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## FROM THE EDITOR IN CHIEF

Health problems that come to the fore in the older age group continue to attract attention not only in terms of mortality and morbidity, but also in terms of their social, psychological and economic dimensions as well. Unfortunately, these problems were often ignored during the pandemic process, and Covid-19 was kept at the forefront by the physicians, health professionals, the elderly and elderly relatives and caregivers in our country, as in the whole World. This situation has led to serious problems both in the control of chronic diseases and in the notification of newly emerging symptoms. As we have strongly emphasized in all our training activities raising awareness of the health professionals both in the therapeutic and preventive medicine area is quite important. I would like to thank our authors, scientific referees and editorial board of the journal and the technical team who enthusiastically continue their work despite adverse conditions during the pandemic.

**Yeşim Gökçe Kutsal**





## RESEARCH

# ACUTE CORONARY SYNDROME IN GERIATRIC PATIENTS IN AN INTENSIVE CARE UNIT

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### ABSTRACT

**Objective:** The advancing age of acute coronary syndrome and the ageing population are leading to an increase in the number of elderly patients with acute coronary syndrome in our clinical practice.

In our study, we aimed to investigate the effect of acute coronary syndrome in the geriatric patient group.

**Materials and Method:** We retrospectively included geriatric patients who were in intensive care units because of different diagnoses, who also showed an acute coronary syndrome, and who had been diagnosed using the sequential organ failure assessment score. This score is used to describe the condition of a patient with sepsis and the extent of organ damage during treatment in an intensive care unit. We reviewed patients who were at Baskent University Faculty of Medicine between 25 March 2015 and 12 March 2020.

**Results:** We included 63 patients aged 77.27±7.65 years. There were 40 (63.5%) males and 23 (36.5%) females. A total of 42 (89.4%) patients died in the first 5 months, one (2.1%) died between the 6th and 10th months, two (4.3%) between the 11th and 20th months, and two (4.3%) between the 21st and 30th months. We found a significant relationship between the sequential organ failure assessment score and mortality rate ( $p<0.05$ ). The sequential organ failure assessment score was reliable in predicting mortality in geriatric patients with acute coronary syndrome, with 57% sensitivity and 75% specificity.

**Conclusion:** Mortality of geriatric patients with acute coronary syndrome can be significantly determined using the sequential organ failure assessment scores.

**Keywords:** Geriatrics; Acute coronary syndrome; Intensive Care Units; Mortality.

## INTRODUCTION

A simple but effective method for describing organ dysfunction or organ failure in critically ill patients is the sequential organ failure assessment (SOFA) score. The SOFA score was designed to provide insights into the acute morbidity of intensive care patients at the population level, but its use has expanded considerably in recent years. The SOFA score is now used at the individual patient level as a key criterion for diagnosing sepsis syndrome (1-4). Due to good medical treatment, the age of the population is increasing, which implies that acute coronary syndrome is now more common in geriatric patients (5).

Despite improvements in patient care and advanced treatment modalities, mortality remains a significant problem in geriatric patients. Elderly patients have a high risk of bleeding (6,7) and ischemic complications (8), among other conditions. For this reason, careful risk stratification for ischemic risk and bleeding risk must be carried out, taking into account the assessment of frailty, quality of life, care goals, and individual preferences (9). With the help of the SOFA score, we aimed to identify the survival of elderly patients with acute coronary syndrome who were treated in the intensive care unit of our clinic.

## MATERIALS AND METHOD

We retrospectively included geriatric patients who were in the intensive care unit because of different diagnoses and who also showed an acute coronary syndrome at Baskent University Faculty of Medicine between 25 March 2015 and 12 March 2020.

We analysed the demographic, clinical and biochemical data of these patients. We also applied the SOFA score to the patients. The sequential organ failure assessment score (SOFA score) is used to monitor a person's condition or failure rate to determine the extent of organ function during a person's stay in the intensive care unit (ICU). The score

is based on six different scores, each for the respiratory, cardiovascular, liver, coagulation, kidney, and neurological systems. The SOFA score helps healthcare providers estimate the risk of morbidity and mortality from sepsis.

## Statistics

We examined various demographic and clinical factors, including age, sex, age, coronary artery disease, hyperlipidaemia, diabetes, hypertension, and this was followed by a ROC curve and Fisher's Exact Test analysis to determine the independent predictors of mortality.

This study was approved by Baskent University Institutional Review Board (Project no: KA21/23) and supported by Baskent University Research Fund.

## RESULTS

We included 63 patients aged  $77.27 \pm 7.65$  years. There were 40 (63.5%) males and 23 (36.5%) females. The demographic and clinical properties of the study population are presented in Table 1. A total of 47 (75.0%) patients died at a mean follow-up duration of  $3.0 \pm 7.0$  (range 0–30) months. Thirty-two (68.1%) of these patients died in the hospital, while 15 (31.9%) died outside the hospital.

In the first 5 months, 42 (89.4%) patients died, whereas one (2.1%) patient died in the 6th to 10th month (2.1%), two (4.3%) between the 11th and 20th month, and two (4.3%) between the 21th and 30th months.

The cut-off value was determined as 6.5 in the diagnosis of individuals with low and high SOFA. Based on this, we examined patients in two groups (SOFA low and SOFA high). For the cut-off value of SOFA of 6.5, the sensitivity value was 0.76.

In our study, we found a significant relationship between SOFA score and mortality rate ( $p < 0.05$ ). The SOFA score was reliable for predicting mortality in geriatric patients with acute coronary syndrome, with 57% sensitivity and 75% specificity.



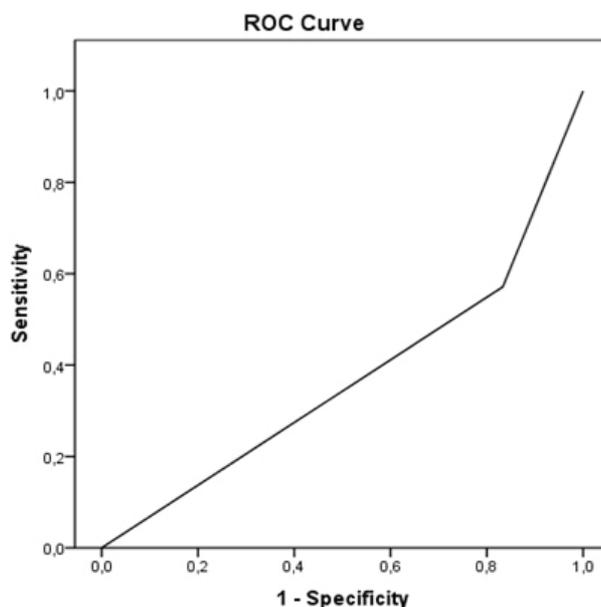
**Table 1.** Demographic and clinical properties of the study population

Characteristic	Results
Sex (Male,%)	63.5%
Age (years, mean $\pm$ SD)	77.27 $\pm$ 7.65
Time to death (month, mean $\pm$ SD)	3.0 $\pm$ 7.0 mean $\pm$ SD
Death (%)	
- Total %	47 (75%)
- In hospital %	32 (68.1%)
- Outside the hospital %	15 (31.9%)
Coronary artery disease (n,%)	28 (44.4 %)
HT (n,%)	45 (71.4%)
HL (n,%)	21 (33.3%)
DM (n,%)	22 (34.9%)
Smoker (n,%)	8 (12.7%)

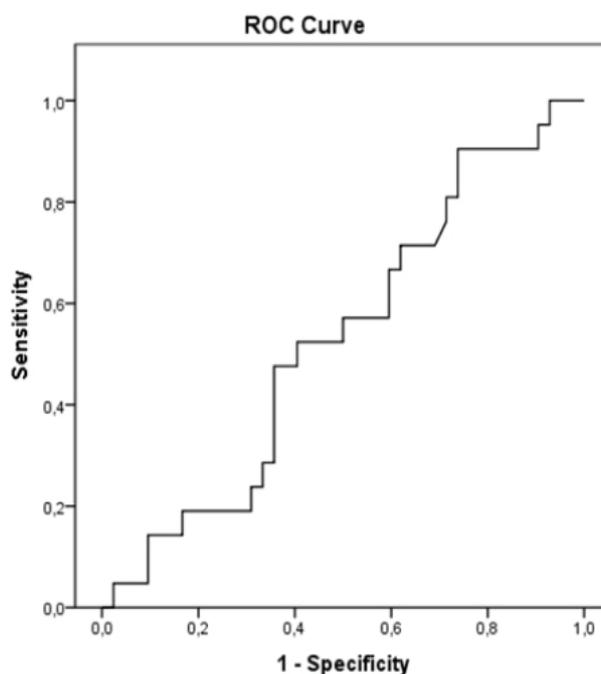
We also found that there was no significant relationship between SOFA score and troponin values ( $p > 0.05$ ). ROC analysis was performed to compare the diagnosing predictability of SOFA score and troponin values obtained as metric. According to ROC analysis, the usefulness of troponin values in distinguishing between individuals with low and high SOFA was not found to be significant (area under the curve = 0.529  $p = 0.710$ ), as shown in Figure 2.

Sensitivity value was set as the rate of accurately diagnosing individuals in the low-SOFA group based on troponin measurement. Similarly, the specificity value was set as the rate at which individuals in the high-SOFA group can be correctly diagnosed. The cut-off value of troponin values in the diagnosis of individuals with low and high SOFA was 1.30. At this cut-off value, the sensitivity of troponin was 0.71. Thus, the diagnosing rate of individuals

**Figure 1.** The SOFA score sensitivity and specificity.



**Figure 2.** Roc analysis of troponin success



whose troponin measurement was lower than 1.30 was 71%.

Further, we found no significant relationship between SOFA scores and CK-MB values ( $p > 0.05$ ). In this case, the sensitivity value was set as the rate of correctly diagnosing individuals in the low-SOFA based on CK-MB measurement. The specificity value was set as the rate at which individuals in the high-SOFA group could be correctly diagnosed. The cut-off value of CK-MB values was determined as 2.45 in the diagnosis of individuals with low and high SOFA. At this cut-off value, the sensitivity of CK-MB was 0.71. This indicates that the rate of diagnosing individuals whose CKMB value was lower than 2.45, who were diagnosed as SOFA-low, was 71%.

## DISCUSSION

Geriatrics refers to the medical care of older adults, who are patients older than 65 years and have chronic illnesses, physical impairments and/or cognitive impairments. With the high quality of current medical treatment, the mean age of geriatric patients has increased, with concurrent increases in the age of patients with acute coronary syndrome. For this reason, the treatment of very old patients has steadily increased (10,11) and has become common practice.

Due to changes and the physiology of ageing, comorbidities, and expectations increase in the elderly. Geriatric patients must be assessed individually, as there can be significant differences between their chronological and biological ages (12). In this context, the SOFA score can be used to assess life expectancy. A simple but effective method for describing organ dysfunction or organ defects for critically ill patients (13).

In our study, we found a significant relationship between SOFA score and mortality rate ( $p < 0.05$ ). The SOFA score showed that it is reliable for predicting mortality in geriatric patients with acute

coronary syndrome, with 57% sensitivity and 75% specificity.

Jones et al. (14) also showed that the SOFA score provides valuable prognostic information on survival in hospital. Machado et al. (15) showed that a mean SOFA average above 5 was associated with mortality in elderly patients with severe sepsis and septic shock. Janssens et al. (16) showed that SOFA scores provide important information on the degree and progression of organ dysfunction in medical and cardiovascular patients.

ACS refers to a range of acute ischemic myocardial conditions. It includes unstable angina and myocardial infarction with or without ST segment elevation. ACS can lead to an increase in cardiac enzymes (17), with an increase in the values of troponin and CK-MB. As part of our study, we carefully examined the relationship between the troponin value and SOFA score and between the CK-MB value and SOFA score. We found that there was no significant relationship between SOFA score and troponin values or CK-MB values ( $p > 0.05$ ).

However, Mannam et al. (18) showed that the mortality in troponin-positive septic patients was significantly higher (45.4% versus 7.7%,  $p < 0.04$ ). Kang et al. (19) showed that elevated troponin levels were significantly associated with short-term and long-term mortality in patients with end-stage kidney disease with sepsis. For this reason, elevated troponin levels should be carefully considered and monitored for undesirable results. Oliveira et al. (20) showed that the severity of septic disease was the only variable that was significantly associated with death. Mehta et al. (21) showed that cardiac troponin is an independent predictor of hospital mortality.

Nevertheless, a skilful clinical assessment remains essential in every patient with suspected ACS and is particularly important in elderly patients who present with specific diagnostic challenges that need to be systematically considered.



## CONCLUSION

The mortality of geriatric patients with acute coronary syndrome can be significantly determined by their SOFA scores. The SOFA scores showed reliability in predicting mortality in geriatric patients with acute coronary syndrome, with 57% sensitivity and 75% specificity. The SOFA score thus provides potentially valuable prognostic information on the survival of geriatric patients in the hospital. It is therefore very well suited for the risk stratification of patients in intensive care units.

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## Study Limitations

The limitations of our study are its retrospective design and the relatively low number of patients.

In addition, patients who were not followed up in our hospital were not included in our study.

## Conflict of Interest

The authors declare no conflict of interest regarding the publication of this manuscript.

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## RESEARCH

# THE EFFECTS OF RENAL INSUFFICIENCY AND AGE ON MORTALITY IN GERIATRIC PATIENTS WITH NON-ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

## ABSTRACT

**Objectives:** Although renal insufficiency is associated with high mortality in patients with acute coronary syndrome, studies have often excluded patients of advanced age who have renal insufficiency. The present study aimed to determine the relationship between renal insufficiency and mortality predictors in patients with non-ST-segment elevation myocardial infarction (NSTEMI) who were aged 65 and older.

**Methods:** The study included 537 NSTEMI patients aged 65 years and over, who were followed up for at least 12 months, who were admitted to the hospital with the diagnosis of NSTEMI and underwent coronary angiography. Sociodemographic and clinical features, laboratory parameters, and clinical evaluation variables were recorded at the time of admission. The patients were divided into four groups according to their ages and creatinine clearance values.

**Results:** The mean age of the patients was  $76.17 \pm 6.64$  years, and 256 (47.7%) of them were women. According to the applied multivariate age-stratified Cox regression analysis, independent predictors of one-year mortality were found to be creatinine clearance ( $p=0.005$ ), left ventricular ejection fraction ( $p<0.001$ ), and coronary revascularization ( $p=0.004$ ).

**Conclusion:** Creatinine clearance, left ventricular ejection fraction, and coronary revascularization are robust and independent predictors of one-year mortality in NSTEMI patients.

**Keywords:** Non-ST Elevated Myocardial Infarction; Renal Insufficiency; Mortality; Acute Coronary Syndrome.

## INTRODUCTION

Non-ST segment elevation myocardial infarction (NSTEMI) is one of the leading causes of mortality and morbidity in patients aged 65 years and older, and these numbers are increasing daily (1, 2). Although there is a decrease due to improvements in reperfusion technology and pharmacology, this patient group's mortality rate is heightened by their tendency toward ischemia and bleeding and increased frequency of comorbidities (3). Currently, the limited number of studies investigating mortality predictors in NSTEMI patients and the narrow inclusion criteria for patients in this research hinders the ability to generalize these studies' results to a patient population in clinical practice (1, 4, 5).

Renal insufficiency (RI) is quite common in hospitalized patients with acute coronary syndrome (ACS) and affects 43% of patients diagnosed with NSTEMI (6). The prevalence of RI increases with age, and arrhythmia and cardiovascular diseases are the leading causes of death in these patients (7). Recent studies have shown that when compared to younger patients, NSTEMI patients who are older than 75 years of age have more significant absolute risk reduction in terms of mortality and morbidity when appropriate follow-up and treatment strategies are applied (8). Nonetheless, the number of studies investigating the validity of this condition is limited since elderly NSTEMI patients with RI are more vulnerable and the pharmacokinetic properties of the medications are varied (9, 10). While a significant number of studies dealing with this issue in Turkey show that RI may be a predictor for mortality (11-13), there are studies showing the opposite (14-16). However, very few of these studies seem to focus on geriatric patients (11, 17). For this reason, it would be useful to investigate the relationship between RI and mortality in this patient group that is likely to benefit from treatment. This study aimed to investigate the effect of RI on patients who had been hospitalized due to NSTEMI and were over

the age of 65 in order to determine the predictors of mortality in a one-year follow-up.

## MATERIAL AND METHODS

### Patient population

The current study's sample consisted of patients aged 65 years or older who were admitted to the hospital and diagnosed with NSTEMI and were performed coronary angiography between 2016 and 2020. The study was planned as an observational report of routine clinical practice. In accordance with the inclusion and exclusion criteria, the study included patients who were undergoing coronary angiography and were treated according to the recommended guidelines and clinical approach. The patients' diagnoses and treatments were made in accordance with the current guidelines (1, 4). The study included patients who were older than 65 years of age and who had been diagnosed with NSTEMI and underwent coronary angiography. Patients younger than 65 years of age, who lacked troponin elevation or had proven troponin elevation due to other causes, and who had malignancies, primary arrhythmia, cardiogenic shock, cardiac arrest, a history of coronary bypass, or severe heart valve disease were excluded from the study. As a result, of the 593 patients who met the inclusion criteria, 56 were excluded, and a total of 537 patients with NSTEMI were included in the study. The approval for the study was obtained from the local ethics committee, and each stage of the study was carried out in accordance with the Helsinki Declaration.

### Study Design and Clinical Evaluation

The study was designed as multicenter and prospective. Erzurum Regional Training and Research Hospital/Erzurum and Ministry of Health, 29 Mayıs State Hospital/Ankara participated in the study. Patients meeting the inclusion criteria were diagnosed with NSTEMI according to current guidelines,



and coronary angiography was applied appropriately (1, 4). Patients who met the exclusion criteria or did not meet the inclusion criteria were excluded at this stage. The patients' sociodemographic characteristics, echocardiography and electrocardiography records, medical history, angiography images, and laboratory parameters were recorded. After the participants were treated according to the appropriate guidelines, they were followed up for at least 12 months (Mean $\pm$ SD: 543.25 $\pm$ 232.39 days, Median: 562 days). Patients were followed up by medical records or telephone. Patients for whom information could not be obtained were excluded from the study. The data recorded in the dataset were statistically analyzed.

The centers participating in the study met the quality assessment criteria for the accuracy of laboratory measurements and follow-up of clinical laboratory measurement results. Routine biochemical and hematological tests of the participants were performed during their hospitalizations. Echocardiographic examinations of the patients were performed using the Vivid 7 (General Electric-Vingmed, Milwaukee, WI, USA) device, and left ventricular ejection fraction (LVEF) measurements were made according to the modified Simpson's method. During follow-up of the patients, GRACE risk calculations were performed by the clinician who performed the follow-up. The coronary angiography images of the patients were examined, and SYNTAX and Gensini scores were calculated by two experienced cardiology specialists. The patients who were treated by coronary bypass or percutaneous methods after coronary angiography were defined as patients who underwent coronary revascularization. Creatinine clearance (CrCl) levels were calculated using the Cockcroft-Gault equation. For the purposes of this study, patients were divided into four categories: those who were 65–74 years of age and had CrCl levels of  $\geq 60$  ml/min; those who were 65–74 years of age and had CrCl levels of  $< 60$  ml/min; those who were  $\geq 75$  years of age and had CrCl levels of  $\geq 60$  ml/min; and those who were  $\geq 75$  years of age and had CrCl levels of  $< 60$  ml/min.

Follow-up controls were planned at the end of one month and one year. In cases of insufficient data, national or hospital records were used.

