in CZA susceptibility testing (7). In contrast, Park et al. found the categorical agreement between BMD and the BD Phoenix 100 automated system to be 97.6% for *Enterobacteriales* and 100% for *P. aeruginosa* (8). Schaumburg et al. reported categorical agreement between DDM and BMD in MDR *P. aeruginosa* and XDR *P. aeruginosa* strains as 79.7% and 88%. The authors also found very major errors (VME) as 1.4% and major errors (ME) as 17.8-30.9%, and accordingly, it was concluded that DDM was not a suitable alternative to BMD (31). Wenzler et al. found that the categorical agreement between DDM and BMD for CR-KP was 98.5% when using a 10/4 µg CZA disk and 82.6% with a 30/20 µg CZA disk. The authors reported that although 10/4 µg CZA disks performed better in determining CZA susceptibility in CR-KP, DDM was not considered a valid alternative to BMD due to the relatively high ME compared to BMD (32). In contrast, Wang et al. reported categorical agreement values of 98.5% and 93.5% between DDM and BMD for *Enterobacteriales* and *P. aeruginosa*, respectively, and concluded that the DDM could be considered as an alternative to the BMD method for *Enterobacteriales* and *P. aeruginosa* (33). Similarly, Daragon et al. compared DDM and the Vitek2 automated system using BMD as the reference and concluded that DDM was a reliable method for determining CZA susceptibility in *P. aeruginosa*, recommending its validation with BMD due to high VME rates observed with the Vitek2 system (34). Zhang et al. found categorical agreement between BMD and DDM to be 100% for *Enterobacteriales* and 95.9% for *P. aeruginosa*, indicating that DDM met the laboratory requirements for CZA susceptibility (35). Sharma et al. also reported a high categorical agreement (94.6%) between DDM and BMD in CRE isolates and suggested DDM as a potential alternative to BMD for determining CZA susceptibility in these isolates (36).

In our study, we aimed to compare DDM and the BD Phoenix automated system, which are considered practical and cost-effective methods for the determination of CZA susceptibility. Among 115 isolates tested by both methods, the categorical agreement was found to be 86.9%. These findings are consistent with those reported by Park et al., Wenzler et al., Wang et al., Daragon et al., Zhang et al., and Sharma et al., who supported the applicability of DDM (8,32-36). The categorical agreement rate in our study was higher than that reported by Shields et al. and Schaumburg et al.,

who did not accept DDM as a viable alternative (7,31). Additionally, when the categorical agreement rates of both methods were examined at the species level, they were determined as 86.7% for CR-KP, 78.6% for CR-EC, and 94.4% for CR-PA. These findings reveal that agreement rates between methods may vary by species and emphasize the importance of determining species-specific susceptibility tests. Further studies using BMD as the reference standard are warranted to validate the accuracy and clinical reliability of both DDM and automated systems for CZA susceptibility testing. In our hospital, CZA susceptibility ranged from 75% to 88% with both the automated system and DDM, and a decline in susceptibility rates was observed over the years using both methods. The decrease in CZA susceptibility over the years may be associated with widespread use of CZA, highlighting the need to investigate the potential resistance mechanisms to prevent further development and dissemination of CZA resistance. Additionally, further studies are needed to evaluate and compare different methods to identify methodological issues that may affect CZA susceptibility.

In conclusion, clinical laboratories must report CZA susceptibility results to healthcare providers using at least one validated method, such as DDM or an automated antimicrobial susceptibility testing system, to support the consideration of CZA as a therapeutic alternative for infections caused by carbapenem-resistant bacteria. In our study, it was observed that the automated system and DDM did not always give consistent results in terms of CZA susceptibility results. Therefore, we emphasize the need for additional studies to determine a reliable susceptibility testing method for CZA and to assess its effectiveness in antimicrobial management.

Conflict of Interest Statement

There is no financial conflict of interest with any organization, institution, or person related to our article, and there is no conflict of interest between the authors.

Ethical Approval

This study was Ethical approval was obtained from the Ethics Committee of Süleyman Demirel Faculty of Medicine (Decision no:38, date May 12, 2025). The study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

Consent to Participate and Publish

Written informed consent to participate and publish was obtained from all individual participants included in the study.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of Data and Materials

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Artificial Intelligence Statement

The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

Authors' Contributions

TAR: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Visualization; Writing-original draft; Validation

YS: Data curation; Formal analysis; Supervision; Visualization; Validation

MTE: Investigation; Data curation; Validation

GB: Investigation; Data curation; Validation

ESC: Project administration; Supervision; Visualization; Writing-original draft; Writing-review and editing; Validation

MCS: Supervision; Writing-review and editing; Validation.

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Reliability and Agreement of Four Radiographic Methods for Measuring Posterior Tibial Slope on Lateral Knee Radiographs

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Cite this article as: Yuksel Y, Kose O. Reliability and Agreement of Four Radiographic Methods for Measuring Posterior Tibial Slope on Lateral Knee Radiographs. Med J SDU 2025;32(4):327-335.

Abstract

Objective

The posterior tibial slope (PTS) is a critical anatomical parameter influencing knee biomechanics and ligamentous stability. Despite its clinical relevance, no consensus exists on the most reliable radiographic method for measuring PTS. This study aimed to evaluate the inter- and intra-observer reliability and agreement of four radiographic techniques for PTS measurement on standard lateral knee radiographs.

Material and Method

A retrospective analysis was conducted on 70 adult patients with high-quality true lateral knee radiographs. Four commonly used methods were applied to measure the PTS: the fibular shaft axis (FSA), anterior cortical line (ACL), posterior cortical line (PCL), and proximal anatomical axis (PAA). Two experienced observers performed all measurements twice, 15 days apart, using a standardized protocol. Intraclass correlation coefficients (ICCs) were calculated to assess reliability, and Pearson correlation coefficients

were used to evaluate the agreement between measurements and demographic characteristics.

Results

All four methods showed excellent intra-observer reliability (ICC, range 0.916–0.975) and good-to-excellent inter-observer reliability (ICC, range 0.813–0.968). Mean PTS values differed by method: ACL $12.4^\circ \pm 3.2^\circ$, PCL $7.2^\circ \pm 3.1^\circ$, FSA $10.1^\circ \pm 3.2^\circ$, PAA $9.6^\circ \pm 3.0^\circ$ ($p = 0.001$). Pairwise correlations were strong for all methods ($p < 0.001$). PTS showed no significant association with age, sex, height, weight, or body mass index.

Conclusion

Although reliability was high for all techniques, differences in absolute values indicate that methods are not interchangeable. Standardized reference axes should be specified to ensure consistent reporting across clinical and research settings.

Keywords: posterior tibial slope, knee radiograph, measurement reliability, observer agreement, anatomical axis

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Received: 24.08.2025 • **Accepted:** 31.10.2025

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Introduction

The posterior tibial slope (PTS) is the posterior inclination of the tibial plateau relative to the tibial axis in the sagittal plane. It plays a crucial role in maintaining knee biomechanics, influencing the ligamentous stability and kinematic behavior of the joint (1). An increased PTS has been associated with anterior tibial translation, heightened risk of anterior cruciate ligament injury, and increased stress on knee prostheses. In contrast, a reduced slope may impair the function of the posterior cruciate ligament and restrict flexion in total knee arthroplasty settings (2, 3).

Despite its clinical relevance, no universally accepted method for measuring PTS on plain radiographs exists. Various anatomical reference axes have been proposed, including the proximal anatomical axis, posterior cortex, anterior cortex, and fibular shaft axis, which yield different angular values (4–6). The variability in reference lines used in the literature contributes to inconsistencies across studies, complicating the comparison and interpretation of findings (7–10).

The accuracy of PTS measurements is also affected by the type of imaging modality used. Long-leg computed tomography (CT) and long-leg lateral radiographs are considered most accurate due to their ability to encompass the entire tibial shaft, which minimizes errors introduced by tibial bowing (11–14). However, in daily clinical practice, standard short lateral knee radiographs are more commonly available, despite their limited representation of the tibial longitudinal axis. Previous studies have also demonstrated that the degree of anterior tibial bowing can lead to significant underestimation of the true PTS on short radiographs (12).

Multiple studies have investigated the absolute values of PTS in different populations and using various methods. However, few have comprehensively compared the inter- and intra-observer reliability of various radiographic techniques on lateral knee X-rays (15–18). Establishing the reproducibility of PTS measurements is crucial for informed clinical decision-making, particularly in surgical planning for ligament reconstruction or joint replacement. The purpose of this study was to compare the inter- and intra-observer reliability and the level of agreement among four commonly used radiographic methods for measuring the PTS on standard lateral knee radiographs. By evaluating the consistency and agreement of these methods, we aimed to identify the most reliable approach for clinical and research applications.

Material and Method

Patients and Study Design

This retrospective observational study included adult patients (>18 years of age) who underwent lateral knee radiographs for various clinical indications between January 2023 and March 2025 at a tertiary care institution. Radiographs were retrospectively retrieved and screened from the institutional Picture Archiving and Communication System (PACS) database to assess eligibility. Patients were excluded if they had severe osteoarthritis, a history of previous surgery involving the tibia or femur, acute or healed fractures, any type of orthopedic implant, or congenital deformities. Additionally, radiographs deemed unsuitable for PTS measurement were excluded. The radiographic inclusion criteria required (i) a true lateral view of the knee, characterized by complete overlap of the posterior femoral condyles, and (ii) adequate tibial length, defined as the inclusion of at least 15 cm of the tibial shaft distal to the joint line. Radiographs failing to meet these criteria, such as those obtained with excessive rotational malalignment or insufficient tibial length, were excluded from the study.