### Statistical Analyses

The descriptive analyses were presented as numbers and percentages for categorical variables and as means and standard deviations for continuous variables. The Pearson Chi-square test was used to evaluate the categorical data from the group comparison. After the assessment of the parametric assumptions in the comparison of continuous variables, one-way ANOVA and Tukey tests were used in post-hoc analysis. Kaplan-Meier plots were used to compare survival rates between the four groups. Then, in order to show the differences in hazard between the age groups, a stratified Cox regression model approach was used. Hazard ratios (HR) and associated 95% Confidential Intervals (CI) were presented to show the differences in mortality risk between the age groups. Special relationships between the potential predictors and survival were tested by using a univariate stratified Cox regression. Variables that were statistically significant in univariate analyses were included in the multivariate models. Only existing variables were considered to be potential predictors. "Survival probability" was calculated for each patient, and its relationship with mortality predictors was examined by using the stratified Cox regression model. Statistical analyses of the data were performed using SPSS version 22 software (SPSS, Inc., Chicago, IL). A value of  $p \leq 0.05$  was considered statistically significant.

### RESULTS

The mean age of the patients was  $76.17 \pm 6.64$  years. At least 281 (52.3%) of the participants were male and 256 (47.7%) were female. In 101 (43.5%) of the 232 (43.2%) patients aged 65–74, CrCl levels were  $< 60$  ml/min, and in 131 (56.5%) patients, CrCl levels were  $\geq 60$  ml/min. By comparison, in 256

(83.9%) of the 305 (56.8%) patients aged 75 years and older, CrCl levels were  $< 60$  ml/min, and in 49 (16.1%) patients, CrCl levels were  $\geq 60$  ml/min. Table 1 presents the comparison of the clinical features of the participants in the four study groups. Accordingly, we found statistical differences between the groups in terms of age ( $p < 0.001$ ), gender ( $p < 0.001$ ), smoking ( $p = 0.001$ ), diabetes mellitus ( $p = 0.001$ ), hypertension ( $p < 0.001$ ), atrial fibrillation ( $p < 0.001$ ), coronary artery disease ( $p < 0.001$ ), percutaneous coronary intervention history ( $p < 0.001$ ), and stroke history ( $p < 0.001$ ). Statistical differences between the four groups were also found in ST-segment deviation ( $p = 0.034$ ), coronary revascularization ( $p = 0.014$ ), LVEF ( $p = 0.028$ ), and GRACE scores ( $p < 0.001$ ). After patients were discharged, statistically significant differences were found between the groups' use of warfarin ( $p < 0.001$ ), new oral anticoagulant ( $p < 0.001$ ), renin-angiotensin system blockers ( $p = 0.031$ ), Beta-blockers ( $p = 0.008$ ), and statin ( $p = 0.002$ ). In addition, we found statistically significant differences between all causes of mortality, one-month follow-up ( $p = 0.016$ ), and one-year follow-up ( $p < 0.001$ ).

Mortality predictors for elderly NSTEMI patients were examined using the age-stratified Cox regression model (Table 2). In the univariate model, the differences between ST-segment deviation (HR: 1.973, 95% CI: 0.1.349–3.428,  $p = 0.004$ ), coronary revascularization (HR: 0.492, 95% CI: 0.308–0.786,  $p = 0.003$ ), CrCl (HR: 0.963, 95% CI: 0.948–0.977,  $p < 0.001$ ), LVEF (HR: 0.921, 95% CI: 0.900–0.943,  $p < 0.001$ ), hemoglobin (HR: 0.841, 95% CI: 0.740–0.956,  $p = 0.008$ ), and SYNTAX scores (HR: 1.029, 95% CI: 1.007–1.052,  $p = 0.010$ ) were found to be statistically significant. In the multivariate stratified Cox regression model, the differences between coronary revascularization (HR: 0.447, 95% CI: 0.258–0.776,  $p = 0.004$ ), CrCl (HR: 0.973, 95% CI: 0.954–0.991,  $p = 0.005$ ), and LVEF (HR: 0.944, 95% CI: 0.919–0.970,  $p < 0.001$ ) were statistically significant (-2 Log Likelihood: 578.438). Figure 1 and Figure 2 present the

relationships between each patient's survival probability (calculated by multivariate stratified Cox regression analysis) and age, diabetes mellitus, gender, CrCl, hemoglobin, LVEF, coronary revascularization, ST-segment deviation, and SYNTAX scores. Figure 3 shows the one-year survival probability curves according to the creatinine clearance (Adjusted to: age, gender, ST segment deviation, revascularization, LVEF, hemoglobin, diabetes mellitus and SYNTAX).

## DISCUSSION

The most prominent finding from the current study, which examined the relationship between renal failure and one-year mortality rates for all causes in NSTEMI patients aged 65 years and older, was that CrCl, LVEF, and coronary revascularization are independent predictors of one-year mortality, regardless of age. We believe that the results of our study are important since they may be instructive for predicting mortality in patients with NSTEMI aged 65 and over.

A number of atherosclerotic processes are activated due to the disruption of vascular elasticity, changes in coagulation and hemostasis mechanisms, endothelial dysfunction, and changes in regeneration capacity with aging or the addition of comorbidities. Moreover, an increasing majority of patients with ACS consist of patients aged 65 and older (18). These individuals are at a high risk of experiencing ischemic events and bleeding due to their higher rates of comorbidities. Although treatment guidelines recommend that elderly patients should be approached in a similar way to that of young patients, there are limited data regarding risk and treatment management for these patient groups since they are excluded in most randomized trials (5, 19). In elderly patients, admission to the hospital and diagnosis are delayed due to atypical symptoms, and interventional or strong antiaggregant treatments are performed less than in



**Table 1.** Baseline characteristics of study subjects according to age and CrCl.

Variable	Patients aged 65-74 years (n=232)		Patients aged ≥75 years (n=305)		P-Value
	CrCl<60 (n=101)	CrCl≥60 (n=131)	CrCl<60 (n=256)	CrCl≥60 (n=49)	
CrCl Groups					
Age (years) (Mean±SD)	70.94±2.53	69.48±2.71*	81.29±4.88*#	78.10±3.02*#£	<0.001
Gender (female)	47 (46.5%)	35 (26.7%)*	157 (61.3%)*#	17 (34.7%)£	<0.001
Current Smoke	15 (14.9%)	31 (23.7%)	24 (10.5%)#	4 (8.2%)#	0.001
Diabetes Mellitus	43 (42.6%)	29 (22.1%)*	90 (35.2%)#	9 (18.4%)*£	0.001
Hypertension	86 (85.1%)	73 (55.7%)*	187 (73.0%)*#	35 (71.4%)*	<0.001
Atrial Fibrillation	20 (19.8%)	7 (5.3%)*	76 (29.7%)#	8 (16.3%)#	<0.001
Prior CAD	60 (59.4%)	30 (22.9%)*	118 (46.1%)*#	21 (42.9%)#	<0.001
Prior PCI	40 (39.6%)	4 (3.1%)*	52 (20.3%)*#	8 (16.3%)*#	<0.001
Prior Stroke	0 (0)	1 (0.8%)	21 (8.2%)*#	0 (0) £	<0.001
ST segment deviation	28 (27.7%)	29 (22.1%)	13 (26.5%)#	92 (35.9%)	0.034
Coronary Revascularization	75 (74.6%)	99 (75.6%)	157 (61.3%)*#	32 (65.3%)	0.014
LVEF (%) (mean±SD)	49.23±10.29	51.14±8.56	50.18±9.67	53.91±8.20*	0.028
SYNTAX Score (mean±SD)	10.36±8.77	11.58±8.59	11.57±11.27	11.24±9.73	0.802
Grace Score (mean±SD)	130.08±17.61	120.36±13.30*	147.31±22.79*#	129.09±17.75£	<0.001
Gensini Score (mean±SD)	27.07±18.21	30.22±17.72	32.11±25.88	23.87±18.27	0.123
Hemoglobin (mean±SD)	12.30±2.02	13.73±2.09*	12.24±1.65#	14.07±1.49*£	<0.001
Creatinine (mean±SD)	1.77±1.25	0.98±0.19*	1.38±0.68*#	0.96±0.18*£	<0.001
Creatinine clearance (mean±SD)	44.43±12.66	77.91±13.56*	44.09±10.77#	68.16±6.82*#£	<0.001
Discharge Medications					
Acetyl Salicylic Aside	81 (80.2%)	119 (90.8%)	211 (82.4%)	41 (83.7%)	0.104
Clopidogrel	81 (80.2%)	104 (79.4%)	205 (80.1%)	36 (73.5%)	0.763
Warfarin	24 (23.8%)	10 (7.6%)*	24 (9.4%)*	2 (4.1%)*	<0.001
New oral anticoagulant	4 (4.3%)	0	44 (190%)*#	8 (24.2%)*#	<0.001
RAS blockers	63 (62.4%)	82 (62.6%)	186 (72.7%)#	27 (55.1%)£	0.031
Beta-Blockers	84 (83.2%)	115 (87.8%)	238 (93.0%)*	39 (79.6%)£	0.008
Statin	57 (56.4%)	104 (79.4%)*	165 (64.5%)#	33 (67.3%)	0.002
Hospitalization days (mean±SD)	6.78±6.90	6.54±7.38	6.94±5.58	4.95±3.40	0.229
One-month mortality	8 (7.9%)	1 (0.8%)*	11 (4.3%)	0 (0)*	0.016
One-year mortality	9 (8.9%)	7 (5.3%)	49 (19.1%)*#	6 (12.2%)	<0.001

CrCl: Creatinine clearance (ml/min.); SD: Standard deviation; CAD: Coronary Artery Disease; LVEF: Left ventricular ejection fraction; PCI: Percutaneous Coronary Intervention; RAS: Renin-angiotensin aldosterone system. The p-value indicates the statistical difference between the four groups.

\* P < 0.05, vs. Patients aged 65-74 years and CrCl<60

# P < 0.05, vs. Patients aged 65-74 years and CrCl≥60

£ P < 0.05, vs. Patients aged ≥75 years and CrCl<60

**Table 2.** Predictors of one-year mortality: Univariable and multivariable age-stratified Cox regression analysis

Predictor	Univariable		Multivariable	
	Hazard Ratio (95% CI)	P-Value	Hazard Ratio (95% CI)	P-Value
All Patients				
ST segment deviation	1.973 (1.349-3.428)	0.004	1.518 (0.853-2.702)	0.156
Revascularization	0.492 (0.308-0.786)	0.003	0.447 (0.258-0.776)	0.004
CrCl (ml/min.) (one-point increase)	0.963 (0.948-0.977)	<0.001	0.973 (0.954-0.991)	0.005
LVEF (%) (one-point increase)	0.921 (0.900-0.943)	<0.001	0.944 (0.919-0.970)	<0.001
Hemoglobin (mg/dl) (one-point increase)	0.841 (0.740-0.956)	0.008	1.094 (0.943-1.269)	0.234
Diabetes Mellitus	1.343 (0.832-2.169)	0.228		
SYNTAX Score (one-point increase)	1.029 (1.007-1.052)	0.010	1.022 (0.999-1.046)	0.064

CrCl: Creatinine clearance (ml/min.); LVEF: Left ventricular ejection fraction.

younger populations due to increased risk of bleeding and comorbidities. Therefore, elderly patients face a higher risk of mortality (9, 19, 20). As in other studies in the literature, age was shown to be associated with mortality in the present study (5, 11).

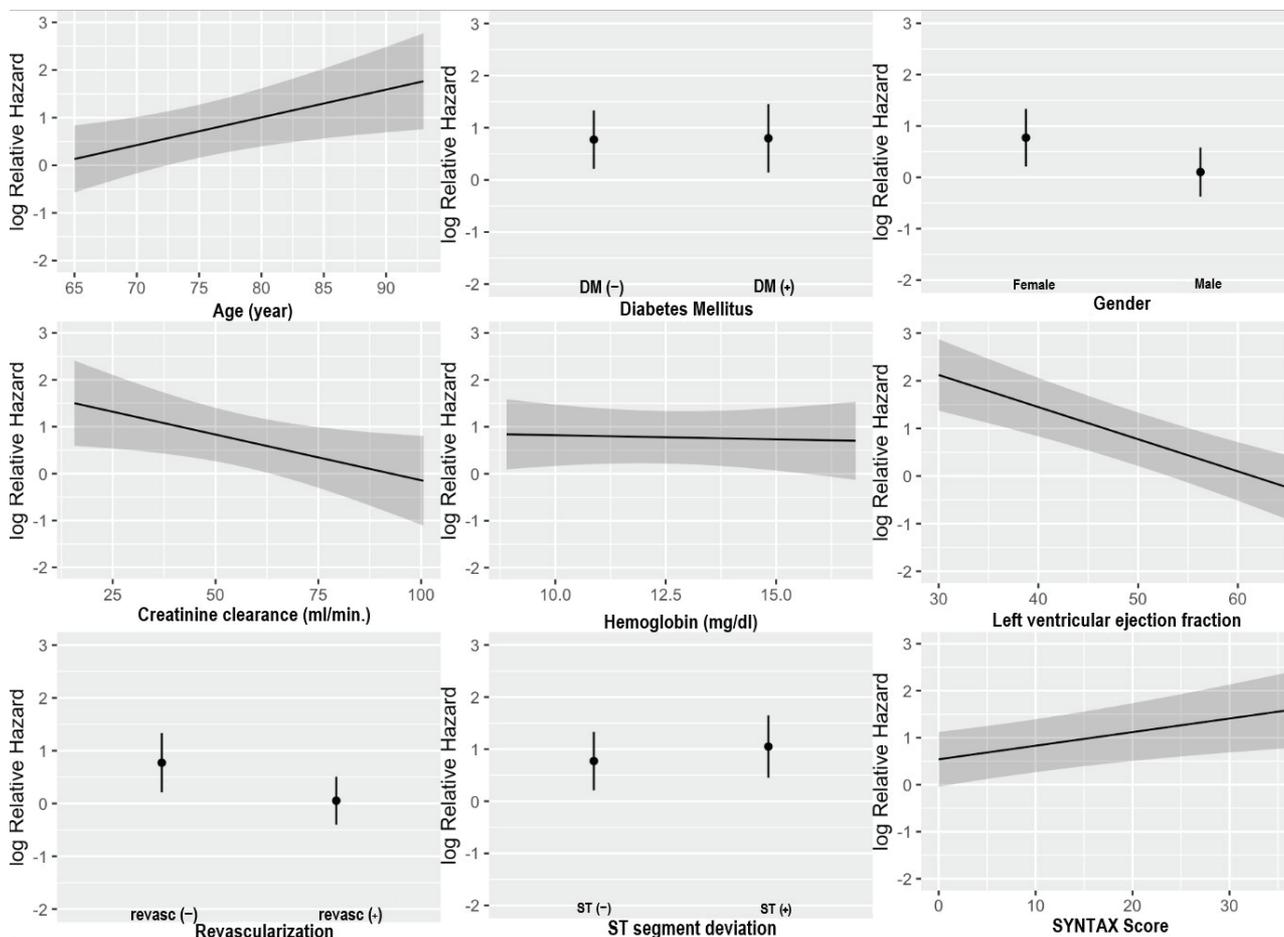
One of the most important and common comorbidities affecting mortality in ACS patients is RI (21, 22). Although coronary artery disease and post-ACS mortality are more common in patients with end-stage renal failure or dialysis, several studies have indicated that mortality rates are also high in patients with mild-to-moderate chronic kidney disease (22). In a study examining the length of hospital stays in NSTEMI patients, RI was associated with prolonged hospital stays, transfers to the catheter lab were delayed, and fewer of the recommended treatments were applied (5). In another study investigating the causes of mortality in NSTEMI patients

aged 75 years and older, mortality was found to be associated with CrCl, hemoglobin levels, age, and LVEF (23). In an ACUITY study that investigated the one-year mortality of 2627 patients, anatomical SYNTAX scores, CrCl, age, and LVEF were found to be indicators of mortality and were included in the Core model, which was recommended as a new scoring system (24).

In the present study, CrCl has been shown to be a predictor of mortality in ACS patients, similar to a significant portion of the literature (11, 12, 21). However, there are limited number of studies conducted with geriatric patients in our country (17). Likewise, few of the studies focus on NSTEMI patients (11, 12). Considering that geriatric NSTEMI patients may benefit relatively more from appropriate follow-up and treatment, the results of present study gain importance (23). However, it should be



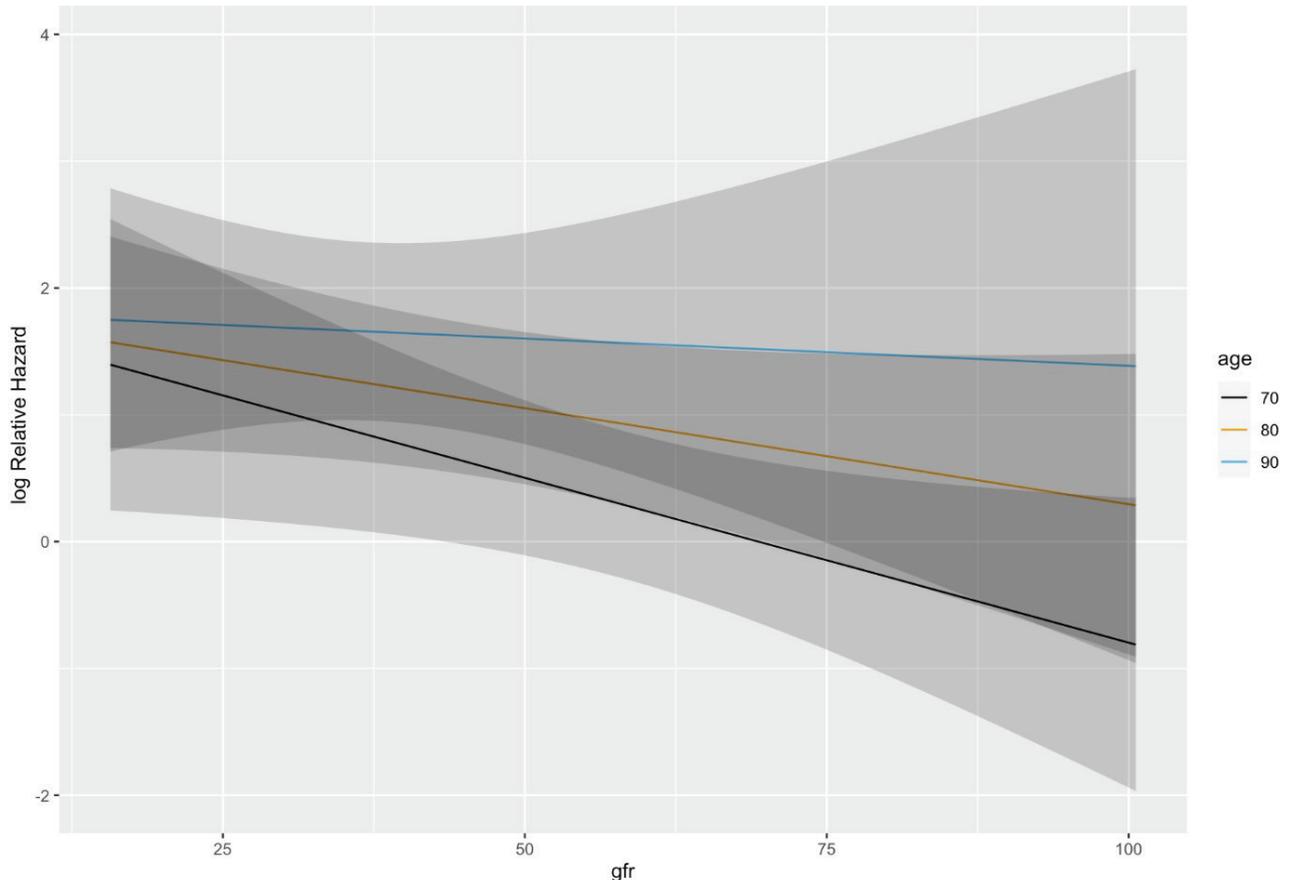
**Figure 1.** Relative Hazard plots for the effects of predictors on mortality.



considered that the results of present study will be useful in clarifying the relationship between CrCl and mortality, since there are few studies conducted in Turkey on this patient group and some of these studies did not find a relationship between CrCl and mortality. Various factors may describe the relationship between mortality and RI in patients with geriatric NSTEMI. The most probable causes of this condition can include increased frequency of heart disease due to oxidative stress, vascular endothelial dysfunction, acceleration of cellular apoptosis, and the contribution of various immune

system disorders, in addition to factors related to atherosclerosis in RI patients, which may include lipid disorders, hypertension, concomitant diabetes mellitus, or chronic inflammation processes (25). These patients may also experience higher rates of mortality due to the decreased frequency in which they undergo coronary revascularization or treatments involving antiaggregants, beta-blockers, RAS blockers, and statins, which are administered less often to patients with RI during hospitalization and after discharge (26). In our study, the rates of usage RAS blockers, beta-blockers in discharge are

**Figure 2.** Graphical representation of the relationship between survival probability and creatinine clearance according to the age.



lower in older than 75 years with RI than the other patients' groups. This may be a reason for the difference in mortality between patient groups. However, this statement may not apply to statins because the beneficial effects of statin therapy appear after at least one year of treatment (27).

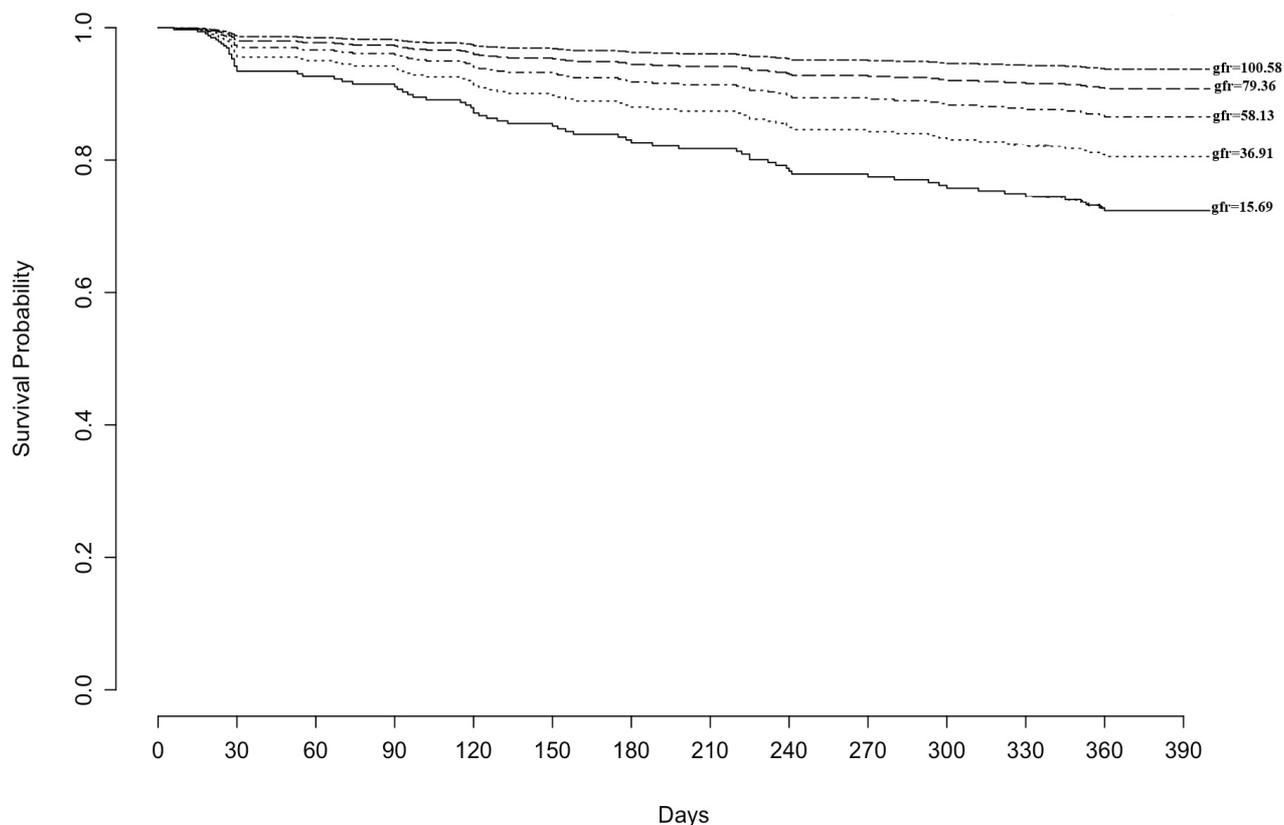
According to guidelines, it is recommended that elderly NSTEMI patients receive individualized therapy and adhere to the same treatment strategies as younger patients (1, 4). In the literature, revascularization has been shown to decrease mortality and morbidity in elderly NSTEMI patients (5, 23). However, in clinical practice, clinicians opt for less

invasive therapies since they consider advanced age to act as an obstacle to invasive intervention (11, 23, 28). Advanced age can also lead to delays in invasive intervention and to increases in undesired results (5). Similar to the findings from the literature, the results of the current study indicated that coronary revascularization is associated with reductions in one-year mortality. These results indicate that, unlike clinical practice, invasive intervention is effective in reducing mortality and morbidity regardless of age.

Although predictors of mortality in NSTEMI patients have been demonstrated in previous studies,



**Figure 3.** The survival probability in patients according to the creatinine clearance.



Adjusted to: age, gender, ST segment deviation, Revascularization, LVEF, Hemoglobin, Diabetes Mellitus, SYNTAX

patients aged 75 years and older and patients with additional comorbidities such as chronic renal failure were excluded from randomized controlled trials until the last few years. In spite of the fact that is recommended to receive similar treatments with other patients in this risky patient group among current treatment recommendations, both invasive and non-invasive treatment applications are insufficient in real life. Because these patients have many comorbidities, multidrug using and some metabolic changes so the clinicians are far from applying the same treatment as younger patients (29). Our study draws attention to a group of patients with high

mortality and may be a warning to be more devoted in providing follow-up and treatment optimization in these patients.

Many studies have shown LVEF to be a consistent predictor of short- and long-term mortality in patients with ACS (30, 31). In addition, recommendations have been made to include LVEF in risk scoring systems, such as GRACE (32). In the present study, LVEF was found to be an important independent predictor of one-year mortality in elderly NSTEMI patients. Therefore, we recommend using the LVEF assessment, which is a parameter of echocardiographic measurement, as an easily accessible

and noninvasive method during the follow-up and risk assessment of patients.

### Limitations

Our study has some important limitations. First, the follow-up period of our study was brief, and it presented all causes of mortality. It would be more beneficial to present cardiac-related mortality, specifically. It is also worth noting that neglecting the factors that can affect mortality, such as possible complications due to invasive treatment, may have affected the results. In addition, clinicians may have taken different approaches in treating the patients. The study was also limited by discrepancies between how clinics applied LVEF measurements and because some clinics did not discharge LVEF measurements.

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### CONCLUSION

Elderly NSTEMI patients with RI are at high risk for mortality, and the administration of guideline-based therapies is controversial. CrCl, coronary revascularization, and LVEF are potent and independent predictors of one-year mortality of all causes. Our results support the available information in the literature and provide new insights into the risk assessment of this complex patient population. Considering these predictors together can prove useful during early risk assessments. In addition, careful application of guidelines for elderly NSTEMI patients with RI should be considered effective in reducing mortality. Future studies should focus on optimizing more aggressive treatments to manage mortality in this patient group.

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## RESEARCH

# THE EFFECT OF OBESITY ON MORTALITY IN GERIATRIC PATIENTS FOLLOWED IN THE INTENSIVE CARE UNIT

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## ABSTRACT

**Introduction:** This study was intended to evaluate the relationship between the presence of obesity in geriatric patients, which is becoming more and more common in the intensive care unit, with the intensive care process and mortality.

**Materials and Method:** In this retrospective study, data on 2,114 patients aged 65 and over who were followed in the intensive care unit between January 2013-January 2020 were obtained electronically and evaluated.

**Results:** Patients were divided into two groups of 1,632 (77.2%) non-obese and 482 (22.8%) obese patients. It was determined that acute kidney injury development was more common in obese patients (326; 67.6%) than non-obese patients (937; 57.4%) and obese patients required more frequent dialysis ( $p < 0.05$ ). It was determined that obese patients required more frequent mechanical ventilator support, had higher positive end-expiratory pressure and peak pressure Work of Breathing ventilator values, and had lower compliance (34 [29–41]) ( $p < 0.05$ ). Although obese patients were given fewer daily calories than non-obese patients, their mean blood glucose was higher ( $p < 0.001$ ). Obese patients (5.70 [2.43–12.31]) had longer intensive care durations than non-obese patients (4.41 [2.01–10.45]) ( $p < 0.05$ ). Finally, intensive care mortality was determined to be 37.6% (181) in obese patients and 36.0% (588) in non-obese patients ( $p > 0.05$ ).

**Conclusion:** Obese patients' increased complication rate and duration of stay in the intensive care show that obesity increases intensive care morbidity in geriatric patients, but it has no relationship with mortality.

**Keywords:** Geriatrics; Aged; Obesity; Intensive Care Units; Body Mass Index; Respiration, Artificial.

## INTRODUCTION

Obesity, which is defined as abnormally increased fat accumulation that may adversely affect health, is accepted as an important public health problem and has an increasing prevalence worldwide (1). In recent years, the increase in the rate of obesity in the general population has had an effect on the profile of patients admitted to the intensive care unit (ICU), resulting in an increase in the number of obese patients (2). The management of obese patients is difficult due to accompanying metabolic dysfunction, impaired glucose intolerance, and respiratory and cardiovascular diseases (3). Concerning the drugs used in treatment, especially those with lipophilic properties, drug response may be altered due to increased fat mass (4). As a result of decreased vascular access due to large body habitus and affected blood pressure measurement accuracy, the frequency of invasive procedures, such as central venous access and intra-arterial cannulation, increases, and nursing care becomes difficult (4). Previous studies on obese patients in the ICU have determined that obesity prolonged the length of stay in the ICU (5,6). However, studies examining the relationship between obesity and mortality in the ICU have yielded complicated results (5-8). Some studies reported an increase in mortality (7), while others found no difference in mortality (5). Nevertheless, some studies have revealed an obesity paradox, in which obesity is not harmful but, in fact, protective (6,8).

In recent years, a worldwide increase in obesity has been observed in the geriatric population (9). According to the estimates of the United Nations, it is predicted that the global elderly population, which was 9.0% in 2019, will increase to 11.7% in 2030 and 16% in 2050 (10). According to a study conducted in the United States, 37.5% of women over 60 and 39.4% of men over 60 were obese (9). Patients over the age of 65 constitute approximately half of the ICU admissions (11). Moreover, the ICU readmission rate and mortality risk are higher in

this patient group (11). In addition to the increased prevalence of obesity in society, the increase in the number of geriatric patients has resulted in the development of a geriatric obese patient profile, which is becoming more prominent in ICUs. In geriatric patients, obesity has been associated with an increased risk of coronary heart disease due to diabetes mellitus, hypertension, dyslipidemia, and physical inactivity (12).

In addition to the rapid increase in the number of geriatric patients, the complicated results of studies investigating the mortality of obese patients may cause a paradox associated with the consequences of obesity in geriatric patients in the ICU. In order to resolve this paradox, our study is intended to determine the relationship between obesity and mortality in geriatric patients followed in an ICU in a large center and within a large sample.

## MATERIALS AND METHODS

### Data Center

This retrospective study was carried out in the ICU of a third-level training and research hospital in Istanbul, Turkey's most populous city.

When a patient is admitted to the ICU, after removing his or her clothes and jewellery, the patient's height and weight are measured by the nurse and recorded in the clinical decision support system. After the height and weight information is entered into the clinical decision support system, the system automatically calculates the body mass index (BMI) with the loaded algorithm and saves it in the patient file. Due to the electronic ecosystem, all bedside monitor information measured during the ICU follow-up of the patient, mechanical ventilation parameters, laboratory examination results, extracorporeal applications, and information on all infusions are transmitted from the utilized devices to the clinical decision support system.



## DATA COLLECTION

The data on all patients followed up between January 2013 and January 2020 from the *EMRall-Qlin-ICUImdSoftMetavision* Clinical Decision Support System used in the ICU were obtained and evaluated through Structured Query Language (SQL) queries.

### Sample

During the study period, 9,544 patients were admitted to the ICU. After the exclusion of 7,430 patients from the study according to the exclusion criteria, the remaining 2,114 patients constituted the study population. All patients included in the study were divided into two groups according to the BMI criteria determined by the World Health Organization, including 1,632 (77.2%) patients with a BMI <30 kg/m<sup>2</sup> and 482 (22.8%) patients with a BMI ≥ 30 kg/m<sup>2</sup>.

### Inclusion criteria

The study was intended to include all patients aged 65 and over who had spent more than 24 hours in intensive care.

### Exclusion criteria

Patients younger than 65 (n: 4,864), those who were taken to the service within the first 24 hours after ICU admission (n: 980), those who developed mortality (n: 774), and those with missing data (n: 812) were excluded from the study.

### Primary outcome

Evaluating the relationship between obesity and mortality in patients over 65 years of age who were followed in ICU was the primary aim of the study.

### Secondary outcome

The secondary aims of the study were to compare

patients' comorbidities at admission, primary diagnoses, calculated ICU scores, interventions, and treatments.

### Ethical aspects

Before beginning the research, ethics committee approval and institutional permission were obtained from the Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (Protocol code: 2021/218; Approval no: 2021-08; Approval date: 19.04.2021).

### Evaluation of data (statistical analysis)

The data collected in the study were evaluated using SPSS 22.00 software. A Shapiro-Wilk test was used to test the distribution of the numerical data. Categorical variables were expressed in terms of frequencies and percentages. Numerical variables with a normal distribution were given as means ± standard deviations, while numerical data not conforming to a normal distribution were given as medians and interquartile intervals (IQRs). An independent-samples t-test was used in comparing the numerical data, and a Mann-Whitney U-test was used when the assumptions of the t-test could not be met. The Chi-square test was used for comparing categorical variables, and Fisher's exact test was used when the conditions of the Chi-square test were not met. A Kaplan-Meier survival analysis was used to determine the association between BMI groups and 28-day mortality. It was thought that the severity of acute illness and chronic health conditions might be different in these groups of patients. In order to avoid these differences potentially affecting results and provide better randomization, patients were divided into four quartiles according to their acute physiology and chronic health evaluation (APACHE) II scores (16, 17-23, 24-29, and ≤30). Additionally, receiver operating characteristic (ROC) curves were created to determine the differences in mortality risk between patients in each quartile. A

p-value <0.05 was accepted as the level of significance.

## RESULTS

Table 1 shows the general characteristics of the patients, who were divided into two groups based on their BMI: non-obese and obese. Of the 2,114 patients, 1,632 (77.2%) were non-obese, and 482 (22.8%) were obese. The average age of the non-obese patients (77 [70–83]) was higher than that of the obese patients (75 [70–82]) ( $p < 0.05$ ). It was determined that the female gender (937; 57.4%) was more common in non-obese patients, whereas the male gender (376; 78.0%) was more common in obese patients ( $p < 0.001$ ). Median BMI values were 27.34 (25.39–28.69) in non-obese patients and 36.73 (33.20–41.62) in obese patients. The frequency of comorbidity was similar between groups. The frequencies of diabetes mellitus and hypertension were increased in obese patients ( $p < 0.05$ ). An examination of the admission diagnoses of the patients in the ICU revealed that the most common admission diagnosis in both groups was sepsis. The rate of patients diagnosed with sepsis was similar between groups. The most common sepsis source in both groups was intraabdominal sepsis. Other common diagnoses in obese patients (due to chronic obstructive pulmonary disease (COPD), pneumonia, and other causes) were pulmonary diseases (95; 19.7%), postoperative follow-up (61; 12.7%), and cerebrovascular disease (47; 9.8%). While malignancy (129; 7.9%) was more common in non-obese patients than obese patients, diagnoses of COPD (37; 7.7%), renal-metabolic diseases (42; 8.7%), and hepatic cirrhosis (8; 1.7%) were more common in obese patients than non-obese patients ( $p < 0.05$ ) (Table 1).

The ICU scores, interventions, and treatments of the patients are shown in Table 2. The numbers of arterial catheters applied to the groups were similar. More central venous catheters were applied to obese patients than to non-obese patients (502,

56.5%,  $p < 0.05$ ). There was no difference between the groups regarding the use of vasoactive drugs, antibiotics, and Total parenteral nutrition (TPN) ( $p > 0.05$ ). When the complications that developed in the ICU were examined, it was found that the rate of acute kidney injury (AKI) in obese patients (326; 67.6%) was higher than that in non-obese patients (937; 57.4%) ( $p < 0.001$ ). Obese patients (124; 25.7%) required dialysis more frequently than non-obese patients (318; 19.5%). Pressure sores were more common in obese patients (76; 15.8%) than non-obese patients (145; 8.9%) ( $p < 0.001$ ).

### Mechanical ventilation

While 68.4% (1,191) of non-obese patients required mechanical ventilator support, this rate increased to 74.3% (358) in obese patients ( $p < 0.05$ ). When mechanical ventilator parameters were examined, while positive end-expiratory pressure (5.6 [5.1–6.0]), peak pressure (14 [12–16]), and Work of Breathing ventilator (WOBv) (1.16 [0.99–1.31]) values were higher in obese patients, pulmonary compliance (34 [29–41]) was lower ( $p < 0.05$ ). There was no difference in mean tidal volume between the groups, but tidal volume, in ml/kg adjusted for ideal weight, was higher in obese patients ( $p < 0.001$ ). Between the groups,  $FiO_2$ , respiratory rate per minute, and mechanical power did not differ significantly (Table 2). Mechanical ventilation duration was higher in obese patients, but this difference was not statistically significant ( $p > 0.05$ ).

### Laboratory parameters

The laboratory parameters of the patients are given in Table 2. When blood gas values were examined,  $pCO_2$  was higher and PH was lower in obese patients ( $p < 0.05$ ). In the two groups,  $PO_2$ ,  $HCO_3$ , and lactate levels were similar ( $p > 0.05$ ). Fewer daily calories could be given to obese patients (1,524 [1,382–1,697]) than non-obese patients (1,652 [1,461–1,881]) ( $p < 0.001$ ). Despite lower calorie input, the mean



**Table 1.** Characteristics of patients groups and admission diagnosis.

Parameters	Non-Obese n=1632 (%77.2)	Obese n=482 (%22.8)	P-value
Body mass index, median (IQR) (kg/m <sup>2</sup> )	27.34(25.39-28.69)	36.73(33.20-41.62)	
<b>Age (year)</b>	77(70-83)	75(70-82)	0.026
65-74	668(40.9)	219(45.4)	0.427
75-84	613(37.6)	188(39.0)	0.759
≥85	351(21.5)	75(15.6)	0.055
<b>Gender</b>			>0.001
Female	695(42.6)	376(78.0)	
Male	937(57.4)	106(22.0)	
<b>Comorbidity</b>	1512(92.6)	455(94.4)	0.184
Hypertension	839(51.4)	307(63.7)	<0.001
Diabetes	422(25.9)	190(39.4)	<0.001
Cerebrovascular disease	204(12.5)	46(9.5)	0.77
CAD	346(79.9)	87(18.0)	0.132
COPD	242(14.8)	86(17.8)	0.108
CRF	194(11.9)	73(15.1)	0.059
Malignancy	226(13.8)	54(11.2)	0.132
Hepatic disease	23(1.4)	8(1.7)	0.668
Psychiatric disorder	13(0.8)	6(1.2)	0.360
Dementia	147(9.0)	34(7.1)	0.178
Other	121(7.4)	32(6.6)	0.564
<b>Admission diagnosis</b>			
Cerebrovascular disease	210(12.9)	47(9.8)	0.066
Cardiac	111(6.8)	34(7.1)	0.847
Pulmonary	266(16.3)	95(19.7)	0.080
Pneumonia	160(9.8)	43(8.9)	0.563
COPD	73(4.5)	37(7.7)	0.005
Pulmonary, Other	33(2.0)	15(3.1)	0.158
Renal-metabolic	96(5.9)	42(8.7)	0.027
Hepatic cirrhosis	11(0.7)	8(1.7)	0.044
Trauma	38(2.3)	15(3.1)	0.334

Sepsis	455(27.9)	136(28.2)	0.885
Pneumosepsis	96(5.9)	20(4.1)	0.142
Intra- abdominal sepsis	217(13.3)	75(15.6)	0.206
Urosepsis	50(3.1)	14(2.9)	0.858
Sepsis, other	92(5.6)	27(5.6)	0.976
Malignancy	129(7.9)	18(3.7)	0.002
Postoperative	220(13.5)	64(13.3)	0.909
GIB-Hemorrhage	54(3.3)	8(1.7)	0.059
Other	42(2.6)	15(3.1)	0.420

CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; CRF, chronic renal failure; GIB: gastrointestinal bleeding; IQR: inter quartile range.

blood sugar of obese patients (156 [131–193]) was higher than that of non-obese patients (144 [121–176]) ( $p < 0.001$ ). Other laboratory parameters were found to be similar, except that obese patients had higher white blood cells (WBCs), and non-obese patients had higher procalcitonin levels.