Sample Size Calculation

The sample size estimation was guided by the expected level of agreement among two raters, quantified using the intraclass correlation coefficient (ICC) for radiographic angular measurements (continuous variable). The expected ICC was set at 0.800, with an acceptable minimum ICC of 0.700, based on a two-way random-effects model for consistency. To achieve 95% power at a significance level of 0.05, each of the two raters performed two repeated measurements per patient. According to Bonett's method, a minimum of 52 patients was required to reliably detect the expected ICC (19). Although the minimum required sample size was calculated as 52, the study was conducted on 70 patients to account for potential exclusions due to suboptimal radiographs and increase the statistical power of the reliability analysis.

Radiological Measurements

The PTS was measured using four radiographic methods, as illustrated in Figure 1 (5). Fibular shaft axis (FSA) method (Figure 1a): The reference axis was defined by a line drawn along the shaft of the fibula, and the posterior tibial slope angle was measured between a line tangent to the lateral tibial plateau and a line perpendicular to this fibular axis. Anterior cortical line (ACL) method (Figure 1b): The anterior cortical line was constructed by connecting mid-diaphyseal points located 5 cm and 15 cm distal to the tibial plateau along the anterior

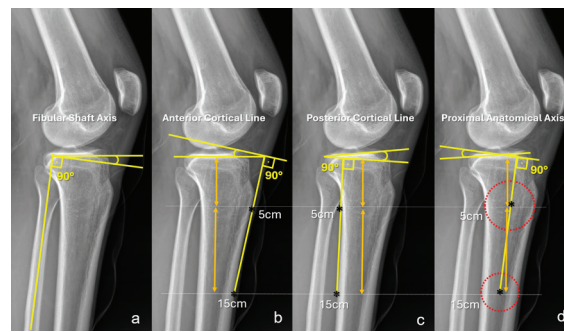


Figure 1

Radiographic illustration of four different posterior tibial slope measurement methods: (a) Fibular Shaft Axis, (b) Anterior Cortical Line, (c) Posterior Cortical Line, and (d) Proximal Anatomical Axis.

cortex. The angle between the plateau tangent and the perpendicular to this anterior cortical line was recorded as the posterior tibial slope angle. Posterior cortical line (PCL) method (Figure 1c): This method used the posterior tibial cortex as the reference. The posterior cortical line was constructed by connecting mid-diaphyseal points located 5 cm and 15 cm distal to the tibial plateau along the posterior cortex, and the posterior tibial slope angle was defined as that between the plateau tangent and a line perpendicular to the posterior cortical line. Proximal anatomical axis (PAA) method (Figure 1d): The anatomical axis of the proximal tibia was determined by connecting two mid-diaphyseal points located 5 cm and 15 cm distal to the tibial plateau. Posterior tibial slope was measured as the angle between the plateau tangent and a line perpendicular to this proximal anatomical axis.

PTS was measured using a global tibial plateau tangent. Specifically, the tangent was drawn to the native subchondral contour spanning the medial and lateral plateaus, providing a single global slope reference. In the presence of osteophytes or marginal irregularities, the tangent was fitted to the presumed anatomic plateau by excluding osteophytic lips and remodeled edges and following the smooth subchondral line of the load-bearing region on each side. All radiographic measurements were performed digitally using RadiAnt DICOM Viewer software (Version 2022.2, Medixant), with calibration applied to a standardized scale to ensure accuracy and reproducibility.

Reliability Study

To evaluate the reliability of the measurements, the PTS was independently assessed on all radiographs by two observers: an orthopedic surgeon with over 15 years of clinical experience in knee surgery and a radiologist with 10 years of experience. Each observer measured the PTS using all four methods described. To assess intra-observer reliability, all measurements

were repeated by the same observers following a 15-day washout period to minimize recall bias. Both observers were masked to each other's measurements and their own previous assessments. Before the evaluations, a standardized measurement protocol and an illustrative reference diagram were provided to ensure consistency across measurements.

Statistical Analysis

Descriptive statistics were reported as means and standard deviations for continuous variables and as frequencies and percentages for categorical variables. The normality of continuous data was evaluated using the Shapiro–Wilk test. Sex-based comparisons of PTS measurements obtained using the four methods were conducted using the Mann–Whitney U test due to non-normal data distribution. Friedman's test was used to compare PTS values across the four measurement techniques within each sex subgroup. Intra- and inter-observer reliability were assessed using the ICC with 95% confidence intervals, based on a two-way random-effects model for absolute agreement. Both single- and average-measure ICCs were calculated. According to commonly accepted thresholds, ICC values below 0.50 were interpreted as poor, between 0.50 and 0.75 as moderate, between 0.75 and 0.90 as good, and above 0.90 as excellent reliability (20). The relationship between demographic variables (age, weight, height, and body mass index) and PTS values obtained from each method was examined using Pearson correlation coefficients. A p-value <0.05 was considered statistically significant.

Results

A total of 70 patients (50 men (71.4%), 20 women (28.6%)) with a mean age of 34.6 ± 14.4 years (range: 18–76) were included. The mean body mass index (BMI) was 25.5 ± 3.3 kg/m², the mean height was 171.1 ± 7.3 cm, and the mean weight was $74.7 \pm$

Table 1 Demographic characteristics of the patients.

Variables	Data
Number of patients	70
Age (years $\pm$ SD) (min-max)	34.6 $\pm$ 14.4 (18-76)
Gender (n,%)	
Male	50 (71.4%)
Female	20 (28.6%)
Weight (kg $\pm$ SD)	74.7 $\pm$ 11.0
Height (cm $\pm$ SD)	171.1 $\pm$ 7.3
Body Mass Index (kg/m ² $\pm$ SD)	25.5 $\pm$ 3.3
Side (n,%)	
Right	27 (38.6%)
Left	43 (61.4%)

Abbreviations, SD: Standard deviation

11.0 kg. The right knee was evaluated in 27 patients (38.6%) and the left knee in 43 patients (61.4%). The demographic characteristics of the participants are presented in Table 1.

The inter- and intra-observer reliability for each PTS measurement method is summarized in Table 2. All four methods demonstrated excellent intra-observer reliability, with ICCs ranging from 0.916 to 0.975. The highest intra-observer reliability was noted for the anterior cortical line method by Observer B (ICC

= 0.975), whereas the lowest was for the posterior cortical line by the same observer (ICC = 0.916). Inter-observer reliability was also high across all methods, with ICC values ranging from 0.813 to 0.968. The anterior cortical line and fibular shaft axis methods demonstrated excellent inter-observer agreement (ICC up to 0.966). The proximal anatomical axis showed slightly lower, yet still good, reliability in the first measurement round (ICC = 0.813), improving to excellent (ICC = 0.955) in the second round.

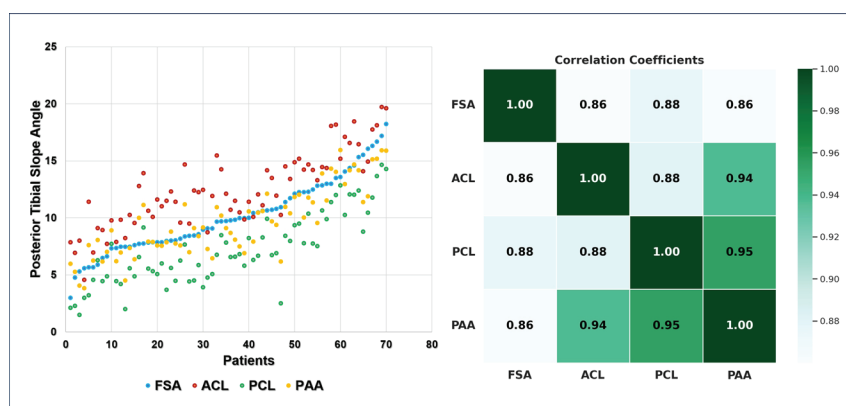


Figure 2

Distribution of posterior tibial slope measurements by method (left) and the correlation matrix of pairwise comparisons between the four radiographic techniques (right). Abbreviations: FSA: Fibular Shaft Axis, ACL: Anterior Cortical Line, PCL: Posterior Cortical Line, PAA: Proximal Anatomical Axis.

Table 2 Inter and Intra-observer Reliability of the Different Posterior Tibial Slope Measurements.