### ICU duration and mortality

Obese patients (5.70 [2.43–12.31]) had longer ICU stays than non-obese patients (4.41 [2.01–10.45]) ( $p < 0.05$ ). When 28-day mortality was examined via Kaplan-Meier survival analysis, it was determined that there was no difference between the groups (Log-rank:  $p=0.191$ ) (Figure 1). Also, ICU mortality was determined to be 37.6% (181) in obese patients and 36.0% (588) in non-obese patients ( $p > 0.05$ ). In the subgroup analysis performed according to the admission diagnoses of the patients, there was no difference in mortality between the groups with any admission diagnosis (Table 3). Considering that the clinical weights of the patients may differ and this may affect the mortality data, the patients were divided into four quartiles according to APACHE II score. Thereby, patients with similar disease severity were grouped together. In order to determine the relationship between BMI and mortality, an ROC

analysis, including patients in the four APACHE II groups, was performed. No significant relationship was found between BMI and mortality in any of the groups, regardless of disease severity (Figure 2).

### DISCUSSION

As a result of this study, which investigated the effect of obesity on mortality in geriatric ICU patients, it was determined that the mortality rate of obese patients was similar to that of non-obese patients. Mortality was found to be similar between the groups in the subgroup analyses for all admission diagnoses. Even when geriatric patients with similar disease severity were grouped, obesity had no effect on mortality. An attempt to find a BMI cut-off value that would affect mortality was unsuccessful. The paradox that associates obesity with better survival in geriatric patients in the ICU could not be statistically confirmed. The results of previous studies investigating the ICU mortality of obese patients contradict one another. While ICU mortality has been shown to be lower in obese patients in some studies (5), no difference in mortality was observed in other studies (6), and obesity was even found to cause higher mortality in one subgroup of obese patients (13). In another study, obesity was



**Table 2.** Scores, interventions, mechanical ventilator values, blood parameters and treatments during the ICU stay.

Parameters	Non-Obese n=1632 (%77.2) median (IQR)	Obese n=482 (%22.8) median (IQR)	P-value
APACHE 2	23(17-29)	24(17-29)	0.586
APACHE 4	80(58-110)	82(57-118)	0.565
SAPS 3	50(42-58)	49(42-59)	0.951
SOFA	6(3-9)	6(3-10)	0.760
TISS	20(15-26)	22(16-27)	0.171
GCS	9(5-13)	10(6-13)	0.595
RASS	-1(-4-0)	-1(-4-0)	0.624
Interventions			
Arterial catheter	1159(71.0)	344(71.4)	0.881
Central catheter	846(51.8)	284(58.9)	0.006
MV	1116(68.4)	358(74.3)	0.013
Tracheostomy	294(18.0)	88(18.3)	0.903
Dialysis	318(19.5)	124(25.7)	0.003
Treatments			
Nutrition (kcal/day)	1652(1461-1881)	1524(1382-1697)	<0.001
TPN	569(34.9)	172(35.7)	0.740
Antibiotics	1452(89.0)	432(89.6)	0.684
Vasoactive agents	1016(62.3)	303(62.9)	0.809
Mechanical ventilation			
FiO <sub>2</sub> (%)	42(40-47)	43(40-48)	0.082
PEEP (cmH <sub>2</sub> O)	5.3(5.1-5.9)	5.6(5.1-6.0)	<0.001
P peak (cmH <sub>2</sub> O)	14(12-16)	15(13-17)	<0.001
Tidal Volume	479(422-546)	477(423-531)	0.433
Tidal Volume (ml/kg)	6.56(5.84-7.43)	6.92(6.18-7.73)	<0.001
Respiratory rate (min)	19(16-21)	19(16-22)	0.682
Compliance (ml/cmH <sub>2</sub> O)	37(31-48)	34(29-41)	<0.001
WOBv (j/L)	1.06(0.90-1.21)	1.16(0.99-1.31)	<0.001
Mechanical power (J/mien)	9.30(7.76-10.78)	9.29(7.73-10.87)	0.737
Blood gas			
PH	7.40(7.32-7.44)	7.38(7.30-7.43)	0.005

PO <sub>2</sub> (mmHg)	87.1(64.7-109.1)	84.4(63.3-106.7)	0.166
PCO <sub>2</sub> (mmHg)	40.6(35.8-46.6)	42.9(38.0-49.8)	<0.001
HCO <sub>3</sub> (mEq/L)	24.3(20.8-27.7)	24.4(20.6-28.2)	0.608
Lactate (mmol/L)	1.78(1.33-3.11)	1.89(1.41-3.31)	0.068
Laboratory			
Glucose (mg/dl)	144(121-176)	156(131-193)	<0.001
Hemoglobin (g/dl)	9.64(8.71-10.96)	9.57(8.63-10.91)	0.174
Hematocrit (%)	30.26(27.19-34.09)	29.79(27.19-33.90)	0.437
Platelet (x10 <sup>9</sup> /L)	206(148-275)	218(160-287)	0.039
White blood cell (x10 <sup>9</sup> /L)	12,35(9.30-16.19)	13.54(10.09-17.28)	<0.001
CRP (mg/L)	1.84(0.28-4.99)	2.11(1.01-5.15)	0.191
Procalcitonin (ug/L)	0.93(0.40-4.52)	0.72(0.35-3.35)	0.033
INR	1.20(1.07-1.43)	1.21(1.08-1.43)	0.715
APTT (sec)	32.3(27.0-41.5)	31.2(26.0-40.2)	0.066
AST (U/L)	31(20-57)	31(21-63)	0.490
ALT (U/L)	19(11-37)	20(13-40)	0.063
Creatinine (mg/dl)	0.70(0.47-1.08)	0.76(0.48-1.06)	0.630
Albumine (mg/dl)	2.80(2.33-3.30)	2.90(2.41-3.34)	0.105
Sodium (mmol/L)	139(136-143)	139(136-142)	0.305
Chlorine (mmol/L)	103(99-107)	103(99-107)	0.142
Potassium (mmol/L)	4.1(3.7-4.5)	4.0(3.7-4.4)	0.607
Magnesium (mg/dl)	1.98(1.80-2.19)	1.95(1.77-2.17)	0.057
Complications			
AKI	937(57.4)	326(67.6)	<0.001
Pressure sores	145(8.9)	76(15.8)	<0.001
MV (day)	5.27(2.24-11.99)	5.29(2.48-13.81)	0.298
LOS ICU (day)	4.41(2.01-10.45)	5.70(2.43-12-31)	0.003
28-day mortality	549 (33.6)	162 (33.6)	0.990
ICU mortality	588(36.0)	181(37.6)	0.542

APACHE: acute physiology and chronic health evaluation; SAPS: simplified acute physiology; SOFA: sequential organ failure assessment; TISS: therapeutic intervention scoring system; GCS: glasgow coma score; RASS: Richmond Agitation and Sedation Scale; MV: mechanic ventilation; TPN: total parenteral nutrition; FiO<sub>2</sub>: fraction of inspired oxygen; PEEP: positive end-expiratory pressure; WOBv: work of breathing ventilator; PCO<sub>2</sub>: partial pressure of carbon dioxide; PO<sub>2</sub>: partial pressure of oxygen; HCO<sub>3</sub>: bicarbonate; CRP: C-reactive protein; INR: international normalized ratio; APTT: activated partial thromboplastin time; AST: aspartate aminotransferase; ALT: alanine aminotransferase; AKI: acute kidney injury; LOS: length of stay; ICU: intensive care unit; IQR: inter quartile range.



**Table 3.** Mortality rates of the groups according to the diagnosis of ICU admission.

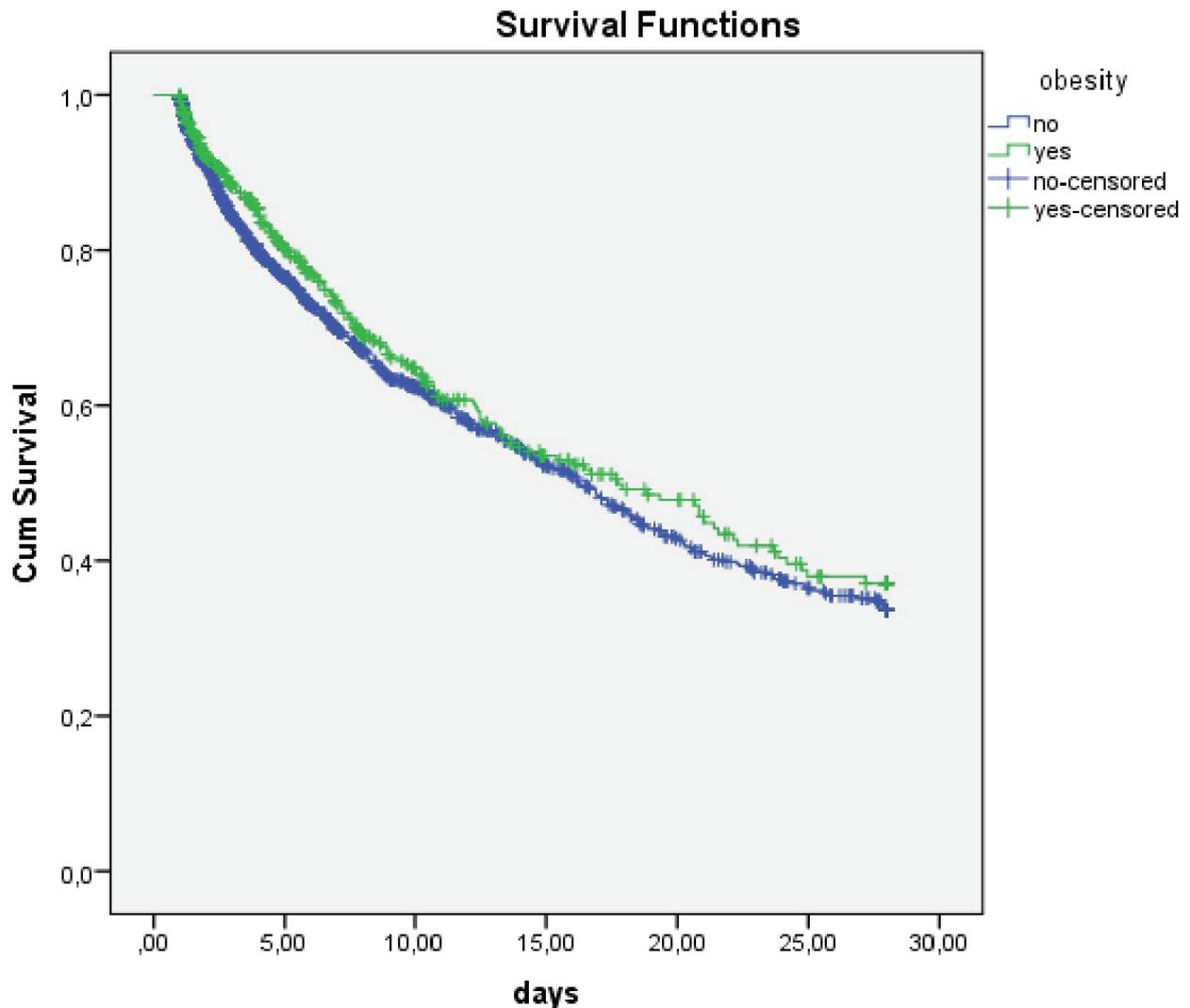
Admission diagnosis	Non-Obese n=1632 (%77.2)	Obese n=482 (%22.8)	P-value
Cerebrovascular disease	61(29.0)	10(21.3)	0.281
Cardiac	42(37.8)	19(55.9)	0.062
Pulmonary	96(36.1)	35(36.8)	0.896
Pneumonia	66(41.3)	20(46.5)	0.535
COPD	19(26.0)	8(21.6)	0.612
Pulmonary, Other	11(33.3)	7 (46.7)	0.326
Renal-metabolic	39(40.6)	21(50)	0.307
Hepatic cirrhosis	7(63.6)	5(62.5)	0.663*
Trauma	11(28.9)	4(26.7)	0.577*
Sepsis	210(46.2)	65(47.8)	0.736
Pneumosepsis	41(42.7)	7(35)	0.524
Intra-abdominal sepsis	102(47.0)	33(44.0)	0.653
Urosepsis	15(30.0)	5(35.7)	0.683
Sepsis, other	52(56.5)	20(74.1)	0.101
Malignancy	40(31.0)	8(44.4)	0.255
Postoperative	38(17.3)	5(7.8)	0.063
GIB-Hemorrhage	29(53.7)	2(25.0)	0.128*
28-day mortality	549 (33.6)	162 (33.6)	0.990
ICU mortality	588(36.0)	181(37.6)	0.542

COPD: chronic obstructive pulmonary disease; GIB: gastrointestinal bleeding. \*Fisher exact test

associated with a decrease in mortality in ICU patients, but no reduction in mortality was found in geriatric obese patients in the same study (14). In a meta-analysis evaluating 32 studies conducted between 1990 and 2013, in which 197,940 adults aged 65 and over were included, it was determined that the relationship between BMI and mortality formed a “U” shaped curve (15). With age, the curve shifts to the right and becomes flat. This change in the curve causes the standard BMI cut-off points to differ in older adults as compared to younger populations. These confusing results can be explained by the use of arbitrary obesity definitions, such as BMI > 28 and BMI > 31, in some studies; differences in comorbidity burden between obese and non-

obese patients; and most importantly, the absence of a single obese patient phenotype. An obesity condition in which adults with dysmetabolic obesity, in which an increase in waist circumference is prominent, die at a younger age and those with a less metabolically active fat mass survive into older age may reflect the absence of this disease rather than representing a healthy state. Therefore, obesity may not have clear negative effects on the geriatric population. The causes of this reversed epidemiological situation, which is called the obesity paradox, are not entirely clear (16). An increased energy reserve that can be consumed during disease can be useful in the “geriatric” population, where many acute and chronic diseases are normal, and adipose tissue

**Figure 1.** Kaplan-Meier analysis performed to determine the relationship between 28-day survival and obesity (Log rank:  $p=0.191$ )

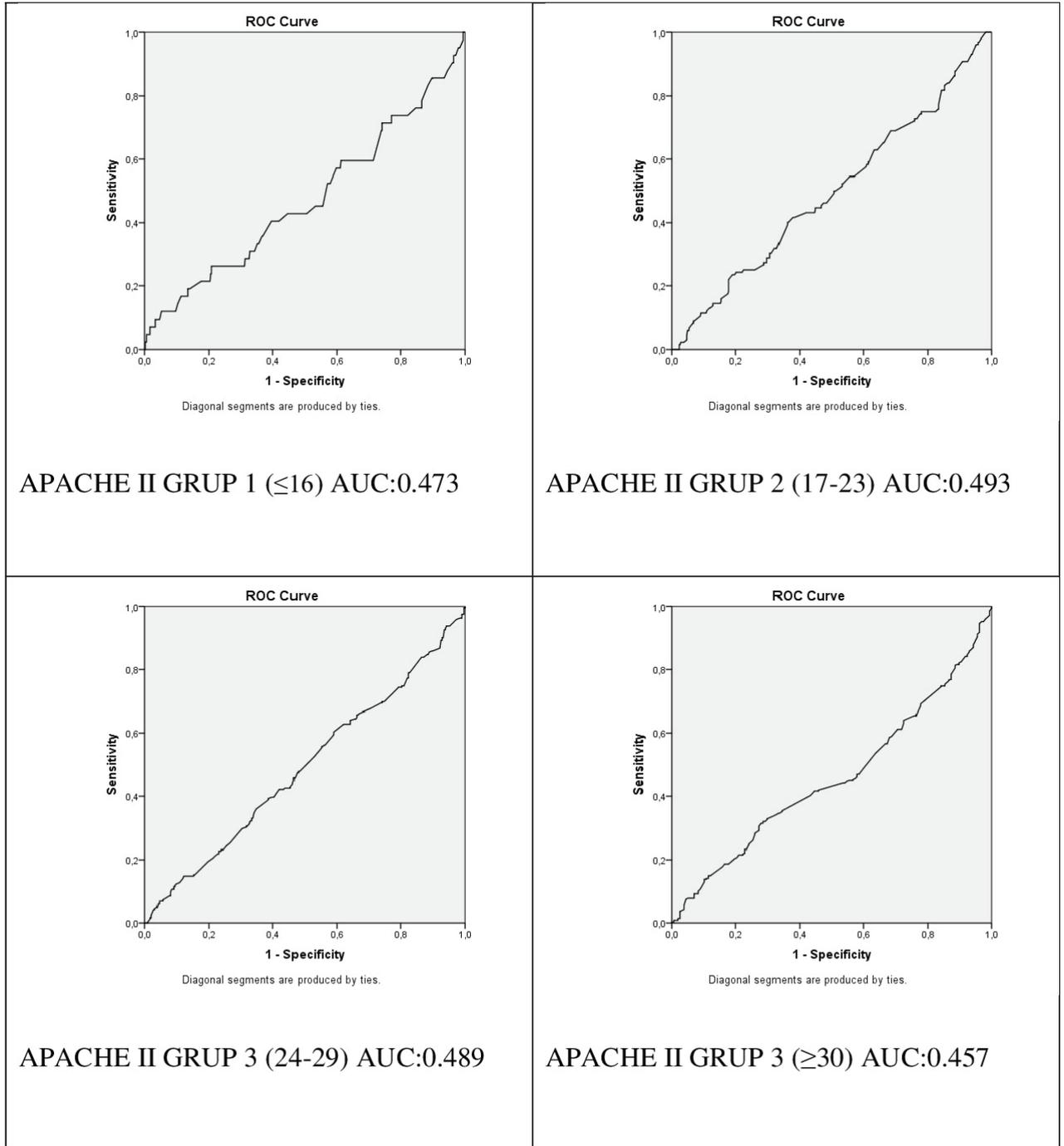


can act as a storage site for harmful metabolites in the circulation (16). Our study, in which higher blood glucose levels were detected in obese patients than non-obese patients despite their lower calorie input, supports this idea. In addition, the fact that BMI measurement does not take into account the distribution of fat in the body or lean muscle mass may cause an incorrect obesity assessment. Neck reduction due to osteoporosis, which is common

with age, may cause an increase in BMI, and while a patient with all the risks of metabolic and clinical obesity due to an increase in visceral fat mass may not be defined as obese, a patient with increased muscle mass and a preserved visceral fat ratio can be defined as obese. Therefore, even the BMI values used in the determination of obesity can cause these complex results.



**Figure 2.** Receiver operating characteristic (ROC) analysis curves of body mass index and mortality according to four different APACHE groups.



The physiology of obesity and its comorbidities are similar to those of aging and age-related diseases. Obesity and aging share a similar phenotypic structure that can be defined by disruptions in genomic integrity, mitochondrial dysfunction, a weakened immune system, increased intracellular macromolecule accumulation, susceptibility to systemic inflammation, and changes in the composition of the body and tissues (17). Also, both obesity and aging are associated with comorbidities, including diabetes mellitus, cardiovascular diseases, and some types of cancer (18). Our research results found that the prevalence of diabetes mellitus and hypertension increased in the obese geriatric population, in accordance with the literature. Obesity and aging are characterized by the deterioration of homeostasis as a result of a gradual decrease in the function of various organs (19). The increased production of reactive oxygen species (ROS), which contributes to aging and obesity, causes oxidative damage and, eventually, DNA damage, which leads to telomere shortening and cell death (20). The resulting DNA damage plays a role in all pathologies associated with obesity and aging.