Variable	Reliability		ICC	95%CI	Interpretation
Fibular Shaft Axis	Intra-observer reliability				
	Observer A t ₁	Observer A t ₂	0.952	0.923-0.970	Excellent
	Observer B t ₁	Observer B t ₂	0.974	0.958-0.984	Excellent
	Inter-observer reliability				
	Observer A t ₁	Observer B t ₁	0.886	0.817-0.929	Good
	Observer A t ₂	Observer B t ₂	0.966	0.946-0.979	Excellent
Anterior Cortical Line	Intra-observer reliability				
	Observer A t ₁	Observer A t ₂	0.939	0.902-0.962	Excellent
	Observer B t ₁	Observer B t ₂	0.975	0.960-0.985	Excellent
	Inter-observer reliability				
	Observer A t ₁	Observer B t ₁	0.875	0.800-0.923	Good
	Observer A t ₂	Observer B t ₂	0.955	0.928-0.972	Excellent
Posterior Cortical Line	Intra-observer reliability				
	Observer A t ₁	Observer A t ₂	0.946	0.913-0.966	Excellent
	Observer B t ₁	Observer B t ₂	0.916	0.865-0.948	Excellent
	Inter-observer reliability				
	Observer A t ₁	Observer B t ₁	0.862	0.777-0.914	Good
	Observer A t ₂	Observer B t ₂	0.968	0.949-0.980	Excellent
Proximal Anatomical Axis	Intra-observer reliability				
	Observer A t ₁	Observer A t ₂	0.928	0.885-0.955	Excellent
	Observer B t ₁	Observer B t ₂	0.944	0.912-0.965	Excellent
	Inter-observer reliability				
	Observer A t ₁	Observer B t ₁	0.813	0.700-0.884	Good
	Observer A t ₂	Observer B t ₂	0.955	0.928-0.986	Excellent

Abbreviations: t₁: First time, t₂: Second time, ICC: Interclass Correlation Coefficient, CI: Confidence Interval

Sex-based comparisons of the PTS values are presented in Table 3. No statistically significant differences were found between men and women for any of the four measurement techniques ($p > 0.05$). The mean PTS values for the total cohort were $10.1^\circ \pm 3.2^\circ$ (fibular shaft axis), $12.4^\circ \pm 3.2^\circ$ (anterior cortical line), $7.2^\circ \pm 3.1^\circ$ (posterior cortical line), and $9.6^\circ \pm 3.0^\circ$ (proximal anatomical axis). The PTS angles demonstrated significant variability depending on the radiographic method used ($p = 0.001$).

Correlation analyses between demographic characteristics and the PTS measurements revealed no statistically significant associations ($p > 0.05$ for all).

The Pearson correlation coefficients between age, weight, height, BMI, and PTS values for each method ranged from -0.198 to $+0.018$, indicating weak and non-significant correlations (Table 4).

Scatter plots were generated to evaluate the pairwise correlations between the four measurement methods. The results demonstrated strong and statistically significant positive correlations ($p < 0.001$ for all pairwise analyses) between all methods (Figure 2). The highest correlation was observed between the proximal anatomical axis method and the anterior and posterior cortical line methods ($r = 0.94$ and $r = 0.95$, respectively).

Table 3 Comparison of the PTS measurement between genders.

Measurements	Total	Male	Female	p-value
Fibular Shaft Axis (°±SD)	10.1±3.2	10.4±3.4	9.2±2.6	0.200 ¹
Anterior Cortical Line (°±SD)	12.4±3.2	12.4±3.6	12.4±2.4	0.750 ¹
Posterior Cortical Line (°±SD)	7.2±3.1	7.2±3.3	7.2±2.6	0.760 ¹
Proximal Anatomical Axis (°±SD)	9.6±3.0	9.5±3.2	9.9±2.5	0.380 ¹
p-value	0.001 ²	0.001 ²	0.001 ²	

Abbreviations, SD: Standard Deviation, ¹ Mann-Whitney U test, ² Friedman's test

Table 4 Correlation between demographic characteristics and the PTS measurements

Correlations		FSA	ACL	PCL	PAA
Age	rho	-0.198	-0.172	-0.138	-0.143
	p-value	0.101	0.155	0.256	0.238
Weight	rho	-0.044	-0.046	-0.010	-0.031
	p-value	0.719	0.703	0.936	0.796
Height	rho	0.018	0.001	-0.059	-0.050
	p-value	0.882	0.994	0.629	0.683
BMI	rho	-0.054	-0.045	0.031	0.001
	p-value	0.656	0.711	0.800	0.995

Abbreviations: FSA: Fibular Shaft Axis, ACL: Anterior Cortical Line, PCL: Posterior Cortical Line, PAA: Proximal Anatomical Axis, BMI: Body Mass Index

Discussion

We aimed to evaluate and compare the reliability and agreement of four commonly used radiographic methods for measuring the PTS on standard lateral knee radiographs. All four methods-fibular shaft axis, anterior cortical line, posterior cortical line, and proximal anatomical axis-exhibited excellent intra-observer and good-to-excellent inter-observer reliability (ICC > 0.800), confirming their reproducibility across independent raters. Despite the high reliability of each method, we observed substantial variation in the absolute PTS values across anatomical reference lines, indicating that different approaches can yield significantly divergent slope measurements. However, strong, statistically significant positive correlations across all pairs of measurement techniques suggest that these methods are directionally consistent

and comparably valid, though not interchangeable. Notably, the PTS measurements did not significantly differ between male and female patients, and no significant correlations were found between PTS values and the demographic variables of age, height, weight, or BMI. These findings suggest that PTS values are independent of patient-specific anthropometric characteristics and that consistent, reliable measurements can be obtained regardless of demographic differences, provided standardized imaging protocols and clearly defined anatomical landmarks are used.

The observed reliability data are broadly consistent with, and in many cases exceed, those reported in the existing literature. For instance, Lee et al. (21) reported moderate to good interobserver reliability depending on the method used, with ICC values ranging from

0.61 to 0.89. Similarly, Abdul Wahid et al. (17) observed inter-rater agreement ranging between 0.68 and 0.85. In a detailed comparative study of multiple radiographic techniques, Fletcher et al. (22) reported a wider ICC range from 0.529 to 0.926, highlighting the variability in reliability across methods. In their analysis, techniques based on the posterior tibial cortex and mechanical axis yielded higher reliability, whereas those referencing the fibular shaft or anterior cortex demonstrated lower reproducibility. The consistently high ICC values observed in our study across all four methods may be attributed to several methodological strengths. These include the use of standardized true lateral radiographs with adequate tibial length (≥ 15 cm distal to the plateau), a clearly defined measurement protocol, and evaluations conducted by experienced observers. Taken together, our results underscore the importance of technical rigor in imaging and measurement procedures. They also suggest that when appropriately applied, all four methods can yield highly reliable inter-observer assessments of the PTS.

The accuracy of PTS measurements is highly dependent on the choice of anatomical reference axis and the imaging modality used. In our study, although all four radiographic techniques demonstrated excellent reliability, the mean PTS values varied substantially depending on the chosen reference line, ranging from 7.2° (posterior cortical line) to 12.4° (anterior cortical line). Yoo et al. (5) emphasized that different reference axes yield significantly different PTS values, with posterior cortex-based measurements being more consistent and reproducible, whereas anterior cortex- or anatomical-axis-based approaches may be affected by tibial bowing or malalignment. Hashemi et al. (8) similarly showed that PTS values can shift significantly depending on the axis used, and such differences can alter biomechanical interpretations, particularly in anterior cruciate ligament injury risk assessments. Fletcher et al. (22) later noted that short lateral knee radiographs may introduce projection errors and underrepresent the tibial axis, and recommended full-length CT scans for more accurate tibial alignment and slope assessment. These findings collectively support the critical need for standardization in both reference axis selection and imaging modality to ensure clinically meaningful and reproducible PTS measurements.

Whether PTS differs between sexes remains debated in the literature. In our study, no statistically significant differences were observed between male and female patients across any of the four radiographic measurement techniques ($p > 0.05$). This finding aligns with the results of Clinger et al. (23), who reported no significant sex-based differences in medial,

lateral, or global PTS in a cadaveric study of 250 specimens. Similarly, Pangaud et al. (24) found that men exhibited slightly higher global and lateral PTS values than women, but no difference was observed in the medial PTS. In contrast, Weinberg et al. (25), in a large osteological analysis, reported that women had significantly greater medial and lateral PTS values compared to men. These conflicting results may reflect differences in imaging modalities, anatomical reference axes, and the demographic composition of the study populations. In our study, we also found no significant correlations between PTS values and the demographic variables of age, height, weight, and BMI. This suggests that PTS may be largely independent of individual anthropometric characteristics.

This study has several notable strengths. First, it is one of the few studies to systematically compare four commonly used radiographic methods for measuring PTS on standardized lateral knee radiographs. Second, this study benefited from a standardized imaging protocol, predefined measurement definitions, and blinded, repeated readings by experienced specialists, yielding excellent intra- and inter-observer reliability. These features enhance the internal validity and reproducibility of the measurements within the study setting. Third, the strict inclusion criteria ensured high-quality radiographs with adequate tibial length, enhancing measurement consistency and validity. Finally, the use of digital DICOM-based measurements with calibration further strengthened the methodological rigor and reproducibility.

Several limitations must be acknowledged, however. The study was conducted in a single tertiary care center, which may limit the generalizability of the findings. Although the number of radiographs included ($n = 70$) was higher than the calculated minimum sample size, the cohort may still not reflect broader anatomical variability. Additionally, only lateral radiographs were used; the potential influence of patient positioning errors on slope measurements, despite stringent selection criteria, cannot be entirely ruled out. This evaluation was performed by a relatively small number of specialists, which may limit generalizability and could underestimate inter-observer variability in broader clinical practice. Although a standardized protocol and a washout period were used to enhance reproducibility, multi-center validation with larger and more diverse rater cohorts is warranted. Lastly, the study did not include a comparison with advanced imaging modalities, such as computed tomography (CT) or magnetic resonance imaging (MRI), which may provide a more precise assessment of the tibial slope.