In our study, it was determined that geriatric obese patients required mechanical ventilation more frequently, but the duration of mechanical ventilation was similar to that observed for non-obese patients. Previous studies investigating the relationship between obesity and MV duration in patients have yielded controversial results (2,21). While the duration of mechanical ventilation was longer in obese patients than non-obese patients in one study (2), no such difference was found in another similar study (21). Our research results show that obese patients had higher ventilation pressures and lower compliance. These results are consistent with previous research. Although obese patients are ventilated with higher pressures on mechanical ventilators, they tend to have a lower functional residual capacity and lung volume due to the changes in respiratory mechanics caused by increased

adipose tissue surrounding the chest wall (22). The decreased compliance found in obese patients can be explained by the fact that the mass burden of obesity makes the lungs more susceptible to atelectasis or increased alveolar wall tension due to the disrupted harmony between the lung and chest wall. Increased intra-abdominal pressure due to visceral fat accumulation in the abdominal area may cause an increase in respiratory workload. In addition, studies have determined that obese patients produce more carbon dioxide (23). This may explain the increased respiratory workload as well. In addition to the increased workload caused by obesity, clinicians may be hesitant to admit geriatric obese patients to the ICU and attach them to a mechanical ventilator due to the muscle weakness seen in the geriatric population. However, studies have shown that the results of the use of mechanical ventilators in the geriatric patient group are comparable to those of non-geriatric patients and that ICU admission should not be denied to geriatric patients (24).

In our study, the ICU follow-up duration was found to be significantly longer in obese geriatric patients as compared to non-obese geriatric patients. Similar studies report that obesity increases the duration of ICU stay (5,6). In a meta-analysis of 23 studies, a trend toward an increase in ICU stay in obese patients was detected (6). In another meta-analysis of 14 studies, obesity was found to be associated with increased ICU length of stay and duration of mechanical ventilation (5). However, there are studies that claim the opposite and find the average ICU duration of obese patients to be similar to that of non-obese patients (8). This may be explained by the fact that obese patients have different phenotypes. There is not a single standardized obese patient profile in the ICU. Patients vary in terms of obesity class and comorbid disease burden. Also, some clinicians tend to think that obese patients may have worse outcomes. Therefore, the increased acceptance of obese patients who can be treated more easily in the intensive care unit and



are not very critical may shorten ICU follow-up duration. On the other hand, vascular access problems are common in obese patients, and the frequency of using central catheters has increased in obese patients, as shown in our study. This may lead to infection development and catheter-related complications, prolonging the duration of ICU stay. In addition, increased AKI and pressure sore incidence in obese patients may have prolonged the duration of the ICU. Previous studies have shown that the prevalence of AKI in obese patients followed in the ICU is higher than in non-obese critically ill patients, and the frequency of AKI in critically ill patients increases with BMI (25). Although the pathophysiology of the development of increased AKI in obesity is not fully understood, increased renal blood flow and glomerular filtration rate due to changes in renal hemodynamics may lead to an increase in the filtration fraction, resulting in increased susceptibility to injury. Obese ICU patients are at risk for increased intra-abdominal pressure, which can cause renal dysfunction due to both poor arterial perfusion and venous occlusion (25). As determined in this study in obese patients, the effects of more common comorbid diseases on kidney physiology should not be ignored. Another factor that may contribute to the effect of obesity on AKI is the difficulty in assessing intravascular volume status and determining adequate fluid therapy or vasoactive drug dose. In addition, providing nursing care to obese patients is more difficult than providing care to normal-weight patients due to obese patients' high body weight and large body surface area. The difficulty involved in position changes for these patients creates the risk of pressure sores and lacerations of the skin. The disruption of the protective skin barrier may prolong stays in the ICU by increasing complications such as infection or bleeding in obese patients (4).

The strengths of the study are that it has a large sample and all the data is obtained from the clinical decision support system with electronic queries

for preventing data misses and human errors. There are some limitations of the study. First, having a single-center population prevents the generalization of the results despite the geographical diversity of the patients. The retrospective study design may create confounding factors and a risk of bias. In addition, the absence of data such as waist circumference or waist-hip ratio, to support the definition of obesity, may have affected the accuracy of the groups created according to BMI. The lack of registration of IV fluids and diuretic treatments used before ICU admission may have affected the BMI data by changing the weights of the patients measured in the ICU. Long-term follow-up results of patients who survived in the ICU could not be evaluated due to lack of data. There is a need for well-designed, randomized prospective studies that include geriatric obese patients at the center of the study in order to better understand the effect of obesity on the geriatric population in the ICU.

## CONCLUSION

It was determined that obesity does not make a difference in ICU mortality for geriatric patients. The obesity paradox in the ICU is supported by the lack of a difference in mortality when patients are grouped by admission diagnosis and disease severity. According to our results, obesity increases ICU morbidity in geriatric patients, but it is not associated with mortality. In an environment with limited resources, the careful selection of geriatric patients to be admitted to the ICU is important, and obese geriatric patients may have positive outcomes.

**Conflict of Interest:** The authors declare they have no conflict of interest.

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## RESEARCH

# THE EFFECT OF COVID-19 PANDEMIC ON SARCOPENIA, QUALITY OF LIFE AND PAIN: A ONE-YEAR FOLLOW-UP STUDY

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## ABSTRACT

**Introduction:** This study evaluated the effect of coronavirus disease 2019 pandemic on sarcopenia, quality of life and pain severity in elderly patients and investigated which patients were affected more from this pandemic (sarcopenic or not, males or females, and physically active or inactive).

**Materials and Methods:** A total of 225 elderly patients with SARC-F, visual analogue scale-musculoskeletal pain scores, handgrip strength, chair stand test, short form-36, demographic data and phone number records in July 2020 were included in this study. Follow-up was conducted in June 2021 with telephonic interviews. During follow-up, SARC-F, 10-point Likert pain scale, Short Form-36 and physical activity were evaluated.

**Results:** After one year of the COVID-19 pandemic, almost all short form-36 scores decreased; however, the pain and SARC-F scores did not show a significant change. Decrease in short form-36 scores were higher in patients without sarcopenia than in those with sarcopenia. Decrease in Short Form-36 scores were higher in women than in men. Increase in pain scores (active:  $p=0.851$ , inactive:  $p=0.005$ ) and decrease in Short Form-36 scores, were higher in physically active patients than in physically inactive patients. SARC-F scores did not change in any of the study groups.

**Conclusion:** After one-year follow-up in elderly patients, quality of life decreased, severity of pain increased in physically inactive, and SARC-F was unaffected. Females, non-sarcopenic, and physically inactive patients were found to be more affected by the COVID-19 pandemic.

**Keywords:** COVID-19; Pain; Quality of life; Sarcopenia.



## INTRODUCTION

In December 2019, Wuhan city in China reported the first confirmed case of coronavirus disease 2019 (COVID-19), which subsequently caused worldwide outbreak. Consequently, a pandemic was declared by the World Health Organization (WHO). While it is important to focus on controlling COVID-19, it is also necessary to identify the long-term effects of the pandemic. COVID-19 has been shown to have substantial long-term impact on several organs of the musculoskeletal system, especially in the geriatric population, because of restrictions and social isolation. One of the consequences of the COVID-19 pandemic has been a decrease in physical activity (1), which is a risk factor for pain (2), reduced quality of life (3), and sarcopenia (4). In addition, social isolation and increased loneliness (5) can lead to anxiety and depression resulting in lower quality of life in the elderly (6). Furthermore, decreased sunlight exposure, which is associated with lower vitamin D concentrations, is a risk factor for pain and sarcopenia (4).

According to the European Working Group on Sarcopenia in Older People (EWGSOP2), the SARC-F scale is recommended to identify cases of sarcopenia. If the results of SARC-F are negative, the patients are considered non-sarcopenic. In clinical practice, after a positive SARC-F score, low muscle strength is sufficient to start intervention (7).

Only a few studies have investigated the effects of COVID-19 pandemic on the musculoskeletal system (8,9). One of the studies reported increased sarcopenia rates in geriatric patients with diabetes (8). Another study reported pain augmentation in adults during the pandemic (9). Considering that the musculoskeletal system can be affected by many conditions, such as physical activity, sarcopenia, and gender, evaluations should be made taking these conditions into account.

The aims of this one-year follow-up cohort study were as follows: 1) to evaluate the effect of the COVID-19 pandemic on sarcopenia using the SARC-F

scale, quality of life, and pain severity in geriatric patients; and 2) to investigate which patients were affected more when classified on the basis of the presence or absence of sarcopenia, sex, and being physically active or inactive.

## MATERIALS AND METHODS

This cohort study was conducted in patients aged 60 years or older who were admitted to a physical medicine and rehabilitation outpatient clinic in July 2020. Patients with SARC-F scores, visual analog scale (VAS)-musculoskeletal pain scores, handgrip strength, chair stand test, short form-36 (SF-36), demographic data, and phone number records in July 2020 were included in this study. Follow-up was conducted via telephone interviews in June 2021. Patients with an additional chronic disease or surgery within one year; active cancer, cerebrovascular stroke, and other neurological disorders, acute/subacute pain, active infection, active arthritis, impaired cognitive status, advanced hearing loss, those who ever had COVID-19 infection or underwent treatment in a hospital within the past one year and immobilised patients were excluded from the study.

In July 2020, 225 patients were evaluated in terms of demographic data (age; sex; weight; height; education/working/family status; presence of concurrent diseases, such as hypertension, diabetes mellitus, chronic obstructive pulmonary disease, thyroid problems; cane usage; smoking), VAS pain, SARC-F score, handgrip strength, chair stand test, and SF-36 by a physical medicine and rehabilitation specialist (face to face) in physical medicine and rehabilitation outpatient clinic. In June 2021, another physical medicine and rehabilitation specialist who was blind to 2020 records conducted telephone interviews with those patients. Any disease, such as cancer, infection, COVID-19 infection and surgery within one year; the rate of musculoskeletal pain with 10-point likert scale; SARC-F; SF-36; and regular exercise were recorded via telephone interviews

with patients themselves (10-15 minutes), without any visual interview. Telephone interviews were held those who were available at that time, appointments were made those who were not available.

The VAS was used to measure general body musculoskeletal pain, which was assessed from 0 (no pain) to 10 (worst possible pain) (10). One year later, 10-point likert was used for general body musculoskeletal pain. The question for this measurement was the following: "How would you rate your general body pain on a 0–10 scale at the present time? Zero is no pain and ten is pain as bad as could be."

Quality of life assessment was performed using the SF-36 with 36 items on physical function, physical role, emotional role, energy, body pain, mental health, general health, and social function. Each scale ranges from 0 (poor health) to 100 (perfect health) (11). Patients spent almostly an average of 5-10 minutes on answering the SF-36 by telephone.

Ambulation, strength, history of falls, rising from a chair, and stair climbing were evaluated using the SARC-F scale which assesses the risk of sarcopenia. A score lower than 4 was defined as non-sarcopenic. The chair stand test measures the time taken for five rounds of rising from the sitting position without using arms, and was defined as low when the time taken was >15s. Grip strength was measured with a hand-held dynamometer (Baseline, White Plains, New York, USA), and the cut-off thresholds were 32 kg for men and 22 kg for women). The chair stand test and grip strength were measured only in July 2020. Probable sarcopenia was defined according to the EWGSOP2 algorithm as having a low SARC-F score and low muscle strength (grip strength/chair stand test) (7).

Physical activity was assessed by asking patients to perform vigorous and moderate physical activity. Vigorous physical activities were defined as physical effort resulting in faster breathing than normal. Moderate physical activities were defined as moderate physical effort resulting in somewhat faster

breathing than normal. Patients were asked the following questions: 1) 'How many minutes do you spend on vigorous physical activity on an average day for one year?'; 2) 'How many minutes do you spend on moderate physical activity on an average day for one year?'. According to the WHO guidelines (12), at least 150 min of moderate and/or 75 min of vigorous physical activity per week for adults and elderly was defined as 'regular physical activity'.

Verbal informed consent was provided by the patients before the telephonic interview. Ethics approval was received from the local ethics committee 30/03/21-09 (25403353-050.99-181555).

### Statistical Analysis

The distribution of each continuous variable was tested for normality using the Shapiro-Wilk test and is expressed as median value (%25-%75). Non-normally distributed variables were performed using the Mann Whitney U and Wilcoxon Signed Ranks Test for continuous variables. The categorical variables are expressed in frequencies and percentages. The Chi-square test was used to compare categorical variables. A p-value < 0.05 was considered significant. All analyses were performed using the SPSS version 22.0 software (SPSS Inc., Chicago, IL, USA).

### RESULTS

One patient died during the study period. Twenty (8.8%) patients with COVID-19 infection, six (2.6%) with an additional chronic disease (such as cancer, vision loss, cardiac disease, bone marrow disease), three (1.3%) who underwent surgery (discectomy, prostate), four (1.7%) with acute pain in the last month, and 30 (13.3%) who were not contacted by telephone were excluded. Finally, 161 patients (125 women, 36 men; mean age,  $68.4 \pm 6.2$  years) who met the inclusion criteria were enrolled in our study. The demographic characteristics of the patients are presented in Table 1.



**Table 1.** Demographic characteristics of patients

	Frequencies n (%)
<b>Age (years)</b> (median 25-75%)	67 (64-71)
<b>Gender (female/male)</b>	125 (77.6%) / 36 (22.4%)
<b>Weight (kg)</b> (median 25-75%)	76 (69.2-89)
<b>BMI</b> (median 25-75%)	29.3 (26.6-33.1)
<b>Chronic diseases</b>	135 (83.9%)
<b>Working</b>	8 (5%)
<b>Education</b>	
Primary school and lower	138 (85.7%)
High school and higher	23 (14.3%)
<b>Family type</b>	
Alone	22 (13.6%)
Nuclear family	104 (64.5%)
Extended family	35 (21.7%)
<b>Cane usage</b>	19 (11.8%)
<b>Smoking</b>	18 (11.2%)

(kg=kilograms, BMI=Body mass index)

Comparison of patients between June 2020 and July 2021 showed that after approximately one year of COVID-19 pandemic, their SF-36 scores decreased except 'role emotional' (physical function:  $p<0.001$ , role physical:  $p=0.007$ , bodily pain:  $p=0.011$ , energy:  $p<0.001$ , mental health:  $p<0.001$ , general health:  $p=0.006$ , social function:  $p=0.001$ ). However, pain scores and SARC-F scores did not show a statistically significant change (Table 2).

Comparison of patients with and without sarcopenia showed that patients with sarcopenia had higher SARC-F and pain scores and lower SF-36 scores in both 2020 and 2021. In patients with probable sarcopenia, physical function and general health decreased after one year of COVID-19 pandemic. In patients without sarcopenia, only SARC-F and pain scores and emotional role did not change; however, other parameters changed after one year of COVID-19 pandemic (physical function,  $p<0.001$ ; physical role,  $p=0.024$ ; bodily pain,  $p=0.019$ ; energy,  $p<0.001$ ; mental health,  $p<0.001$ ; general health,

$p=0.031$ ; social function,  $p=0.004$ ). On comparing patients with probable sarcopenia with those without sarcopenia, age ( $p=0.006$ ) was found to be lower and the rate of regular exercise ( $p=0.017$ ) was higher in the no sarcopenia group (Table 3).

For female patients, most of the SF-36 scores (physical function,  $<0.001$ ; physical role,  $p=0.019$ ; energy,  $p=0.002$ ; mental health,  $p<0.001$ ; general health,  $p=0.014$ ; social function,  $p=0.004$ ) decreased within one year of the pandemic. For male patients, three of the SF-36 parameters decreased (physical function,  $p=0.004$ ; energy,  $p=0.029$ ; mental health,  $p=0.028$ ). Comparison of patients according to sex showed that females were found to have significantly higher SARC-F and pain scores, whereas many of the SF-36 scores (physical function, physical role, emotional role, energy, mental health) were lower than those of males in both 2020 and 2021. However, social function was similar between the two groups in both 2020 and 2021. On the other hand, females were found to have lower bodily pain and

**Table 2.** Comparison of SARC-F, pain and SF-36 scores of patients between July 2020 (before) and June 2021 (after)

Variables	Before (median 25-75%)	After (median 25-75%)	p
<b>SARC-F score</b>	3 (1-5)	3 (1-5)	0.452
<b>Pain scores</b>	6 (2-8)	5 (3-8)	0.066
<b>SF-36 subgroups</b>			
Physical function	60 (35-80)	55 (35-75)	<b>&lt;0.001</b>
Role physical	50 (0-100)	50 (0-100)	<b>0.007</b>
Role emotional	33.3 (0-66.1)	33.3 (0-66.7)	0.208
Bodily pain	55 (32-88)	55 (32-77)	<b>0.011</b>
Energy	45 (27-60)	42.5 (25-60)	<b>&lt;0.001</b>
Mental health	60 (44-76)	60 (40-76)	<b>&lt;0.001</b>
General health	60 (45-70)	60 (45-70)	<b>0.006</b>
Social function	100 (50-100)	100 (50-100)	<b>0.001</b>

general health than males in 2020; after one year, these values were found to be significantly similar between females and males (Table 4).

Male patients had regular physical activity compared to female patients ( $p=0.003$ ). Many of the parameters did not change during the one-year pandemic in patients who had regular physical activity; only mental health ( $p=0.034$ ) and energy ( $p=0.025$ ) decreased. However, in patients who did not engage in regular physical activity, many of the parameters changed within one year; only SARC-F scores and emotional role did not change. Their pain ( $p=0.005$ ) scores increased, and all of the SF-36 parameters except emotional role (physical function:  $p<0.001$ , role physical:  $p=0.002$ , bodily pain:  $p=0.021$ , energy:  $p=0.003$ , mental health:  $p<0.001$ , general health:  $p<0.001$ , social function:  $p=0.007$ ) decreased. Comparison of patients according to physical activity showed that the patients who regularly engaged in physical activity had lower SARC-F scores and higher SF-36 scores in both 2020 and 2021. Furthermore, pain ( $p=0.001$ ) scores increased significantly more in patients who did not engage

in regular physical activity than in those who performed regular physical activity after one year of the pandemic (Table 5).

## DISCUSSION

Restrictions, travel bans, social isolation, and fear of infection during the COVID-19 pandemic have resulted in an extended home stay for the geriatric population. This study aimed to investigate the effect of the COVID-19 pandemic on the severity of pain, quality of life, and sarcopenia in geriatric patients. Therefore, other causes, such as cancer, infection, and surgery, which may also affect these situations within the past one year, were excluded from our study. Patients who were evaluated face-to-face for pain, sarcopenia, and quality of life in July 2020, were followed up with telephonic interviews in June 2021 as telehealth care became widely used because of the COVID-19 pandemic (13). Within one year, almost all quality-of-life parameters decreased; however, the severity of musculoskeletal pain and SARC-F scores did not change. The severity of pain, quality of life, and SARC-F scores were



**Table 3.** Comparison of age, physical activity levels, SARC-F, pain and SF-36 scores of both sarcopenia probable and no sarcopenia patients between July 2020 (before) and June 2021 (after)

Variables		Sarcopenia probable (median 25-75%) (n=35)	No sarcopenia (median 25-75%) (n=126)	p
Age (years)		70 (65-78)	67 (61.7-70)	<b>0.006</b>
Gender(female/male)n (%)		31(89%)/4(11%)	94(75%)/32(25%)	0.058
Regular physical activity n (%)		7 (20%)	53 (42%)	<b>0.017</b>
SARC-F Score	Before	5 (4-8)	2.5 (1-4)	<b>&lt;0.001</b>
	After	6 (4-7.25)	3 (1-4)	<b>&lt;0.001</b>
	p	0.545	0.638	
Pain scores	Before	8 (6-8)	5 (0-7)	<b>&lt;0.001</b>
	After	8 (5-9)	5 (2-8)	<b>&lt;0.001</b>
	p	0.578	0.083	
<b>SF-36 subgroups</b>				
Physical function	Before	30 (20-50)	70 (50-85)	<b>&lt;0.001</b>
	After	25 (15-40)	65 (45-80)	<b>&lt;0.001</b>
	p	<b>0.008</b>	<b>&lt;0.001</b>	
Physical role	Before	0 (0-50)	75 (25-100)	<b>&lt;0.001</b>
	After	0 (0-50)	75 (25-100)	<b>&lt;0.001</b>
	p	0.131	<b>0.024</b>	
Emotional role	Before	0 (0-33.3)	66.7 (33.3-100)	<b>&lt;0.001</b>
	After	0 (0-33.3)	66.7 (33-100)	<b>&lt;0.001</b>
	p	0.414	0.317	
Bodily pain	Before	32.5 (22.5-55)	67 (45-90)	<b>&lt;0.001</b>
	After	32.5 (10-55)	67 (45-78)	<b>&lt;0.001</b>
	p	0.218	<b>0.019</b>	
Energy	Before	25 (20-40)	50 (35-65)	<b>&lt;0.001</b>
	After	27.5 (15-40)	45 (30-65)	<b>&lt;0.001</b>
	p	0.333	<b>&lt;0.001</b>	
Mental health	Before	44 (32-60)	68 (52-80)	<b>&lt;0.001</b>
	After	46 (36-57)	64 (44-76)	<b>&lt;0.001</b>
	p	0.142	<b>&lt;0.001</b>	
General health	Before	40 (30-55)	65 (50-70)	<b>&lt;0.001</b>
	After	40 (28.7-60)	60 (50-70)	<b>&lt;0.001</b>
	p	<b>0.031</b>	<b>0.031</b>	
Social function	Before	62.5 (25-100)	100 (59-100)	<b>0.005</b>
	After	62.5 (34-100)	100 (50-100)	<b>0.013</b>
	p	0.157	<b>0.004</b>	

(SF-36: Short form-36)

**Table 4.** Comparison of age, SARC-F, pain and SF-36 scores of patients between July 2020 (before) and June 2021 (after) according to gender

Variables		Female (median 25-75%) (n=125)	Male (median 25-75%) (n=36)	P
Regular physical activity (%)		39 (31.2%)	21 (58.3%)	<b>0.003</b>
Age (years)		67 (64-71)	67.5 (62.5-73)	0.722
SARC-F Score	Before	4 (2-5)	1.5 (1-3.7)	<b>0.001</b>
	After	4 (2-5)	2 (1-4)	<b>0.004</b>
	P	0.725	0.325	
Pain scores	Before	6 (3-8)	4 (0-6.2)	<b>0.008</b>
	After	5 (3.5-8)	5 (0.5-7.7)	<b>0.037</b>
	P	0.240	0.086	
<b>SF-36 subgroups</b>				
Physical function	Before	55 (30-72)	80 (65-95)	<b>&lt;0.001</b>
	After	50 (30-70)	75 (55-90)	<b>&lt;0.001</b>
	p	<b>&lt;0.001</b>	<b>0.004</b>	
Physical role	Before	50 (0-100)	100 (56-100)	<b>0.001</b>
	After	50 (0-100)	87.5 (50-100)	<b>0.002</b>
	P	<b>0.019</b>	0.165	
Emotional role	Before	33.3 (0-66.7)	66.7 (8-100)	<b>0.016</b>
	After	33.3 (0-66.7)	66.7 (8-100)	<b>0.006</b>
	p	0.193	1.000	
Bodily pain	Before	55 (32.5-77.5)	67 (55-90)	<b>0.006</b>
	After	55 (32-77)	62 (45-90)	0.083
	P	0.061	0.054	
Energy	Before	40 (25-55)	57 (41-75)	<b>&lt;0.001</b>
	After	40 (21-55)	55 (45-72)	<b>&lt;0.001</b>
	p	<b>0.002</b>	<b>0.029</b>	
Mental health	Before	60 (40-74)	76 (56-80)	<b>0.005</b>
	After	56 (40-71)	72 (56-76)	<b>0.005</b>
	p	<b>&lt;0.001</b>	<b>0.028</b>	
General health	Before	60 (40-70)	62 (55-75)	<b>0.037</b>
	After	60 (40-70)	60 (50-73)	0.156
	p	<b>0.014</b>	0.210	
Social function	Before	100 (50-100)	100 (78-100)	0.129
	After	87.5 (50-100)	100 (53-100)	0.187
	P	<b>0.004</b>	0.144	

(SF-36: Short form-36)



**Table 5.** Comparison of age, SARC-F, pain and SF-36 scores of patients between July 2020 (before) and June 2021 (after) according to making regular physical activity or not.

Variables		Regular physical activity (median 25-75%) (n=60)	No regular physical activity (median 25-75%) (n=101)	P
Age (years)		67.5 (62.2-71)	67 (64-71)	0.564
Gender (female/male) (n)		39 / 21	86 / 15	<b>0.003</b>
SARC-F Score	Before	2 (1-4)	4 (2-5)	<b>0.003</b>
	After	2 (1-4)	4 (2-6)	<b>0.001</b>
	p	0.761	0.259	
Pain scores	Before	5 (0-8)	6 (4-8)	0.059
	After	4 (2-6)	6 (4-8)	<b>0.001</b>
	p	0.851	<b>0.005</b>	
<b>SF-36 subgroups</b>				
Physical function	Before	72.5 (50-85)	55 (30-70)	<b>0.001</b>
	After	70 (45-85)	50 (30-70)	<b>&lt;0.001</b>
	p	0.068	<b>&lt;0.001</b>	
Physical role	Before	100 (25-100)	50 (0-100)	<b>0.008</b>
	After	75 (25-100)	50 (0-75)	<b>0.001</b>
	p	0.668	<b>0.002</b>	
Emotional role	Before	66.7 (0-100)	33.3 (0-66.7)	<b>0.011</b>
	After	66.7 (33-100)	33.3 (0-66.7)	<b>0.001</b>
	p	0.752	0.051	
Bodily pain	Before	67.5 (45-90)	55 (32.5-77.5)	0.057
	After	67.5 (45-80)	55 (32-77)	0.061
	p	0.247	<b>0.021</b>	
Energy	Before	50 (36.2-70)	40 (25-55)	<b>&lt;0.001</b>
	After	50 (36-70)	35 (20-55)	<b>&lt;0.001</b>
	p	<b>0.025</b>	<b>0.003</b>	
Mental health	Before	68 (44-80)	60 (44-76)	0.137
	After	64 (44-76)	56 (40-72)	0.128
	p	<b>0.034</b>	<b>&lt;0.001</b>	
General health	Before	65 (50-75)	55 (40-67)	<b>0.017</b>
	After	65 (51-73)	55 (40-65)	<b>0.002</b>
	p	0.945	<b>&lt;0.001</b>	
Social function	Before	100 (78-100)	87.5 (50-100)	<b>0.013</b>
	After	100 (62-100)	75 (50-100)	<b>0.014</b>
	p	0.102	<b>0.007</b>	

(SF-36: Short form-36)

compared between female and male patients, patients with and without sarcopenia, and physically active and inactive patients.

Decreased physical activity, protein intake, sun exposure, increased sitting-screen time, stress, anxiety, and meal frequency have long-term adverse effects on muscle loss (4). To understand sarcopenic change, only the SARC-F score was used during the telephonic interview, and we could not perform grip strength and chair stand test measurements. The SARC-F scores were found to be similar between 2020 and 2021 in all study groups. A recent study in Japan reported that after the onset of the COVID-19 pandemic skeletal, muscle mass index had decreased in 56 geriatric diabetes patients compared to that before the pandemic with high mean follow-up duration (between the start and the end of the evaluation were 34 months) (8). The SARC-F is an inexpensive and practical method for evaluating sarcopenia in geriatric patients, with a sensitivity of 21% and specificity of 90% (14). It may not be appropriate to use SARC-F alone without objective measurements to evaluate annual changes in the geriatric population. We believe that there would have been a difference in our results if grip strength and chair stand test could be performed or the follow-up period was more than a year.

To the best of our knowledge, this is the first study to evaluate the effects of the COVID-19 pandemic on pain, SARC-F, and quality of life by comparing patients with and without sarcopenia according to the EWGSOP2 algorithm. Interestingly, in patients with sarcopenia, only general health and physical function decreased during the pandemic. Although all parameters were better in patients without sarcopenia in both 2020 and 2021, the pandemic affected patients without sarcopenia more than those with sarcopenia. Almost all quality of life parameters decreased more than those of patients with sarcopenia within one year. Patients with sarcopenia already have impaired physical function, mobility, social isolation, and reduced quality of

life (15). Impaired physical function and mobility result in reduced physical activity, as observed in our study. Therefore, their daily lives may not have been affected to a large extent because of the restrictions and social isolation during the pandemic.

This study did not investigate how physical activity levels change during the pandemic because previous studies have already reported worldwide reduction in levels of physical activity reduced during the COVID-19 pandemic (1). In Turkey, the rate of geriatric physical activity was previously reported to be 33% (16) during the COVID-19 pandemic, similar to the rate observed in our study (38%). These low rates are associated not only with the pandemic but also with the habits of Turkish people. Before the pandemic, Akturk et al. (17) reported the rate of physical activity in geriatric population to be 32%, which supports our findings. According to the WHO, at least 150 min of moderate-intensity physical activity or 75 min of vigorous-intensity physical activity per week is recommended (12). Investigating the factors related to the recommended physical activity level showed that only energy and mental health were affected by the pandemic in patients who engaged in regular physical activity. On the other hand, musculoskeletal pain severity increased, and almost all quality-of-life parameters decreased in physically inactive patients. In addition, SARC-F scores were lower in the physically active patients than in the inactive patients in both 2020 and 2021. This result showed that physical inactivity is related to increased pain, sarcopenia, and decreased quality of life, and it is important for the elderly population to gain and continue physical activity behaviours during a pandemic. In elderly individuals, walking programs have been shown to positively impact the quality of life (18). Web-based home exercise programs or outdoor walking programs should be implemented, which can be useful for both increasing motivation and physical activity.

The relationship between quality of life and physical activity in older people has been reported in a



systematic review (3). Physically inactive elderly individuals are at an increased risk of cardiovascular diseases, cancer, falls, disability, functional limitation, cognitive decline, and depression. Consequently, they experience a lower quality of life (19). However, in our study, energy and mental health were affected not only in physically inactive patients but also in physically active patients. The SF-36 mental health score was previously shown to be related to major depression in the elderly (20). Depressive symptoms were reported to be more prevalent compared to the pre-pandemic times (6). It has also been reported that both physical health and mental health of older people have been affected by the COVID-19 pandemic because of reduced physical activity, social isolation, and fear of COVID-19 infection (5).

The importance of physical activity in the management of pain has been highlighted in many studies (2), in which physical inactivity during the COVID-19 pandemic had a negative effect on pain severity among the elderly population. Similar to the findings of our study, but not in the elderly population, decreased physical activity during the pandemic was reported to be associated with pain augmentation in Japanese workers (9). Although pain severity in both male and female patients, as well as patients with and without sarcopenia, did not seem to be affected during the COVID-19 pandemic, the severity of pain was lower in women than in men and in patients with sarcopenia than in those without sarcopenia at both 2020 and 2021. Similar to our study, Zanin et al. reported a relationship between chronic pain and sarcopenia in 79 elderly women before the pandemic (21). Another study reported that women experience greater pain than men. Sex-based differences can be explained not only by hormonal differences and psychosocial factors, but also with sociodemographic factors (22).

Comparison of patients according to sex showed that not only pain severity but also SARC-F scores and quality of life in women was worse than in men in both 2020 and 2021. In addition, six of the eight

quality-of-life parameters were affected in women, while three of them affected men during the COVID-19 pandemic. This result is consistent with that of previous studies, and poor quality of life and sarcopenia are generally higher in women around the world (23). These results can be explained by the lower physical activity levels of women, as observed in the female patients in our study. Furthermore, the socioeconomic and sociodemographic differences may have influenced the results. In studies investigating the impact of the pandemic on both males and females, Japanese investigators found that suicide deaths occurred more frequently in females since the onset of the pandemic (24). Another study reported that women had more musculoskeletal symptoms than men during the pandemic (25).

The main limitation of our study was evaluation of sarcopenia during follow-up without including objective measurements. The rating of musculoskeletal pain was done face to face interview in 2020, however one year later by telephone, they might not be equivalent, this was also a limitation of our study. In this pandemic, the Turkish elderly could not get outside for months, the questions asked in this study may not be sufficient to clearly reveal the troubles of this period, this is also another limitation of our study. However, to the best of our knowledge, our study is the first to evaluate the COVID-19 pandemic on the severity of pain, SARC-F, and quality of life in older patients. The strength of our cohort study was reporting the one-year follow-up results of patients according to having sarcopenia/not, sex, and being physically active/inactive. Further studies are needed to investigate the effects of this pandemic on sarcopenia using objective measurements.

In conclusion, the following findings were observed after one-year follow-up of elderly patients during the COVID-19 pandemic: 1) their quality of life decreased; 2) patients without sarcopenia were affected more than those with sarcopenia in terms of decrease in quality of life; 3) females were affect-

ed more than males in terms of decrease in quality of life; 4) physically inactive patients were affected from this pandemic more than physically active patients in terms of not only decrease in quality of life, but also increase in the severity of pain; and 5) SARC-F scores did not change in any study group. This pandemic has and will continue to affect the quality of life and cause multiple lifestyle changes

among older adults. Therefore, improving quality of life and increasing physical activities of older people are both economic and public health imperatives.

### Conflict of Interest

All authors declare no conflict of interest.

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## RESEARCH

# EVALUATION OF THE FACTORS PROLONGING THE DISCHARGE HOME OF PATIENTS IN A PALLIATIVE CARE CENTER

## ABSTRACT

**Introduction:** The need for palliative care increases with advanced age and chronic diseases. We evaluated the factors that prolong discharge from palliative care center to improve the efficient use of existing palliative care beds.

**Materials and Methods:** This retrospective study included patients discharged from a palliative care center. The demographic and clinical features of the two groups, differentiated by length of stay, were compared.

**Results:** This study included 103 patients Group 1, n = 56, aged  $67.7 \pm 16.4$  years and Group 2, n = 47, aged  $67.6 \pm 14.1$  years. The length of stay in the center was  $12.4 \pm 4.8$  days for Group 1 and  $42.4 \pm 15.8$  days for Group 2. The number of patients with heart failure was higher in Group 2 than in Group 1 ( $p = 0.006$ ), and the number of patients receiving oral nutrition was higher in Group 1 ( $p = 0.031$ ). The gastrostomy status of Group 2 was higher than that of Group 1 ( $p = 0.035$ ). Grades 1 and 3-4 decubitus ulcers were more common in Group 1 than in Group 2 ( $p = 0.009$ ), and the lowest sodium levels were lower in Group 1 ( $p = 0.033$ ).

**Conclusion:** Anoxic brain injury as a referral diagnosis, presence of heart failure, and lower serum sodium levels were associated with a longer length of stay in palliative care center. It is important to determine the factors affecting long-term hospitalization and discharge so that more patients can benefit from inpatient palliative care services.

**Keywords:** Palliative Care; Length of Stay; Patient Discharge.



## INTRODUCTION

Palliative care (PC) is defined as an approach that improves the quality of life of patients and their families when facing life-threatening diseases (1). The need for PC is growing due to the increases in the elderly population and the prevalence of chronic life-threatening diseases (2). Determining the factors affecting the discharge of patients treated in a palliative care center (PCC) may contribute to the efficient use of existing PCC beds (3). The aim of this study was to evaluate the factors that prolong patients' discharge from a PCC.

## MATERIALS AND METHODS

### Ethical approval and study protocol

This study was approved by the Institutional Ethical Committee of our university-affiliated training and research hospital in Ankara, Turkey (December 28, 2020, number 101/08, Chairperson: Professor GS; Clinicaltrials.gov identifier: NCT04755374). Written informed consent was obtained from all patients or their relatives. All procedures were performed in accordance with the principles of the Declaration of Helsinki.

The records of patients referred to our university-affiliated training and research hospital's PCC between August 2018 and September 2020 and those who were discharged were evaluated retrospectively. Patients were excluded if their records were incomplete, they refused to participate in the study, they were transferred to intensive care, or they died.

### Data sources

The data were obtained from the hospital computerized database. The following data were recorded: age, gender, body mass index, length of stay (LOS) in the PCC, diagnosis (cancer, cerebrovascular disease, Alzheimer's disease/dementia, motor neurone disease, Parkinson's disease, chronic obstructive pulmonary disease [COPD], trauma, infec-

tion), a comorbid disease (hypertension, diabetes mellitus, heart failure, chronic kidney disease, epilepsy), performance assessed on the Karnofsky performance scale (KPS), clinical features (spontaneous breathing, tracheostomy, invasive home mechanical ventilation, oral nutrition, parenteral nutrition, gastrostomy, decubitus ulcers, mobilization), education status of the patient and their caregiver, lowest and highest hemoglobin values, serum sodium (Na) levels, and white blood cell counts. The KPS measures a patient's health status based on their self-care capacity, ability to carry out daily tasks, and general functioning for survival. The KPS comprises 11 classes, which progress from 0 (death) to 100 points (normal condition without any disease) (4). The patients discharged home were grouped according to their LOS in the PCC as Group 1 (discharged in less than or equal to 21 days) or Group 2 (discharged after more than 21 days) and analyzed accordingly (5).

### Data analysis

Statistical analyzes were performed using IBM SPSS for Windows Version 22.0 package program. Numerical variables are mean  $\pm$  standard deviation or median [25–75. percentile] values and categorical variables were summarized with numbers and percentages. Parametric test assumptions (normality and homogeneity of variances) were checked before comparing the groups in terms of numerical variables. Whether the numerical variables showed normal distribution was examined by Shapiro Wilks test. The homogeneity of the variances of the compared groups was examined using the Levene test. The difference between the two independent groups in terms of numerical variables was examined using the t test in the independent groups if the parametric test conditions were met and with the Mann Whitney U test if they were not. Comparison of more than two groups in terms of numerical variables was made with the Kruskal Wallis test. Whether there was a difference between the groups in terms of categorical variables was examined us-

ing the chi-square test or Fisher's exact test. The relationship between numerical variables was given by Spearman correlation coefficient. Multiple stepwise linear regression analysis was applied to determine the factors determining the length of hospital stay. A value of  $p < 0.05$  was accepted as statistically significant.

## RESULTS

During the 2-year study period, 197 patients were admitted to the PCC. Among them, 34 patients died, and 30 patients were transferred to intensive care unit; therefore, they were excluded from the study. Data from 103 patients (Group 1,  $n = 56$ ; Group 2,  $n = 47$ ) were included in the final analyses (Figure 1). All patients were referred from an intensive care unit. The LOS was  $12.4 \pm 4.8$  (4–21) days and  $41.4 \pm 15.8$  (22–90) days in Groups 1 and 2, respectively. The groups were comparable with respect to patient and caregiver characteristics, except for patient body mass index, which was higher in Group 2 (Table 1).

The frequencies of diagnoses and conditions of the patients are listed in Table 2. The number of patients with heart failure was significantly higher in Group 2 than in Group 1 (14 [25.0%] vs. 25 [53.2%];  $p = 0.006$ ). More patients in Group 1 received oral nutrition (27 [48.2%]) than in Group 2 (12 [25.5%],  $p = 0.031$ ), and the gastrostomy status of Group 2 patients (28 [50.0%]) was higher than that of Group 1 patients (34 [72.3%],  $p = 0.035$ ). Grades 1 and 3-4 decubitus ulcers were observed more frequently in Group 1 than in Group 2 (10 [17.9%] vs. 8 [17.0%] patients and 7 [12.5%] vs. 2 [4.3%] patients, respectively;  $p = 0.009$ ). There were no statistically significant differences in mobilization status ( $p = 0.057$ ) or Karnofsky performance scale scores ( $p = 0.254$ ) between the groups (Table 2). The lowest recorded Na level was significantly lower in Group 1 than Group 2 ( $133.8 \pm 4.95$  mmol/L vs  $135.8 \pm 4.5$  mmol/L;  $p = 0.033$ ) (Table 3).