This evaluation was performed by a relatively small number of specialists (two observers), which may underestimate inter-observer variability in wider practice. Although a standardized protocol and a washout period were used to enhance reproducibility, multi-center validation with larger, more diverse rater cohorts is warranted.

Conclusion

This study demonstrated that all four radiographic methods used to measure the PTS yielded high intra- and inter-observer reliability, confirming the reproducibility and consistency of these techniques when applied under standardized conditions. Despite strong correlations among the methods, absolute PTS values differed systematically by method, and the techniques are not interchangeable. This suggests that the choice of anatomical reference axis plays a more critical role in determining the measured slope than the measurement technique itself. Therefore, although each method offers internal consistency, caution must be exercised when comparing PTS values across studies because differences in reference axes may significantly influence the reported results. To ensure comparability and reproducibility, clinicians and researchers should pre-specify a single reference axis and use it consistently within a study or clinical pathway. Moreover, no significant associations were found between PTS values and patient demographics such as sex, age, height, and weight, indicating that these variables may not be major determinants of slope variation in radiographic assessments. Overall, our findings highlight the importance of clearly defining the measurement method in clinical evaluations and scientific reporting to ensure the accurate interpretation and meaningful comparison of PTS data.

Abbreviations

PTS - Posterior Tibial Slope; FSA-Fibular Shaft Axis; ACL - Anterior Cortical Line; PCL - Posterior Cortical Line; PAA – Proximal Anatomical Axis; ICC – Intraclass Correlation Coefficient; SD - Standard Deviation; CI - Confidence Interval; CT - Computed Tomography; MRI - Magnetic Resonance Imaging; DICOM - Digital Imaging and Communications in Medicine

Conflict of Interest Statement

The authors have no conflict of interest to declare.

Ethical Approval

Alaaddin Keykubat University Ethics Committee approved the study protocol. Date:11.06.2025 Issue:10-2. The study was conducted in line with the principles of the "Helsinki Declaration".

Consent to Participate and Publish

This retrospective observational study involved no human participation and was based solely on radiographic evaluations.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of Data and Materials

Data available on request from the authors.

Artificial Intelligence Statement

The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

Authors Contributions

YY: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Visualization; Writing-original draft.

OK: Investigation; Validation; Writing-original draft; Data curation; Formal analysis; Writing- review & editing.

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Comparison of Fistula Rates After Urethrocutaneous Fistula Repair Versus Primary Hypospadias Repair for Distal Hypospadias

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Cite this article as: Khalilova P, Ergun E, Gollu G, Ates U, Bingol Kologlu M, Yagmurlu A, Cakmak M. Comparison of Fistula Rates After Urethrocutaneous Fistula Repair Versus Primary Hypospadias Repair for Distal Hypospadias. Med J SDU 2025;32(4):337-341.

Abstract

Objective

To investigate the incidence of fistula formation following distal hypospadias repair and the recurrence rate after fistula correction within a 15-year period.

Material and Method

Postoperative fistula development rates of patients who underwent primary distal hypospadias repair between the years 2007-2022 were analyzed. The rates of recurrence of fistula after fistula repair were examined.

Results

A total of 417 patients were included in the study. Fistula developed in 54 patients (13%) after the first surgery. The mean age of the patients at the time of

the first operation was 39 months. It was observed that there was fistula approximately 10 months after the operation. Re-fistula formation was observed in 14 (25%) of 54 patients who underwent fistula repair. Re-fistula occurrence time after fistula repair was 5 days-18 months. The most common fistula location after the first operation was the coronal level (53%), with 28 patients where as the most location after the fistula repair was also coronal level (71% with 10 patients).

Conclusions

In patients who develop fistula after distal hypospadias repair, the risk of developing a fistula after the repair is higher than the risk of developing a fistula after the primary repair. These results may be related to the techniques and methods used in primary repair.

Keywords: hypospadias, fistula, children

Introduction

Hypospadias is one of the congenital anomalies seen in every 200-300 births and considered as a midline defect (1). Different causes regarding its etiology and epidemiology were mentioned (1,2). Hormonal

irregularity in the maternal period is one of the mostly stated ones in the current literature (3). No matter how advanced surgical techniques and materials are, there is not a single gold standard treatment method for hypospadias repair (4). Location of the urethra, whether it is accompanied by penile curvature,

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Received: 07.09.2025 • **Accepted:** 10.11.2025

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the size of penis, urethral groove status, etc. are important factors that effect the choice of repair (5). Tubularized incised plate urethroplasty (TIPU) which has been performed with an increased frequency may be performed to repair hypospadias with mild penile ventral curvature (6). Although it is considered as one of the techniques that may be learned easily and has a high success rate, postoperative complications are inevitable (7,8). Urethrocuteaneous fistula is one of the most common complications after hypospadias repair (9). This rate varies between 5-50%, depending on the degree of hypospadias and the surgical technique (9). As it is in primary surgery, in case of urethrocuteaneous fistula, the time of repair and technique and many variables effect the outcome (10). In this study, it was aimed to present the results of postoperative urethrocuteaneous fistula repairs in children who underwent hypospadias surgery due to distal hypospadias within 15 years.

Material and Method

Patients who underwent primary distal hypospadias repair between 2007 and 2022 and patients who developed fistula on the postoperative period were

included in the study. Demographic data, comorbidities, location of the urethral opening, surgical technique, duration and materials, and postoperative follow-up of the patients were analyzed and the recurrence rates of fistula after fistula repair were examined. The time of recurrence in fistulas, time for repair, the repair technique, and the materials used were recorded.

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 23 (IBM Corp., Armonk, NY, USA). Categorical variables were analyzed using the Chi-square (χ^2) test. A p-value of less than 0.05 was considered to indicate statistical significance ($p < 0.05$).

Results

A total of 417 patients who underwent distal hypospadias repair within 15 years were included in the study. The mean age of the patients was 39 (6-156) months. Megameatus was observed in 69 patients, glanular hypospadias in 72 patients, coronal in 100 patients, subcoronal in 121 patients and midpenile in 55 patients. Table 1 provides a detailed presentation of the information.

Table 1 Urethra Locations and Fistula Rates

Primary	Rate of fistula	Fistula	Re-fistula	Re-fistula	Re-fistula
Megameatus (16.55%;n=69)	2,8 %	Glanular (n=1)			
		Coronal (n=1)			
Glanular (17.26%;n=72)	5,5 %	Glanular (n=2)			
		Coronal (n=2)	Coronal (n=1)	Coronal(n=1)	Coronal(n=1)
Coronal (23.98%;n=100)	22 %	Glanular (n=5)			
		Coronal (n=10)	Coronal (n=3)	Coronal(n=1)	
			Subcoronal(n=1)		
		Subcoronal(n=5)			
Subcoronal (29,01%;n=121)	14 %	Midpenile (n=2)			
		Coronal (n=11)	Coronal (n=3)		
		Subcoronal(n=6)	Subcoronal(n=1)		
Midpenile (13.19%;n=55)	16 %	Glanular (n=1)	Glanular (n=1)		
		Coronal (n=4)	Coronal (n=2)		
		Subcoronal(n=3)	Subcoronal(n=1)		
		Midpenile (n=1)	Coronal (n=1)		

Additional urinary anomalies (inguinal hernia, undescended testicle, hydrocele, ureteropelvic junction obstruction, Wilms' tumor, renal stone) were accompanied in 29 patients (7%). There was a comorbidity in 43 patients (10.5%), 21 of whom were cardiovascular pathologies. Tubularization was performed with the Snodgrass technique in 94,4 % (n=393) patients. Meatoplasty or glanuloplasty was sufficient in the remaining patients (5.6%, n=24). Early complications such as hematoma, bleeding and edema were encountered 12 % of the patients in the present study (n=50). There were 22 children (5,2 %) with meatal stenosis after the primary repair and in 18 % of them urethrocuteaneous fistula was occurred (n=4). Glans dehiscence was not encountered in any children. Fistula developed in 54 patients (13%) after the hypospadias repair. Mean time for fistula formation was 10 months (1-129 months). In 42 patients (78%), the fistula size was less than 2 mm, while in 12 patients (22%), it was greater than 2 mm. Fistula repairs were performed on these patients 13 months (8-20 months) after the hypospadias repair. Re-fistula formation was observed in 14 (25%) of 54 patients who underwent fistula repair. The most common fistula location after the first operation was at the coronal level (53%), with 28 patients. Re-fistula was observed approximately 8 months after the operation. Recurrent fistula occurred at the coronal level in most children (71% with 10 patients). We performed simple fistula repair in 46,3 % (n=25), simple ligation in 24 % (n=13), Mathieu technique in 18,6 % (n=10) and TIPU in 11,1 % (n=6). Among these, refistula developed in 6 children (24%) who underwent simple fistula repair, in 4 (30%) who underwent simple ligation, in 2 (20%) who underwent Mathieu technique, and in 2 (33%) who underwent TIPU. A child required third and other required fourth operations due to recurrent fistulas.

Discussion

The present study demonstrated that recurrent fistula rate after urethrocuteaneous fistula repair is higher than primary fistula formation in children who underwent surgery due to distal hypospadias (25%

vs 13%, respectively). Even though the number of patients are not relatively big, there are some studies supporting these data (11,12). The reason for such a high rate compared to the literature may be that there are multiple surgeons and therefore the diversity of techniques and skills is high (13). Our long follow up time is also another reason for encountering high fistula rate.

Considering all the complications of hypospadias, a rate of 1-90% is stated (11). Early complications include bleeding or hematoma, edema, wound infection, skin necrosis, flap or graft necrosis, wound dehiscence, catheter problems, penile erection, and bladder spasms. In the late period, meatal and urethral strictures, diverticula development, continuation of curvature, psychological and cosmetic problems are encountered (14,15). Urethrocuteaneous fistulas are seen in both the short and long term period (10,15). Due to the lack of long term follow up, some of these complications can not be addressed.

In general, there are some risk factors in the formation of fistula and other complications: the level of hypospadias, the length of the damaged urethra, the use of tissue with poor blood supply, the use of inappropriate techniques and materials, meatal and urethral stenosis, diverticula, urinary tract or wound infection. (6,15). The increased rate of recurrent fistula may be a result of damaged urethra and deteriorated blood supply of surrounding structures.

Preoperative use of testosterone and low growth hormone in patients are also mentioned to be risk factors for fistula formation. There are debates that androgens delay wound healing and increase inflammation (16–18). None of the patients received hormone treatment before or after the first operation.

The short time between hypospadias and fistula repair is another risk factor (9,12). Although six months was considered sufficient in the past, it is recommended in the current literature that this period should be extended up to one year (12,19). Our approach

Table 2 Comparison of Fistula Rates Based on the Use of Dartos Flap

Group	Use of Dartos Flap	Number of Fistulas, n (%)
Group 1 (203 patients)	Yes	35 (17.2%)
Group 2 (214 patients)	No	19 (8.8%)

regarding repair time seems to be in line with current literature. Conventional approach of the authors regarding repair time of urethrocutaneous fistula may be a factor on the increased re-fistula rates. But the studies also support that recurrence rate increases 3 times in recurrent fistulas (11). A similar rate was achieved in our study (13/25, 1,92 times). The time may not be the one and only cause of this increase. Also in terms of meatal and urethral stenosis, the risk of fistula formation increases due to proximal urinary pressure (12).

In recurrent fistulas, one of the important approaches is to determine the location and number of the fistula. In large urethrocutaneous fistulas with a high flow rate, 'pinpoint' fistulas may be overlooked because the urine pressure will be low. Therefore, an examination should be performed by administering isotonic solution, methylene blue, antiseptic or pomade-like substances from the meatus before the operation. Coronal region may be a highly risked location in both primary and recurrent fistulas. In the present study, 53% of the fistulas developed in this area after the primary repair (n=28).

The reason for this is that the blood supply to that area is weak, and it is difficult to bring the supportive tissues over the urethral anastomosis (12). This situation could explain why the recurrent fistulas in our study are located at the coronal level.

It is reported that the use of supportive tissues reduce the rate of fistula (10). However, our results indicate a higher fistula rate in patients with Dartos flap application (17.2%) compared to those without it (8.8%). This unexpected finding may be attributed to the complexity of the cases where a Dartos flap was used, potential surgical technique variations, or compromised vascularization in previously operated tissues. Further studies are needed to clarify this association (Table 2). In the study of Snodgrass et al., 50% (5/10) fistulas were seen in reoperative TIPU cases without the use of supporting tissue (dartos, t. vaginalis), while 4% (2/51) were observed in those used. There are different techniques in fistula repair and the results have started to be more satisfactory day by day (7,14,20–22). Simple fistula repair with primary closure is the most commonly used repair technique. Here, the choice depends on the surgeon's preference. A series of 40 patients with simple ligation was presented by Shirazi et al. and it is recommended for cases smaller than 4 mm (5). Repair with double ligation is recommended by Karakuş et al. for fistulas smaller than 2 mm (23). Modified Cecil-Culp technique, which is one of the preferred methods in recurrent

fistulas, gives successful results. The use of buccal and lingual mucosa can also be preferred in recurrent fistulas (10). Repairs using fascia lata, amniotic membrane, rectal mucosa are the substitution tissues and the Mathieu technique and TUPU are other alternative techniques for repairing fistulas (21,22). We performed simple fistula repair in 46,3 % (n=25), simple ligation in 24 % (n=13), Mathieu technique in 18,6 % (n=10) and TIPU in 11,1 % (n=6). The fact that Mathieu was applied in patients with refistula caught our attention.

The overlapping of the suture lines is a negative situation both because it creates malnutrition and prepares the ground for the urethral epithelium to walk on the skin. The technique preferred in the first repair is effective in the formation of the fistula as well as in its spontaneous closure (24). Spontaneous closure may be seen in pinpoint fistulas, especially in patients undergoing spongioplasty (25,26). There was no spontaneous closure in our study.

Conclusion

In patients who develop fistula after distal hypospadias repair, the risk of developing a fistula after the repair is higher than the risk of developing a fistula after the primary repair.

Conflict of Interest Statement

The authors declare no conflict of interest.

Ethical Approval

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ankara University Faculty of Medicine Clinical Research Ethics Committee, No: i10-811-24.

Funding

No financial assistance was received to support this study.

Availability of Data and Materials

The data of the study were retrieved from electronic patient record of Hospital Authority.

Artificial Intelligence Statement

Generative AI and AI-assisted technologies were NOT used in the preparation of this work.

Authors Contributions

PK: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Visualization; Writing-original draft.

EE: Data curation; Formal analysis; Writing- review & editing.

GG: Investigation; Validation; Writing-original draft.

UA: Investigation; Validation; Writing-original draft.

MBK: Investigation; Validation; Writing-original draft.

AY: Data curation; Formal analysis; Writing- review & editing.

MC: Data curation; Formal analysis; Writing- review & editing.

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Expectations of Medical School Students for Leisure Time Activities

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Cite this article as: Ercan S, Taş FU, Arslan E, Savran M, Şenol N. Expectations of Medical School Students for Leisure Time Activities. Med J SDU 2025;32(4):343-352.

Abstract

Objective

This study aimed to examine the expectations of medical students towards leisure time activities, reasons for participation, barriers they face, and their attitudes towards leisure time management within the framework of semester differences.

Material and Method

Süleyman Demirel University Faculty of Medicine students were included in the study on a voluntary basis. Participants were evaluated using a descriptive data form, the Leisure Time Management Scale, the Leisure Time Facilitators Scale, and the Leisure Time Barriers Scale. The data obtained were analyzed using SPSS software.

Results

458 students participated in the study. Participation in social activities was the lowest in class 2 ($p=0.008$). The reasons for participation were having fun, getting away from stress, and socializing, while the reasons

for not participating were the intensity of the course and the incompatibility of activity times. Participants' scores on the Scales of Leisure Time Management, Leisure Time Facilitators, and Leisure Time Barriers show class differences. Among the activities requested by students, music/concerts, social excursion programs, and hobby workshops were the most requested. These findings suggest that students have different attitudes towards social activities and leisure time management.

Conclusion

Medical students' expectations for leisure time activities change as the academic class progresses; intensive academic programs and structural barriers limit participation in social activities. These findings provide clues to educational administrators in terms of developing students' leisure time management strategies and supporting their psychosocial well-being.

Keywords: Leisure time, leisure time management, social activities, barriers, facilitators.

Introduction

Time is a concept that cannot be substituted or replenished, and whose value becomes more apparent once it is lost. Although it has been defined in various ways for thousands of years, time remains

a unique phenomenon that is not treated equally by everyone and is used at the discretion of the individual (1). Leisure time is defined as the period available for personal use after fulfilling obligations such as work, employment, sleep, and household tasks. It has also been recognized as a legal right in Article 24 of the

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Received: 30.05.2025 • **Accepted:** 15.11.2025

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Universal Declaration of Human Rights, which states, “Everyone has the right to rest and leisure, including reasonable limitation of working hours and periodic holidays with pay.” Technology advancements and rising living standards have made the place of leisure time in society’s structure more crucial. The World Leisure and Recreation Association defines leisure as a specific time period in which individuals can engage in activities that enhance their creativity and provide them with enjoyment and satisfaction (2). The concept of recreation emerged after the Industrial Revolution and was enriched in content following World War II, as increased personal income and rapid urbanization contributed to greater social mobility (3).

How leisure time is utilized depends entirely on the individual’s free will and common sense. Recreational activities used to occupy leisure time have become indispensable elements of modern social life (4). Although sports, music, and fine arts are commonly the first areas that come to mind in discussions of leisure (5), any activity that allows individuals to pursue interests aligned with their abilities and to discover themselves through those abilities can be considered a leisure activity (6). It has been noted that individuals seek to spend their leisure time for various reasons and expectations, often sharing a common purpose in participating in such activities. The purpose of engaging in leisure activities may not only include gaining knowledge, performing physical activity, or producing visual-auditory outputs, but also simply escaping from time that might otherwise be filled with boredom (7). Leisure can thus be defined as a period in which the individual exercises autonomy, experiences enjoyment, satisfaction, and happiness, undertakes activities voluntarily and without material gain, and lives fulfilling experiences independent of external pressures (8,9).

It has been found that medical students who do not engage in extracurricular activities are at higher risk of experiencing stress. Extracurricular activities are seen as a means through which students can express their autonomy, and they can enhance motivation both for academic success and broader life goals (10).