Multiple logistic regression was used to model LOS and patient characteristics. Compatibility tests with chi-square and pseudo  $R^2$  tests were used to test the compatibility of the model and explain the

**Table 1.** Comparison of patients characteristics between groups

		Group 1 Discharged $\leq 21$ days (n=56)	Group 2 Prolonged discharge >21 days (n=47)	p value
Gender <sup>a</sup>	Female	26 (46.4)	20 (42.6)	0.845
	Male	30 (53.6)	27 (57.4)	
Age, ( years) <sup>b</sup>		$67.7 \pm 16.4$	$67.6 \pm 14.1$	0.971
BMI (kg/m <sup>2</sup> ) <sup>b</sup>		$25.4 \pm 3.3$	$26.8 \pm 3.0$	0.029 *
Education Status of the Patient, <sup>a</sup>	Illiterate	11 (19.6)	8 (17.0)	0.586
	Primary school	22 (39.3)	24 (51.1)	
	High school	19 (33.9)	11 (23.4)	
	University	4 (7.1)	4 (8.5)	
Education Status of the Patient's Care giver, <sup>a</sup>	Illiterate	1 (1.8)	3 (6.4)	0.103
	Primary school	14 (25.0)	15 (31.9)	
	High school	34 (60.7)	18 (38.3)	
	University	7 (12.5)	11 (23.4)	

<sup>a</sup> numbers (percentage), <sup>b</sup>mean  $\pm$  standard deviation, BMI: body mass index

\*Statistically significant p values are highlighted.



**Table 2.** Comparison of diagnose, co-morbid disease and the clinical features between groups

	<b>Group 1 Discharged ≤21 days (n=56)</b>	<b>Group 2 Prononged discharge &gt;21 days (n=47)</b>	<b>p value</b>	
Cancer, <sup>a</sup>	8 (14.3)	6 (12.8)	1.000	
Cerebrovascular disease, <sup>a</sup>	16 (28.6)	18 (38.3)	0.404	
Alzheimer's- Dementia, <sup>a</sup>	18 (32.1)	10 (21.3)	0.311	
Anoxic brain injury, <sup>a</sup>	3 (5.4)	6 ( 12.8)	0.294	
Motor neurone disease, <sup>a</sup>	1 (1.8)	1 (2.1)	NA	
Parkinson's disease , <sup>a</sup>	4 (7.1)	3 (6.4)	1.000	
COPD, <sup>a</sup>	10 (17.9)	2 (4.3)	0.067	
Trauma, <sup>a</sup>	7 (12.5)	6 (12.8)	1.000	
Infection, <sup>a</sup>	5 (8.9)	9 (19.1)	0.223	
Hypertension, <sup>a</sup>	35 (62.5)	31 (66.0)	0.874	
Diabetes mellitus, <sup>a</sup>	18 (32.1)	17 (36.2)	0.825	
Heart failure, <sup>a</sup>	14 (25.0)	25 (53.2)	0.006*	
Chronic kidney disease, <sup>a</sup>	4 (7.1)	5 (10.6)	0.729	
Epilepsy, <sup>a</sup>	13 (23.2)	11 (23.4)	1.000	
Number of patient having >1 co-morbidity, <sup>a</sup>	51(91.1)	43(91.5)	1.000	
Number of patient having > 3 co-morbidity, <sup>a</sup>	9(16.1)	12(25.5)	0.346	
Spontaneous breathing, <sup>a</sup>	47 (83.9)	32 (68.1)	0.097	
Spontaneous breathing with tracheostomy, <sup>a</sup>	7 (12.5)	13 (27.7)	0.092	
Invasive home mechanical ventilation, <sup>a</sup>	3 (5.4)	4 (8.5)	0.699	
Oral nutrition, <sup>a</sup>	27 (48.2)	12 (25.5)	0.031*	
Parenteral nutrition, <sup>a</sup>	1 (1.8)	1 (2.1)	NA	
Gastrostomy present, <sup>a</sup>	28 (50.0)	34 (72.3)	0.035*	
Decubitus ulcers, <sup>a</sup>	27 (48.2)	32 (68.1)	0.067	
	Grade 1	10 (17.9)	8 (17,0)	0.009*
	Grade 2	10 (17.9)	22 (46,8)	
	Grade 3-4	7 (12.5)	2 (4.3)	
Mobilization	20 (35.7)	8 (17.5)	0.057	
Karnofsky Performance Status, <sup>b</sup>	45 ± 8.5	43.6 ± 7.9	0.254	

<sup>a</sup> numbers (percentage), <sup>b</sup>mean ± standard deviation, COPD: chronic obstructive pulmonary disease, KPS: Karnofsky performance scale scores (0 to 100 points)

\*Statistically significant p values are highlighted.

**Table 3.** Comparison of laboratory variables between groups.

	Group 1 Discharged in ≤21 days (n=56)	Group 2 Prolonged discharge >21 days (n=47)	p value
Lowest hemoglobin (g/dL), <sup>a</sup>	10.22 ± 2.00	10.72 ± 1.98	0.211
Highest hemoglobin (g/dL), <sup>a</sup>	11.61 ± 2.01	12.27 ± 2.00	0.102
Lowest serum sodium (mmol/L), <sup>a</sup>	133.82 ± 4.95	135.87 ± 4.56	0.033*
Highest serum sodium (mmol/L), <sup>a</sup>	141.48 ± 6.23	142.26 ± 5.69	0.516
Lowest white blood cell (x10 <sup>3</sup> /μL), <sup>a</sup>	7.26 ± 2.08	7.91 ± 2.39	0.328
Highest white blood cell (x10 <sup>3</sup> /μL), <sup>a</sup>	13.71 ± 4.94	14.70 ± 5.24	0.148

<sup>a</sup> mean ± standard deviation

\*Statistically significant p values are highlighted.

**Table 4.** Multiple linear regression analysis of the factors affecting length of stay

	B (95% CI)	Beta	p
Heart failure	11.16 (4.37 – 17.95)	0.29	0.002
COPD	-14.96 (-25.24 - 4.69)	-0.26	0.005
Lowest recorded sodium level (mmol/L)	0.93 (0.25 – 1.61)	0.24	0.008
Anoxic brain injury	15.14 (3.42 – 26.86)	0.23	0.012

F=7.69 (p<0.001), R<sup>2</sup>=%23.9

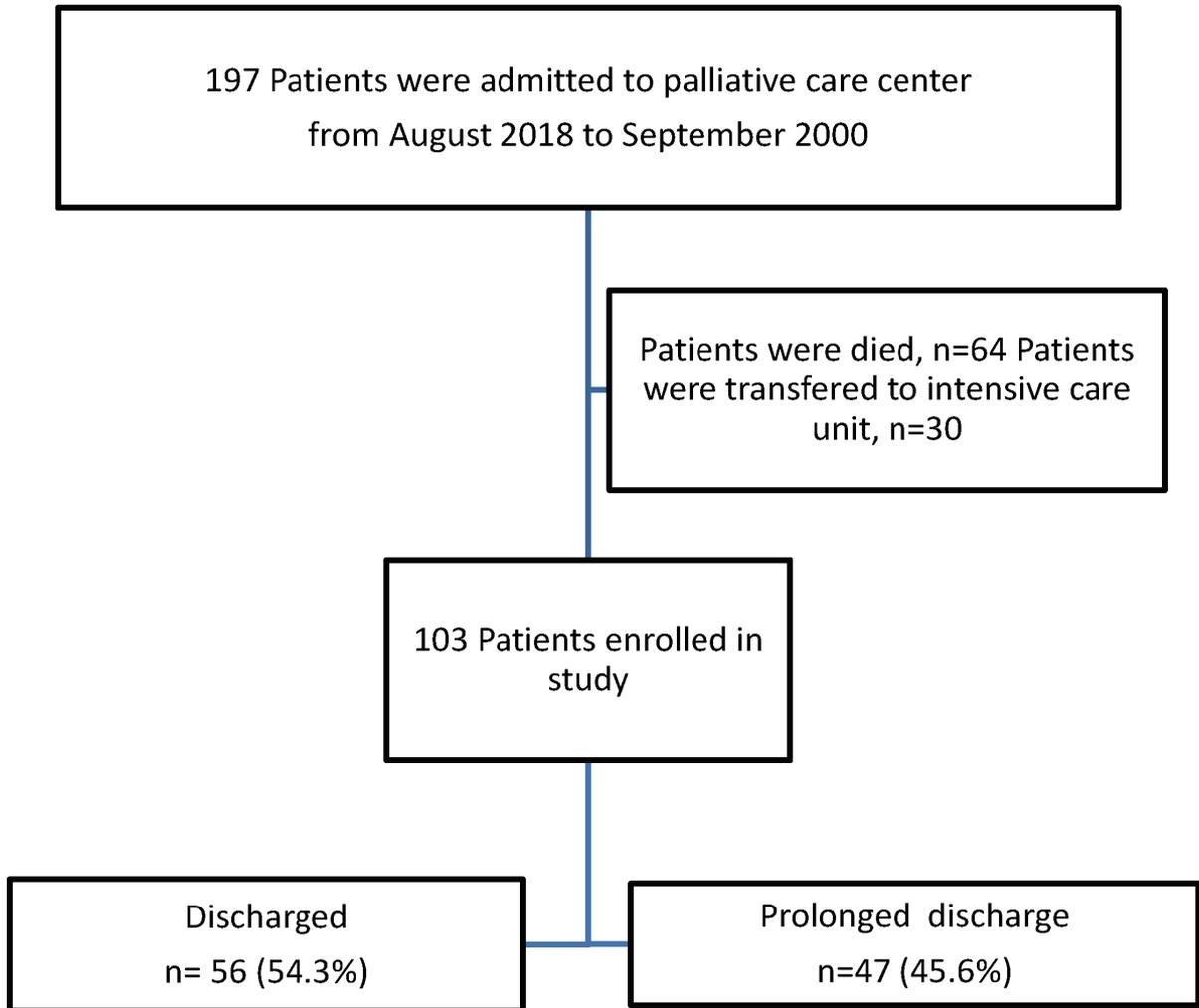
changes in the data. According to the Nagelkerke test result, the independent variables included in the model explained approximately 23.9% of the changes in LOS, which was the dependent variable. Utilizing a stepwise regression to identify the predictive factors for our regression model, we found that heart failure, the lowest Na level, and anoxic brain injury were associated with a significantly longer LOS, while a COPD diagnosis was associated with a significantly shorter LOS (Table 4). The analyses showed that a 1- mmol/L increase in serum Na levels caused a 0.93-day increase in LOS (F = 7.69, R<sup>2</sup> = 23.9, p = 0.008).

## DISCUSSION

It is important to determine the factors that affect long-term hospitalization and discharge so that more patients can benefit from inpatient PC services. In this study, we examined the LOS in the PCC at a training and research hospital in Turkey and identified the possible factors related to prolonged hospitalization. The results showed that presence of heart failure, anoxic brain injury as a referral diagnosis, and lower serum Na levels were associated with a significantly longer LOS, while a COPD diagnosis was associated with a significantly shorter LOS.



Figure 1. Flowchart of patient enrolment in the study



PC is provided for a variety of serious illnesses and conditions for patients across a wide range of ages with the aim of increasing quality of life by providing symptom control and decreasing suffering (1, 6). The capacity of PCCs and clinical experience in this field in Turkey is limited (3). Patients can be discharged home from PCCs when they are stable, symptom control is achieved, and family support is sufficient.

The diagnoses and clinical features of patients admitted to PCCs can affect their LOS (3). The patients in the current study had multiple chronic diseases, and the mean KPS scores showed that most of the patients required considerable assistance and were disabled with the need for special care and assistance. The majority of patients were admitted for diagnosis other than cancer. The most prevalent diagnoses were neurological disorders

followed by COPD, trauma-related conditions, and infections. The most common comorbid diseases were hypertension, diabetes mellitus, heart failure, and epilepsy. We did not document the differences in comorbid diseases between the groups given the number of such diseases, which suggests that it is not the number of comorbid diseases but the severity of the comorbidity that has an impact on LOS.

Anoxic brain injury is a medical condition with devastating consequences caused by prolonged hypoxia (7). In a study investigating the LOS in a PCC of patients with traumatic brain injury, the mean LOS was 34.0 days (8). Notably, the LOS in the PCC was significantly higher among patients with a gastrostomy who were immobile and not fed orally.

Anemia can contribute to the symptoms of PC patients (9). Infection and decubitus ulcers are factors that can affect PCC LOS (3), and urinary tract infections are common in PC patients (10). In a study reporting a mean  $27.2 \pm 30.9$  day stay in a PCC, advanced age, cancer, a diagnosis of hypoxic brain injury, the presence of hypertension, gastrostomy, parenteral nutrition, and infectious complications increased the LOS (3). In the patient group in our study, infection, anemia, and decubitus ulcers were not associated with a prolonged time to discharge.

Heart failure is more common with increasing age and is a worldwide public health problem (11). It is a complex clinical syndrome associated with various symptoms, including dyspnea, fatigue, peripheral edema, and depression. Heart failure is one of the factors that affect PCC LOS (12). One study concluded that care pathways for the treatment of heart failure decreased mortality rates and the length of hospital stay, but no differences were observed in the readmission rates and hospitalization costs (13). In our study, patients with heart failure had a longer time to discharge from the PCC.

Hyponatremia is defined as a sodium level  $< 135$  mmol/L (14). Hyponatremia management can improve the quality of life of patients with PC (15). Symptoms of hyponatremia may include nausea,

vomiting, headache, stupor, coma, seizures, fatigue, and cognitive impairment. Hyponatremia may be a contributing factor to the symptoms of PC patients (16) and is associated with increased mortality, prolonged hospital stay, and increased healthcare costs (17). Comorbid conditions may be the main cause of mortality in patients with severe hyponatremia (18). In a study investigating the incidence of hyponatremia in patients referred for PC, 61.1% of patients with a malignant disease and 39.9% of those with a non-malignant disease were found to have hyponatremia (15). In hospitalized cancer patients, hyponatremia may be the reason for long hospital stay (19). A study found a significant association between Na levels and length of hospitalization; for those discharged to their homes, the LOS was 16%–29% longer when the patients' Na levels were below 135 mmol/L (14).

In the present study, the absolute value of the "lowest Na level" in the prolonged discharge group (Group 2) was well within normal ranges; however, the fact that the LOS was higher in the patient group with the higher "lowest Na level" indicated that these patients needed to be hospitalized longer to correct their hyponatremia. Therefore, our interpretation of the results pertaining to the LOS–Na level relationship was that in patients with hyponatremia, a 1-mmol/L improvement in serum Na levels required a 0.93-day increase in LOS.

PC is difficult for patients with COPD because of its unpredictable disease course (20). In patients with COPD, PC is not limited to the terminal stage and can be provided at an early stage alongside curative care (21).

This study has several limitations. First, it was a retrospective study, and the number of included patients was small. Second, we did not include the patients' serum Na levels on admission in the analyses; therefore, we could not comment on this issue. Furthermore, patients' medications and simultaneous glucose levels during hyponatremia may have affected our results, but we did not include such



data in our analyses. Additionally, we did not stratify patients with COPD and heart failure according to disease severity, which may have affected our results.

It is important to determine the factors that affect long-term hospitalization and discharge so that more patients can benefit from inpatient PC services. A better understanding of the factors that may cause prolonged hospitalization in PC units and the ability to cope with these problems may

help shorten the length of hospitalization.

In conclusion, we demonstrated that anoxic brain injury as a referral diagnosis, the presence of heart failure, and serum Na levels were associated with a significantly longer LOS in the PCC, while a COPD diagnosis was associated with a significantly shorter LOS.

**Conflict of interest:** The authors declare no conflicts of interest.

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## RESEARCH

# MYOCARDIAL INJURY AFTER NONCARDIAC SURGERY IN GERIATRIC PATIENTS

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## ABSTRACT

**Background:** Myocardial injury after noncardiac surgery is an independent predictor of mortality in the postoperative period, and the risk is higher in geriatric patients than it is for other groups. However, this condition is thought to be underdiagnosed. To obtain a diagnosis, measuring high-sensitivity cardiac troponin is critical during postoperative monitoring. This study aimed to evaluate the presence of myocardial injury after noncardiac surgery occurring in geriatric patients during the perioperative period.

**Methods:** This study included 259 patients over 65 years of age. A peak high-sensitivity cardiac troponin value of  $\geq 0.03$  ng/mL was accepted as a diagnostic criterion for myocardial injury after noncardiac surgery. The patients were divided into two groups—those who were diagnosed with myocardial injury after noncardiac surgery (Group A) and those who were not (Group B). Incidence rates, 30-day mortality rates, hospital stay durations, levels of urgency, and comorbidities were compared between the two groups.

**Results:** The mortality rate in Group A (25%) was significantly higher than that in Group B (5.8%;  $p < 0.001$ ). In addition, the hospital stay duration was significantly longer in Group A. Finally, the rates of diabetes, coronary artery disease, and chronic renal failure were significantly higher in Group A.

**Conclusions:** The results of our study indicated that the mortality rate and hospital stay duration were significantly higher in geriatric patients with myocardial injury after noncardiac surgery. We think that high-sensitivity cardiac troponin values should be routinely monitored in the postoperative period in patients over 65 years of age for timely treatment of myocardial injury.

**Keywords:** Postoperative Complications; Troponin; Mortality; Geriatrics.

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## INTRODUCTION

After noncardiac surgery, major adverse cardiac events are leading causes of morbidity and mortality in patients (1). More than 200 million adults who undergo noncardiac surgery develop a myocardial injury each year, and this is estimated to result in 1 million deaths annually (2). Myocardial injury after noncardiac surgery (MINS) is a relatively new term for postoperative myocardial injury, and it is thought to be underdiagnosed.

Diagnosis of MINS is difficult because patients are unable to describe certain symptoms, such as angina pectoris and dyspnea, because of analgesia, sedation, and intubation, as well as because changes in electrocardiography (ECG) are nonspecific (1, 3-5). Therefore, assessing high-sensitivity cardiac troponin (hs-cTnT) is critical for detecting acute myocardial injury (6-11). MINS is diagnosed from postoperative hs-cTnT elevation in the presence or absence of clinical symptoms. It is seen in 8%–22% of adults who undergo noncardiac surgeries, and it is an independent predictor of 30-day and 1-year mortality (7,12). Previous studies have investigated the role of hs-cTnT in perioperative myocardial ischemic events and have demonstrated the prognostic function of postoperative hs-cTnT elevation (4, 13).

In a prospective study of more than 15,065 patients who underwent noncardiac surgery, the patients were screened within the first 3 days postoperatively for troponin elevation and ischemic symptoms. Although troponin elevation was observed in 8% of the patients, myocardial ischemic findings were detected in only half of this group (7). In a Perioperative Ischemic Evaluation (POISE) study, 5.0% of patients had a perioperative myocardial infarction, 65.3% of patients did not experience ischemic symptoms and the 30-day mortality rate was 11.6% (4).

Performing perioperative troponin follow-up can play a potentially critical role in improving patient outcomes (2). For this reason, routine monitoring

of cardiac troponin is recommended to identify patients at risk for early postoperative cardiovascular events (14). This new definition has been recommended as a guide for timely diagnosis and intervention (15). Although studies have investigated this topic, no specific study has paired the issue of MINS with geriatric patients. Moreover, geriatric patients have insufficient cardiovascular compensation and extra concomitant comorbidities compared with other patients. For these reasons, we examined myocardial damage in geriatric patients during the perioperative period. The primary outcome was a comparison of mortality rates in patients with MINS diagnoses. The secondary outcomes were troponin levels, hospital stay durations, operation durations, comorbidities and their associations with MINS, and the rates of MINS in emergency cases.