In terms of participation in leisure activities, various barriers and facilitators come into play. The Leisure Facilitators Scale was developed by Raymore (2002) (11). In this scale, individual characteristics are categorized as intrapersonal facilitators, support from close social networks as interpersonal facilitators, and factors such as financial status and gender as structural facilitators, thereby dividing the scale into three dimensions (9). The concept of “barrier” refers

to the reasons experienced by individuals that limit or prevent their participation in leisure activities (12). Alexandris and Carroll (1997) classified barriers into six distinct dimensions: individual psychology, lack of information, inadequate facilities, lack of companions, time constraints, and low interest (13). Gurbuz et al. (2020) conducted a validity and reliability study to adapt this scale to Turkish culture (14). In the literature, some studies have categorized the barriers more concisely into internal and external factors rather than six separate sub-dimensions (15).

The university period is a critical time for individuals to explore themselves and their surroundings, and it is also considered the most advantageous stage for allocating time to leisure activities (16). Although the education in medical faculties is generally longer and more intensive compared to other faculties, this period still represents the most favorable time for medical students, given the demanding nature of their future professional lives. Future physicians, who must navigate stressful periods at a young age while developing a healthy sense of self-confidence, may nevertheless face various challenges stemming from either internal or external sources in participating in leisure activities.

The aim of this study is to examine how medical students utilize their leisure time, identify the challenges they encounter in doing so, and provide data that may serve as a guide for administrators and stakeholders interested in this topic.

Material and Method

Students enrolled at Süleyman Demirel University Faculty of Medicine during the 2023–2024 academic year who voluntarily agreed to participate were included in the study. Internship-level students (6th-year medical interns) were excluded owing to their distinct, shift-based clinical workload and limited control over leisure time, which would bias comparisons with pre-internship students.

After collecting descriptive information from the participants, they were asked to complete a paper-based questionnaire consisting of items from the Leisure Time Management Scale (17,18), the Leisure Facilitators Scale (19, 20), and the Leisure Constraints Scale (13, 14). The questionnaire was administered in a face-to-face setting.

Descriptive Data Form

This form, developed by the researchers, gathered information on students’ sociodemographic charac-

teristics, their reasons for participating or not participating in social activities, and the types of social activities they were interested in.

Leisure Time Management Scale

This scale consists of 15 items grouped under four subdimensions: "Goal Setting and Evaluation" (6 items), "Leisure Attitude" (3 items), "Evaluation" (3 items), and "Scheduling" (3 items). Items are rated on a 5-point Likert scale ranging from 1 (Strongly Disagree) to 5 (Strongly Agree). Items under the "Scheduling" subdimension are reverse-scored due to their negative phrasing, while the others are positively phrased. Higher scores indicate more effective leisure time management (17,18). The scale was adapted into Turkish by Akgul et al. (18).

Leisure Facilitators Scale

This 16-item scale is structured into three factors: Intrapersonal, Interpersonal, and Structural Facilitators. Items are rated on a 5-point Likert scale ranging from 1 (Not Important at All) to 5 (Very Important) (19, 20). Gurbuz et al. adapted the scale into Turkish (20).

Leisure Constraints Scale – Short Form

This scale comprises 18 items distributed across six subdimensions: Lack of Companionship, Lack of Interest, Facilities, Time, Individual Psychology, and Lack of Information. Items are rated on a 4-point Likert scale ranging from 1 (Not Important at All) to 4 (Very Important) (14, 19). The Turkish adaptation of the scale was developed by Gurbuz et al. (14).

Power Analysis / Sample Size

The study population consisted of 1.398 students enrolled at Süleyman Demirel University Faculty of Medicine during the 2023–2024 academic year. Assuming a 5% margin of error and a 99% confidence level, the required sample size was calculated to be 451 participants.

Statistical Analysis

Quantitative data were analyzed using the SPSS v.23 software package (IBM Corp., Armonk, NY, USA). The normality of data distribution was assessed using the Shapiro-Wilk test, followed by descriptive analyses. After grouping the students according to their academic year (14), different analyses were conducted using the Kruskal-Wallis test, independent t test and the Chi-Square test with Monte Carlo correction. Data were presented as median (25th–75th percentile) and percentages (n).

A p-value of <0.05 was considered statistically significant. For continuous variables not conforming

to a normal distribution, the Spearman correlation test was applied. Correlation coefficients (r values) were interpreted as follows: $0 < r < 0.20$: very weak correlation, $0.20 \leq r < 0.40$: weak correlation, $0.40 \leq r < 0.60$: moderate correlation, $0.60 \leq r < 0.80$: strong correlation, $0.80 \leq r < 1.00$: very strong correlation (21).

Results

A total of 458 students participated in the study, with 56.6% (n=259) identifying as female and 43.4% (n=199) as male. An evaluation of the students' descriptive characteristics revealed that as the academic year progressed, there was a shift toward living alone ($p < 0.001$). The frequency of participation in social activities was determined to be 5 (3–10) times per month, with the lowest level of participation observed among second-year students ($p = 0.008$) (Table 1).

When considering all students, the most common reasons for participating in social activities were entertainment, stress relief, and socialization/making friends. First-year students were more likely to cite "developing skills" as a reason for participating, whereas this reason was less prominent among fourth-year students ($p = 0.011$). As students advanced through medical school, participation in social activities for the purpose of "relieving stress" became more common, especially among fifth-year students ($p = 0.020$) (Table 2).

Among all students, the most frequently cited reasons for not participating in social activities were inappropriate event timing, academic workload, and scheduling conflicts with lectures. Health-related issues were the most prominent barrier among first-year students ($p = 0.004$). Lack of interest in activities was least reported among second-year students ($p = 0.013$). Lack of interest in social activities among peers was lowest in the second year and highest in the fifth year ($p = 0.029$). Academic workload and scheduling conflicts with lectures were most prominent in the fourth year ($p = 0.020$ and $p = 0.025$, respectively) (Table 3).

Among the types of activities students wished to participate in, the top three were music/concert events, social trips, and hobby/craft workshops. These preferences did not significantly differ between academic years ($p > 0.05$) (Table 4).

The median scores obtained by participants were 50 (44–57) on the Leisure Time Management Scale,

Table 1 Identifying Information

	Total (n=458)	Year 1 (n=92)	Year 2 (n=61)	Year 3 (n=94)	Year 4 (n=116)	Year 5 (n=95)	p Value
Age (years)	22 (20-23)	19 (18-20) ^a	20 (20-21) ^b	21 (21-22) ^c	22 (22-23) ^d	23 (23-24) ^e	<0.001*
Gender (K/E), % (n)	56.6 (259) / 43.4 (199)	52.2 (48) / 47.8 (44)	55.7 (34) / 44.3 (27)	57.4 (54) / 42.6 (40)	62.1 (72) / 37.9 (44)	53.7 (51) / 46.3 (44)	0.648
Residence status, % (n)							<0.001*
With family	25.6 (117)	35.2 (32) ^a	14.8 (9) ^a	33 (31) ^a	22.4 (26) ^a	20 (19) ^a	
With friend(s)	20.6 (94)	25.3 (23) ^{a,b}	26.2 (16) ^{a,b}	26.6 (25) ^b	17.3 (20) ^{a,b}	10.5 (10) ^a	
Alone	53.8 (247)	39.5 (37) ^a	59 (36) ^{a,b}	40.4 (38) ^a	60.3 (70) ^b	69.5 (66) ^b	
Economic status, % (n)							0.123
Good	24.9 (114)	25.3 (23)	21.3 (13)	26.6 (25)	31.1 (36)	17.9 (17)	
Moderate	68.8 (315)	69.2 (64)	63.9 (39)	67 (63)	65.5 (76)	76.8 (73)	
Poor	6.3 (29)	5.4 (5)	14.8 (9)	6.4 (6)	3.4 (4)	5.3 (5)	
Health status, % (n)							0.264
Good	77.6 (356)	80.2 (74)	67.2 (41)	80.6 (76)	77.6 (90)	78.9 (75)	
Moderate	20 (91)	17.6 (16)	26.2 (16)	19.4 (18)	19 (22)	20 (19)	
Poor	2.4 (11)	2.2 (2)	6.6 (4)	0 (0)	3.4 (4)	1.1 (1)	
Leisure time (hours/week)	20 (10-35)	20 (10-40)	14 (10-30)	20 (10-35)	19 (10-30)	25 (10-35)	0.074
Participation in social activities (times/month)	5 (3-10)	4 (2-10) ^a	4 (2-5) ^b	5 (3-10) ^a	5 (3-10) ^a	5 (4-10) ^a	0.008*

Data are presented as median (25th–75th percentile) and % (n). Kruskal-Wallis Test and Chi-Square Test with Monte Carlo correction were applied. *: p-value < 0.05 was considered statistically significant. Different superscript letters indicate significant differences between groups.

Table 2 Reasons for Students' Participation in Social Activities

Reason for participating in social activities, % (n)	Total (n=458)	Year 1 (n=92)	Year 2 (n=61)	Year 3 (n=94)	Year 4 (n=116)	Year 5 (n=95)	p Value
Having fun	17.4 (391)	16.5 (79)	16.7 (49)	16.3 (79)	18.8 (96)	18.3 (88)	0.152
Relieving stress	15.2 (343)	12.3 (59) ^a	15.0 (44) ^{a,b}	14.4 (70) ^{a,b}	17.4 (89) ^{a,b}	16.8 (81) ^b	0.020*
Socializing/making friends	13.1 (295)	12.3 (59)	12.2 (36)	13.0 (63)	14.3 (73)	13.3 (64)	0.829
Improving interpersonal relationships	11.2 (252)	12.1 (58)	10.2 (30)	10.9 (53)	11.7 (60)	10.6 (51)	0.426
Gaining experience	9.2 (207)	10.9 (52)	8.2 (24)	9.7 (47)	8.8 (45)	8.1 (39)	0.058
Acquiring new skills	9.1 (204)	9.8 (47)	9.9 (29)	9.3 (45)	7.8 (40)	8.9 (43)	0.136
Maintaining health	8.3 (187)	7.7 (37)	9.5 (28)	8.4 (41)	8.4 (43)	7.9 (38)	0.804
Enhancing skills	8.2 (184)	9.2 (44) ^a	9.5 (28) ^{a,b}	8.4 (41) ^{a,b}	6.1 (31) ^b	8.3 (40) ^{a,b}	0.011*
Developing personality	8.2 (184)	8.6 (41)	8.5 (25)	9.3 (45)	6.8 (35)	7.9 (38)	0.092
Other	0.2 (5)	0.4 (2)	0.3 (1)	0.4 (2)	0 (0)	0 (0)	0.079

The data are presented as % (n). Since multiple responses were allowed, the value of n exceeds the sample size. The Chi-Square Test with Monte Carlo correction was applied. *: p-value is significant at the 0.05 level. There is a significant difference between groups indicated by different superscript letters.

Table 3 Reasons for Students' Non-Participation in Social Activities

Reason for not participating in social activities, % (n)	Total (n=458)	Year 1 (n=92)	Year 2 (n=61)	Year 3 (n=94)	Year 4 (n=116)	Year 5 (n=95)	p Value
Inconvenient timing of activities (day/hour)	20.0 (298)	20.0 (60)	20.3 (37)	18.6 (55)	21.1 (81)	19.5 (65)	0.424
Excessive course workload	18.8 (281)	16.0 (48) ^a	21.4 (39) ^{a,b}	17.3 (51) ^{a,b}	21.9 (84) ^b	17.7 (59) ^{a,b}	0.020*
Conflict between event time and class time	16.0 (239)	13.0 (39) ^a	20.9 (38) ^a	15.3 (45) ^a	18.5 (71) ^b	13.8 (46) ^a	0.025*
Lack of interest in the activity	14.8 (221)	16.7 (50) ^a	12.1 (22) ^b	17.3 (51) ^a	11.7 (45) ^a	15.9 (53) ^a	0.013*
Unawareness of activities	11.5 (171)	15.3 (46)	9.9 (18)	11.5 (34)	9.7 (37)	10.8 (36)	0.054
Lack of interest in social activities among peers	8.5 (127)	8.0 (24) ^{a,b}	6.0 (11) ^b	7.5 (22) ^{a,b}	8.4 (32) ^{a,b}	11.4 (38) ^a	0.029*
Financial constraints	8.0 (119)	5.7 (17)	7.7 (14)	10.5 (31)	7.0 (27)	9.0 (30)	0.119
Health problems	1.6 (24)	4.0 (12) ^a	0.5 (1) ^{a,b}	0.3 (1) ^b	1.3 (5) ^{a,b}	1.5 (5) ^{a,b}	0.004*
Other	0.9 (13)	1.3 (4)	1.1 (2)	1.7 (5)	0.3 (1)	0.3 (1)	0.186

Data are presented as percentages (n). Since multiple responses were allowed, the n value exceeds the sample size.

A Chi-Square Test with Monte Carlo correction was performed. *: p-values less than 0.05 were considered statistically significant.

Significant differences were observed between groups denoted by different superscript letters

Table 4 Activities Requested by Students

	Total (n=458)	Year 1 (n=92)	Year 2 (n=61)	Year 3 (n=94)	Year 4 (n=116)	Year 5 (n=95)	p Value
Music/concert events	17.2 (351)	15.7 (68)	18.0 (46)	16.1 (71)	18.3 (92)	18.3 (74)	0.908
Social trips	16.2 (330)	14.4 (62)	14.5 (37)	16.3 (72)	17.5 (88)	17.6 (71)	0.146
Hobby workshops/ Handicrafts courses	12.8 (260)	11.8 (51)	12.1 (31)	12.7 (56)	12.9 (65)	14.1 (57)	0.800
Sports/exercise activities	12.0 (245)	12.5 (54)	12.9 (33)	10.4 (46)	12.7 (64)	11.9 (48)	0.691
Cultural events	11.1 (227)	10.9 (47)	11.7 (30)	11.8 (52)	9.8 (49)	12.1 (49)	0.412
Intellectual competitions (e.g., chess)	7.0 (142)	7.6 (33)	7.8 (20)	7.2 (32)	6.8 (34)	5.7 (23)	0.443
Science competitions	6.1 (124)	7.6 (33)	6.3 (16)	6.3 (28)	5.4 (27)	5.0 (20)	0.172
Intellectual reading activities (non-academic)	6.1 (125)	6.3 (27)	6.6 (17)	5.9 (26)	7.2 (36)	4.7 (19)	0.451
Community service/Social responsibility projects	5.7 (116)	6.9 (30)	5.5 (14)	6.8 (30)	5.2 (26)	4.0 (16)	0.058
Activities to develop presentation skills	5.4 (110)	6.3 (27)	4.3 (11)	5.9 (26)	4.2 (21)	6.2 (25)	0.212
Other	0.3 (6)	0 (0)	0.4 (1)	0.7 (3)	0 (0)	0.5 (2)	0.577

Data are presented as percentages (n). Since multiple responses were allowed, the n value exceeds the sample size.

The Chi-Square Test with Monte Carlo correction was applied. *: p-values less than 0.05 were considered statistically significant.

Table 5 Students' Attitudes Toward Leisure Time

	Total (n=458)	Year 1 (n=92)	Year 2 (n=61)	Year 3 (n=94)	Year 4 (n=116)	Year 5 (n=95)	p Value
Leisure Time Management Scale	50 (44-57)	49.5 (43.25-57.75)	48 (44-56)	50 (43-58)	48 (44.25-55.75)	52 (46-59)	0.135
Goal Setting and Method	18 (14-22)	18.5 (14-22)	18 (15-22)	17 (13-21)	18 (13-22)	20 (16-23)	0.073
Evaluation	10 (8-12)	10 (8-12)	9 (7.5-12)	9.5 (8-12)	9 (8-12)	10 (8-12)	0.699
Leisure Attitude	13 (11-15)	13 (11-15)	12 (9-15) ^a	13 (11-15)	13 (11-15)	14 (12-15) ^b	0.041*
Scheduling	10 (8-12)	9 (7-11)	10 (6.5-12)	10 (8-12)	10 (8-11)	11 (9-12)	0.107
Leisure Facilitators Scale	62 (55-70)	63 (54-69)	60.5 (51-67.75)	62.5 (56-69.25)	62.5 (54.25-70.75)	64 (58-71)	0.387
Intrapersonal	20 (18-24)	20 (18-24)	19.5 (16-22.75) ^a	20 (19-23)	20 (17-24)	22 (19-24) ^b	0.017*
Interpersonal	14 (12-16)	15 (12-17)	15 (12-16)	14.5 (13-16)	14.5 (12-17.75)	14 (12-16)	0.476
Structural	28 (24-31)	28 (23-30)	26 (22-31)	27 (24-31)	28 (23.25-31)	28 (25-31.5)	0.465
Leisure Constraints Scale	49 (43.75-55)	48 (42-53)	51.5 (44.25-56)	51 (45-56.25)	49 (43-54)	48 (43-55)	0.090
Individual Psychology	8 (7-10)	9 (7-10)	9 (7-9)	9 (7-10)	8 (6-10)	8 (6-9)	0.214
Lack of Information	8 (6-10)	8 (6-10)	9 (6-10)	9 (7-10)	8 (6-9)	8 (6-9)	0.223
Facilities	9 (7-10)	9 (7-10)	9 (7.25-12)	9 (7-11)	9 (7-10)	9 (8-11)	0.163
Lack of Companionship	8 (6-10)	8 (6-10)	9 (7-10.75)	8 (6-10)	9 (6-10)	8 (6-10)	0.303
Time	8 (7-9)	7 (6-9)	9 (7-9)	9 (7-10)	8 (7-9)	8 (7-10)	0.060
Lack of Interest	8 (6-9)	8 (6-9)	8.5 (6-9)	9 (6-10)	8 (6-9)	8 (6-9.5)	0.485

Data are presented as median (25th–75th percentile). The Kruskal-Wallis test was applied. *: p-values less than 0.05 were considered statistically significant. Significant differences were observed between groups indicated by different superscript letters.

Table 6 Distribution of Scale Scores by Gender

	Female (n=259)	Male (n=199)	p Value
Leisure Time Management Scale	50 (45-57)	49 (44-58)	0.356
Goal Setting and Method	18 (14-22)	18 (14-22)	0.955
Evaluation	10 (8-12)	10 (9-12)	0.189
Leisure Attitude	13 (11-15)	13 (11-15)	0.066
Scheduling	10 (9-12)	9 (7-11)	0.010*
Leisure Facilitators Scale	64 (57-70)	61 (54-69)	0.005*
Intrapersonal	20 (18-24)	20 (18-23)	0.367
Interpersonal	15 (13-17)	14 (12-16)	0.002*
Structural	28 (24-32)	26 (23-30)	0.012*
Leisure Constraints Scale	51 (45-56)	47 (42-54)	0.001*
Individual Psychology	9 (7-10)	8 (6-9)	<0.001*
Lack of Information	9 (7-10)	7 (6-9)	<0.001*
Facilities	9 (8-10)	9 (7-11)	0.756
Lack of Companionship	9 (6-10)	8 (6-10)	0.303
Time	9 (7-10)	8 (6-9)	<0.001*
Lack of Interest	8 (6-10)	8 (6-9)	0.362

Data are presented as median (25th–75th percentile). The independent t test was applied. *: p-values less than 0.05 were considered statistically significant.

62 (55–70) on the Leisure Facilitation Scale, and 49 (43.75–55) on the Leisure Constraints Scale. A statistically significant difference in "leisure attitude" was observed between second- and fifth-year students ($p=0.041$). A similar difference was found in the "personal facilitators" subscale of the Leisure Facilitation Scale ($p=0.017$) (Table 5).

When the scale scores were analyzed by gender, statistically significant differences were found in the "programming" subscale of the Leisure Time Management Scale ($p=0.010$), in the total score of the Leisure Facilitation Scale ($p=0.005$), and in the interpersonal ($p=0.002$) and structural ($p=0.012$) subscales. Significant gender-based differences were also seen in the subscales of psychological constraints ($p<0.001$), lack of knowledge ($p<0.001$), and time-related constraints ($p<0.001$), as well as in the overall score of the Leisure Constraints Scale ($p=0.001$) (Table 6). A weak correlation was found between the total score of the Leisure Time Management Scale and the total score of the Leisure Facilitation Scale ($p<0.001$; $r=0.319$).

Discussion

This study examined the expectations, participation motives, encountered barriers, and facilitating factors regarding leisure activities among students of Süleyman Demirel University Faculty of Medicine. Through an evaluation of participation characteristics and scale scores across different academic years, the students' leisure time management and attitudes toward extracurricular activities were explored in detail.

The findings indicate that students participate in social activities an average of 5 (3–10) times per month. However, the lower participation rate observed in second-year students suggests potential challenges during this period related to academic workload, the adaptation process, or difficulties in time management. Overall, the most common reasons for engaging in social activities were enjoyment, stress relief, and socialization. Notably, the greater emphasis on "developing skills" among first-year students implies that, at the beginning of their academic journey, students are more open to personal development and acquiring new abilities. As medical training progresses, the increasing importance of "stress relief" as a motive, especially in the fifth year, highlights the growing impact of academic pressure and stress on students' quality of life.

In a study conducted by Çakır with 250 students from the Faculty of Sports Sciences, it was reported that the

"leisure attitude" and "evaluation" subdimensions of the Leisure Time Management Scale were influenced by age, with participants aged 26 and older scoring higher (22). In our study, a significant difference in the "leisure attitude" subdimension was observed between second- and fifth-year students.

Among the reasons why students cannot participate in social activities, the incompatibility of activity times with course schedules and the intensity of coursework are the most prominent. This reflects the challenges faced by medical students due to the demanding curriculum. Differences are also observed across academic years; for example, health problems are more evident in the first year, whereas the influence of peer groups increases in the fifth year. This situation is thought to stem, in the first year, from students' adaptation to a new environment along with changes in dietary habits and lifestyle; whereas the increasing influence of friendships in the later years appears to be related to the expansion of small groups formed during the clinical training period, which provide greater opportunities for establishing and developing social relationships. Al-Ansari et al. reported that participation in extracurricular activities among dental students in Egypt and Saudi Arabia was low, with most participants engaging in community service, sports, and social activities. Their primary motivation was socialization, and the majority expressed dissatisfaction with school-organized activities (23). Similarly, in the present study, the leading reasons for participation in extracurricular activities were enjoyment, stress relief, and socialization. The motivation to "improve skills" observed in the first year indicates that students initially hold expectations focused on personal development. Almasry et al. noted that second- and third-year medical students participated in extracurricular activities for reasons such as résumé building and teamwork, while identifying lack of time and incompatibility with course schedules as the main barriers (24). In a study conducted at Akdeniz University, the most important reasons for participation were entertainment, spending time with friends, and relaxation, whereas barriers differed by gender: course intensity among women, and lack of interest in activities, financial limitations, and peer disinterest among men (25). These findings in the literature parallel the results of our study.

Both the Leisure Facilitation Scale and the Leisure Constraints Scale were used in a study by Siyahtaş et al. with 220 students from Istanbul University Faculty of Sports Sciences. The results indicated that gender, age, monthly income, and perceived level of welfare significantly influenced scale scores. The main factor hindering participation in leisure activities was identified

as a lack of facilities, while the most effective facilitator was structural facilitators (1). Results from the Leisure Constraints Scale indicated that perceived welfare level was a significant factor in activity participation in a different study that involved 328 students at Adnan Menderes University and sought to determine the reasons why they did not engage in leisure-time activities. Furthermore, significant differences were found between gender and the subdimensions of the scale (26). Similarly, in our study, we observed statistically significant differences in the total and subdimension scores of the Leisure Constraints Scale based on gender. Furthermore, it was determined that gender and academic year influenced the scale scores, and that gender differences existed in interpersonal and structural facilitators as well as in individual psychology, lack of knowledge, and time parameters. In a study by Köse et al., the role of personal and structural facilitators in enhancing leisure motivation was emphasized (27). The differences observed in the “personal” subdimension of the Leisure Facilitators Scale in our study also emphasize the importance of individual factors in managing leisure time. Moreover, our findings revealed statistically significant gender differences in the total score and in the interpersonal and structural subdimensions of the Leisure Facilitators Scale. It indicates that male and female students do not perceive the barriers and facilitators affecting participation in leisure activities in the same way. In the study conducted by Güler et al. with the participation of 324 university students, significant differences were found in the sub-dimension of skill acquisition strategies according to gender, year of study, participation in sports activities, and difficulty in managing leisure time, while significant differences were also reported for age, level of welfare, and adequacy of weekly leisure time. The study concluded that, depending on their sociodemographic characteristics, university students may exhibit diverse coping strategies for the barriers they encounter during leisure time [18].

Fares et al., in a study conducted with first- and second-year medical students in Lebanon, reported that 62% of the 165 participants experienced stress and 75% experienced burnout. They found that participation in extracurricular activities played a significant role in coping with stress. The study also concluded that engagement in music-related activities was associated with lower levels of burnout, whereas participation in social activities was inversely related to academic involvement (28). Consistent with these findings, our study also demonstrated that academic workload and lack of time were among the primary barriers to participation in social activities, highlighting the impact of the demanding nature of medical

education on students' leisure practices.

In a large-scale study conducted by Işıkgöz et al. with 1,894 university students, analysis of the Leisure Time Management Scale data revealed that the most influential subdimensions in leisure management were, in order, “Goal Setting and Method,” “Leisure Attitude,” “Programming,” and “Evaluation.” The study also found that factors such as gender, type of faculty/school, age, housing status, and duration of participation in recreational activities significantly affected leisure time management (29).

The primary limitation of this study is its single-center design: data were collected at one institution in Isparta, a relatively small city. Contextual differences from major metropolitan areas—particularly in leisure opportunities and resources—may limit the generalizability of our findings. In addition, internship-level (6th-year) students were excluded; generalizability to this cohort is limited.

Conclusion

This study identifies medical students' expectations and barriers to leisure participation, offering guidance for social and academic support programs. Administrators should adopt flexible, inclusive practices that protect time for social activity and strengthen motivation. Practical steps include broadening electives, resourcing student clubs, establishing mentorship and community-service opportunities, and providing leisure-time management training to promote efficient time use and reduce maladaptive behaviors. Programming should align with students' interests (e.g., music/concerts, social excursions, hobby workshops, sport/exercise, cultural events) and account for differences across year levels. Participation can be increased by addressing structural constraints—improving campus facilities, preventing clashes between classes and events, and enhancing communication channels for announcements. Future research should examine leisure-time management, motivations, and constraints across diverse subgroups using mixed methods to deepen interpretation.

Acknowledgments

We would like to extend our sincere thanks to all the students who participated in this study. We also express our gratitude to Süleyman Demirel University Faculty of Medicine students M. Emin AĞIR, Kübra BİLİR, Burak KORKMAZ, and Eren BAŞGÖR, as well as to Health Technician Bahtiyar Emine DURAN, for their valuable support during the data collection process.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Ethical Approval

The study was approved by the Ethics Committee of Süleyman Demirel University with the decision dated 13.02.2024 and numbered 73/7. Institutional permission was obtained on 16.02.2024. All students participated in the study on a voluntary basis. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Artificial Intelligence Statement

The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

Authors Contributions

SE: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Writing-original draft; Supervision.

FUT: Investigation; Methodology; Project administration; Resources; Validation; Writing-original draft.

EA: Investigation; Validation; Writing-original draft.

MS: Formal analysis; Investigation; Visualization; Writing-original draft.

NŞ: Resources; Supervision; Writing-review & editing.

Editorial Statement

Despite the fact that SE, a co-author of the article, fulfills the role of field editor for the journal, she did not participate in any phase of the publication process for this particular article.

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