## METHODS

This study received ethical approval from the Clinical Research Ethics Committee of Bakırköy Dr. Sadi Konuk Education and Research Hospital (decision no. 2018/02/29). The study was retrospective, and no written consent was attempted. We included 259 American Society of Anesthesiologists (ASA) Score 1–3 patients older than 65 years of age who had undergone operations at the Bakırköy Dr. Sadi Konuk Education and Research Hospital between January 1, 2017, and January 1, 2018. Patient data, including troponin values, were reviewed and collected retrospectively from the hospital's electronic database and death notification system, and their demographic data and accompanying diseases were recorded. The records were assessed, checked, and verified. The type, duration, and urgency of the operation were noted. Between January 1, 2017, and January 1, 2018, 1,180 patients underwent surgery at the Bakırköy Dr. Sadi Konuk Education and Research Hospital. We excluded patients with ASA 4 status who had undergone intracranial and cardiovascular surgery and patients with incomplete data.

Because myocardial injuries typically occurred



within 3 days after the operation, hs-cTnT values were evaluated using the Elecsys 2010 Troponin T hs STAT test (Roche Diagnostics) for the first 3 days postoperatively. A peak hs-cTnT level of 0.03 ng/mL or higher was accepted as a diagnostic criterion for MINS.

The patients were divided into two groups—those diagnosed with MINS (Group A) and those who had no such diagnosis (Group B). The 30-day mortality rates, hospital stay durations, associations with comorbid diseases, and incidence rates of MINS in emergency cases were compared between the two groups.

### Statistical method

Data are presented as mean  $\pm$  standard deviation or median (range). The normality of distribution was measured with the Kolmogorov–Smirnov test. The Mann–Whitney U test was used to analyze the quantitative independent data, and the chi-square test or Fischer's exact test was used to analyze the qualitative independent data. SPSS v22.0 was used for all analyses.

### RESULTS

This study included 259 geriatric patients (116 [44.8%] women and 143 [55.2%] men). The mean patient age was  $74.12 \pm 7.3$  years. The mean age of the patients with MINS (Group A) was  $76.1 \pm 7.7$  years, whereas the mean age of the patients without a MINS diagnosis (Group B) was  $72.8 \pm 6.8$  years. Thus, the mean age of Group A was significantly higher ( $p < 0.05$ ). The demographic data of the patients participating in the study are shown in Table 1.

The highest troponin levels of the included patients in the first 3 days postoperatively were considered. Patients with hs-cTnT  $> 0.03$  ng/mL were diagnosed as having MINS.

The mortality rate in Group A (25%) was significantly higher than that in Group B (5.8%;  $p < 0.05$ ; Table 2). The mortality rates according to age distribution are presented in Table 2. In addition, the hs-cTnT values were significantly different between the groups (Table 3).

The hospital stay duration in Group A was significantly higher than that in Group B ( $p < 0.05$ ; Table 4).

**Table 1.** Summary of patients' demographic data

Mean $\pm$ SD n (%)		Group A	Group B	p
		Mean $\pm$ SD n (%)		
Age		$76.1 \pm 7.7$	$72.8 \pm 6.8$	<b>0.001<sup>a</sup></b>
Age groups (years)	65–74	49 (47.1%)	105 (67.7%)	<b>0.001<sup>b</sup></b>
	75–84	35 (33.7%)	39 (25.2%)	
	$\geq 85$	20 (19.2%)	11 (7.1%)	
Gender	Female	52 (50.0%)	64 (41.3%)	0.167 <sup>b</sup>
	Male	52 (50.0%)	91 (58.7%)	

<sup>a</sup>Mann–Whitney U test, <sup>b</sup>Chi-square test or Fischer's test

**Table 2.** Comparison of mortality rates between groups

Age (years)	Mortality	Group A		Group B		p
		n	%	n	%	
≥65	Deceased	26	25%	9	5.8%	<0.001
	Alive	78	75%	146	94.2 %	
65–74	Deceased	10	20.4%	5	4.8%	0.003
	Alive	39	79.5%	100	95.2%	
75–84	Deceased	10	28.6%	2	5.1%	0.007
	Alive	25	71.4%	37	94.9%	
≥85	Deceased	6	30.0%	2	18.2%	0.394
	Alive	14	70.0%	9	81.8%	

**Table 3.** Comparison of troponin values between groups

		Deceased	Alive	p
		Mean ± SD	Mean ± SD	
Troponin value	Group A	0.282 ± 0.502	0.153 ± 0.254	<0.001
	Group B	0.020 ± 0.008	0.012 ± 0.008	

The p-values were measured using the Chi-square test or Fischer's test.

**Table 4.** Comparison of length of hospital stay and operation duration between groups

	Group A			Group B			p
	Mean	SD	Median	Mean	SD	Median	
Length of hospital stay (days)	14.6	14.3	8.5	9.7	10	6.0	0.025
Duration of the operation (min)	135	85.2	110.0	183.8	111.3	150.0	0.001

The p-values were measured using the Mann–Whitney U test.



Moreover, the incidence rates of MINS were similar between the patients undergoing emergency surgery (10.6%) and those undergoing elective surgery (5.8%). Longer operation times did not increase the risk of MINS (Table 4). Rates of diabetes, coronary artery disease, and chronic renal failure were significantly higher in Group A patients ( $p < 0.05$ ; Table 5).

## DISCUSSION

Different mechanisms have been suggested for the development of MINS, including surgical stress, catecholamine release, and inflammatory reactions in the perioperative period (16). The physiological response to surgical stress, which lasts up to a few days after surgery, increases oxygen consumption; moreover, hypotension, anemia, hypoxia, and hypovolemia are common in the perioperative period, and these conditions reduce oxygen delivery. The imbalance between myocardial supply and oxygen demand can lead to MINS (3).

One study demonstrated that chronic catecholamine stimulation aggravates myocardial damage by provoking an inflammatory reaction and increasing

myocardial apoptosis (17). If cardiac cellular damage is caused by trauma, ischemia, or any other factor, the cell becomes hyperactive, and intracellular contents spill into the extracellular space and the bloodstream. If the myocyte damage is sufficiently large, these compounds can be detected using biochemical assays. Detection of troponin in the plasma indicates heart injury. Thus, with hs-cTnT level monitoring, myocardial ischemia can be detected without myocardial necrosis; the value increases in proportion to the level of ischemia, appears rapidly in circulation after the onset of ischemia, and remains long enough for detection. It can be easily measured with high sensitivity and reasonable specificity (16).

In a study of 1,087 critically ill patients, 17.3% were diagnosed with MINS. The hs-cTnT levels increased in 59.0% of MINS-diagnosed patients immediately after surgery, 71.8% after 24 h, and 24.5% after 48 h. The authors suggested that the troponin level should be monitored for the first 48 h postoperatively (15). In our research, the highest troponin values seen in the first 72 h were obtained.

**Table 5.** Comparison of comorbidities according to group

	Group A		Group B		P
	n	%	n	%	
Hypertension	24	23,1	26	16.8%	0.208
Diabetes	19	18.3%	10	6.5%	0.003
Coronary artery disease	25	24%	15	9.7%	0.002
Arrhythmia	25	24%	23	14.8%	0.062
Chronic kidney failure	23	22,1%	10	6,5%	<0.001
Cerebrovascular disease	0	0.0%	1	0.6%	1.000
Respiratory system Diseases	24	23.1	26	16.8%	0.217

The p-values were measured using the chi-square test or Fischer's test.

In one study, the mortality rate was 16.9% among patients with peak TnT  $\geq$  0.30 mg/L (18). Van Waes et al. (12) prospectively screened 3,224 patients aged  $\geq$  60 years who underwent noncardiac surgery; postoperative myocardial injury was detected in 715 patients (22%). In our study, the incidence of MINS increased with age in geriatric patients.

Inhibition of platelet function or perioperative suppression of sympathetic effects of the compensatory expansion of surgery has not been found to be beneficial in many clinical trials (19).

One study reported that myocardial injury developed in one of seven patients over 65 years of age who had coronary artery disease, peripheral arterial disease, or stroke (20). In our study, older age and accompanying diseases, such as coronary artery disease, increased the risk of MINS.

In a prospective multicenter study including 3,387 patients undergoing noncardiac surgery, Sabat  et al. (21) found that chronic renal failure was associated with major cardiac and cerebrovascular events. We also observed chronic renal failure more frequently in patients with MINS.

Few studies have evaluated the relationship between operation duration and MINS. Bae et al. (22) reported that the duration of surgery was associated with MINS. In contrast, our data indicated that the operation duration did not increase with the development of MINS; in fact, MINS was more commonly noted in operations of shorter durations.

Studies have demonstrated that emergency operations are independent risk factors for MINS. In these operations, there is not enough preoperative evaluation or preparation because of their urgent nature, intraoperative hypotension and arrhythmia are more common, and blood transfusions are more frequently needed (15). However, the incidence of MINS in our study was similar in emergency and elective cases.

MINS is a frequent complication after noncardiac surgery; it is found early in routine clinical screening, and it has been shown to be associated with short- and long-term mortality (4, 5, 7, 23). In our study, mortality and morbidity rates were significantly higher in patients over 65 years of age who were diagnosed with MINS compared with those who were not diagnosed with MINS. MINS was more common in patients with accompanying diabetes, coronary artery disease, and chronic renal failure.

Many studies have investigated the role of cardiac troponins in diagnosing perioperative myocardial ischemic events and shown the prognostic value of postoperative cardiac troponin elevation (4, 23). Different studies used different values, such as 0.1 ng/mL (5, 23) or 0.14 mg/L (20), to diagnose MINS. As a result, we think that hs-cTnT values should be routinely monitored postoperatively in patients over 65 years of age for early diagnosis and timely treatment. However, additional prospective studies are required on this topic.

### **Limitations of the study**

There are some limitations associated with this study that should be mentioned. The study was retrospective, involved a single center study, and only included patients whose hs-cTnT values were available in the medical records. Prospective studies with a large number of patients and different surgical groups will overcome these limitations, providing clearer information on the topic.

**Conflicts of Interest:** The authors declare no conflicts of interest.

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**Running Head:** MINS in Geriatric Patients



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## RESEARCH

# DO SHOCK INDEX, MODIFIED SHOCK INDEX, AND SHOCK INDEX BY AGE HAVE A PREDICTIVE VALUE IN DETERMINING THE RISK OF POST-SPINAL HYPOTENSION IN ELDERLY PATIENTS?

## ABSTRACT

**Introduction:** Intraoperative hypotension in the elderly, is associated with an increased risk of complications. Predicting intraoperative hypotension will help patients have better outcomes by providing early prevention and intervention. We investigated the predictive value of the shock index, modified shock index, and shock index by age to determine the risk of hypotension in elderly patients undergoing spinal anesthesia in minor elective surgeries.

**Materials and Methods:** Our prospective observational study included 128 patients aged  $\geq 65$  with ASA classifications of I-III undergoing minor elective surgeries under spinal anesthesia lasting  $< 120$  minutes. The patients' preoperative shock index, modified shock index, and shock index by age values were calculated and recorded. Hypotension was defined as mean arterial pressure  $\leq 65$  mmHg on two consecutive measurements or  $< 25\%$  of the baseline value. Hypotensive and normotensive patients' preoperative shock index, modified shock index, and shock index by age values, as well as whether they were admitted to the post-anesthesia care unit, discharge time, and complication rates, were all compared.

**Results:** The incidence of intraoperative hypotension was 50% (n = 64). The modified shock index has predictive value for predicting hypotension (cut-off point of  $< 0.73$ ). Being female increased the risk of hypotension by 20.047 fold, and a 1-point increase in Charlson Comorbidity Index scores increased the risk of hypotension by 2.058 fold.

**Conclusion:** The modified shock index arrived at by dividing heart rate by mean arterial pressure, can be used to predict hypotension due to spinal anesthesia in elderly patients.

**Keywords:** Anesthesia, Spinal; Geriatrics; Hypotension.

## INTRODUCTION

The vascular stiffening observed in the cardiac physiology, autonomic changes, and an increase in the incidence of systolic and diastolic dysfunction make the elderly susceptible to hypotension after anesthesia (1-3). Therefore, the most common intraoperative complication in the elderly is hypotension (4).

It has been shown that an intraoperative decrease of mean arterial pressure (MAP) to <80 mmHg for >10 minutes can disrupt tissue perfusion and cause organ damage (3). Even short-term systolic or MAP drops during noncardiac surgery may result in major cardiac and renal complications (5, 6). The use of preoperative fluid boluses (preloading) in minor surgeries has been shown to improve hemodynamic stability (7). While preoperative dehydration is a preventable factor, preloading therapy is risky and not recommended in elderly patients, due to the high prevalence of cardiac, respiratory, and renal comorbidities (8).

The shock index (SI) is a straightforward equation obtained by dividing the heart rate (HR) by systolic blood pressure. The shock index has a standard range from 0.5 to 0.7. It increases in cases of acute hypovolemia and left ventricular dysfunction, and it aids in the early diagnosis of shock (9). The modified shock index (MSI) is a value arrived at by dividing HR by MAP. It indicates organ perfusion status better than systolic blood pressure (SBP) because it includes the diastolic blood pressure parameter when calculating MAP. The normal value of MSI is between 0.7 and 1.3 (10, 11). Because age has a negative impact on physiological reserve, a shock index by age (SIA) has been created for the elderly, and it is found by multiplying age and SI. If the SIA value is greater than 50, particularly in patients over 55, life-threatening shock may be observed. Additionally, SI, MSI, and SIA are parameters that can be easily measured without the use of any special equipment in the estimation of mortality and morbidity (12-15). Pre-intubation SI, MSI, and SIA values

have been shown to be independent predictors of post-intubation hypotension in studies evaluating SI, MSI, and SIA to predict post-intubation hypotension (15, 16).

Hypovolemia and hypovolemic shock cannot be diagnosed solely based on heart rate or blood pressure parameters. Thus, the shock index should be investigated to determine whether it can be used as a clinical indicator of mortality (14, 17, 18).

Predicting intraoperative hypotension, taking early precautions, and intervening can also be beneficial in the elderly population. Our primary goal in this study is to determine whether SI, MSI, and SIA, as non-invasive parameters that can be measured using only heart rate and blood pressure parameters at the bedside, can predict post-spinal hypotension in patients over 65 years old undergoing elective transurethral interventions.

Our secondary goal is to investigate whether intraoperative hypotension has any adverse effects by comparing pre-operative and post-operative blood tests, as well as whether the post-anesthesia care unit (PACU) was visited, the duration of hospital stay, and postoperative complications.

## MATERIALS AND METHODS

This study began after the approval of the Turkish Ministry of Health, Ankara City Hospital, No. 1 Clinical Research Ethics Committee Presidency (approval number E1-20-787 dated 25/06/20). Clinical trial number (NCT04483765) was obtained. Our study is a prospective, observational study and was conducted in Ankara City Hospital between 01/07/2020 and 01/11/2020. Informed consent was obtained from all patients.

The study involved 128 patients  $\geq 65$  years old who had American Society of Anesthesiologists (ASA) risk scores of I-III, undergone elective transurethral bladder (TUR-B) and prostate resections (TUR-P) under spinal anaesthesia, and surgery times  $\leq 120$  minutes. The existence of valvular disease and



arrhythmia that impaired hemodynamics (for example, high ventricular fast atrial fibrillation), severe heart failure, mental/motor problems that made communicating difficult, neuropsychiatric disease in the patient, and the patient's refusal to participate in the study were accepted as exclusion criteria.

Patients' ages, heights, body weights, body mass indices (BMIs), genders, Charlson Comorbidity Index (CCI) values according to their systemic diseases, pre-operative fasting times, pre-operative HRs, non-invasive SBPs, diastolic blood pressures (DBPs), MAP values, and peripheral oxygen saturation (SpO<sub>2</sub>s) values were recorded. The patients' preoperative SI, MSI, and SIA values were calculated and recorded.

Blood urea nitrogen (BUN), creatine, glomerular filtration rate (GFR), aspartate aminotransferase (AST), alanine aminotransferase (ALT), hemoglobin (Hgb), hematocrit (Htc), and white blood cell count (WBC) values were recorded from the blood tests performed during the pre-operative and post-operative periods. The type of operation that patients were to undergo, operation time, and HR, SBP, DBP, MAP, and SpO<sub>2</sub> values were recorded every 5 minutes in the first 30 minutes of the operation, every 10 minutes after the operation, and every 15 minutes after the 60th post-operative minute. Furthermore, the needle thickness used in spinal anesthesia, the amount of dermatome used for spinal anesthesia, the local anesthetics and doses used for spinal anesthesia, and the sedative drugs applied to the patient and their doses were all recorded.

The amount of total crystalloid/colloid fluid applied intravenously (i.v.) during the intraoperative period and the amount (L) and type of irrigation fluid used during the TUR operation were recorded.

For the first 15 minutes after spinal anesthesia, the sensory block level was determined by applying cold to the patient's skin with an ice tray once per minute. By comparing the patient's shoulder to the dermatome areas of the abdominal skin, where the block was tested, the block level was evaluated

based on the patient's verbal responses. The time elapsed from the moment of spinal anesthesia to the detection of the sensory block was recorded as the onset of sensory block. The patient's sensory block level was recorded as the level of the sensory block that remained constant over three measurements.

Motor block was assessed using the Bromage Scale every 5 minutes. The time elapsed from the moment of spinal anesthesia to the detection of motor block was recorded as the onset of motor block. The evaluation that remained constant three times in a row was recorded as the degree of motor block.

The patient's admissions to the service or PACU, hospitalization times (discharge time), and whether or not there were any postoperative complications were all reported during the postoperative period.

Patients were accepted as hypotensive when two consecutive MAP measurements were  $\leq 65$  mmHg or when MAP was  $< 25\%$  (improved or not improved with intervention) of the baseline value. Normotensive patients were labeled as Group N, whereas hypotensive patients were labeled as Group H. Demographic characteristics (age, gender, and comorbidities) were also compared between these groups.

### Statistical Analysis

The descriptive statistics for the continuous data have been presented as mean, standard deviation, median, minimum, and maximum values, whereas the discrete data have been presented in percentages. The Kolmogorov-Smirnov test was used to assess the data's conformity to a normal distribution. The t-test was used to compare continuous data with a normal distribution in hypotensive and non-hypotensive patients, and the Mann-Whitney U test was used to compare non-normally distributed data. In group comparisons of nominal variables (cross tables), the Chi-Square and Fisher's Exact tests were used. The risk factors affecting the

development of hypotension were investigated using multivariate logistic regression analysis. For the evaluations, the IBM SPSS Statistics 20 program was used, and the statistical significance limit was accepted at  $p < 0.05$ .

### Sample Size

Lee et al. found that the rate of hypotension after intubation was 29% in a study that evaluated the use of SI, MSI, and SIA in hypotension prediction after intubation (15). At a  $d=0.12$  effect size, 80% power, and  $\alpha=0.05$  error level, 127 patients should be recruited into our analysis, assuming that the rate of hypotension in patients may be 10 percentage different. The calculation was performed using the G\*Power 3.1.9.4 statistical package program.

## RESULTS

When patients were accepted as hypotensive when two consecutive MAP measurements made at any time from spinal anesthesia until the end of surgery with  $\leq 65$  mmHg or when MAP was  $< 25\%$  of the preoperative baseline value,  $n=64$  (50%) of patients were found to have developed hypotension.

When the demographic characteristics of Group H and Group N were compared, it was discovered that the patients in Group H had a higher mean ages ( $p < 0.05$ ), shorter average height ( $p < 0.01$ ), higher mean CCI scores ( $p < 0.05$ ), and higher ratio of ASA scores that were 3 (Table 1,  $p < 0.01$ ). Group H had a slightly higher female gender ratio than Group N ( $p < 0.01$ ). Body weight, BMI values, surgery form and length, and fasting periods were identical in Group H and Group N ( $p > 0.05$ ).

Group H and Group N had identical preoperative BUN, creatine, GFR, ALT, Hgb, Htc, WBC, and  $SpO_2$  values ( $p > 0.05$ ), while AST values were higher in Group H (Table 1,  $p < 0.05$ ).

When the applied level of intervertebral space rates of Group H and Group N were compared, Group H had a higher application rate at the L3-L4 level than Group N ( $n = 34, 53.1\%$ ,  $n = 15, 23.4\%$ ,  $p < 0.001$ , respectively), and the rate at the L5-S1 level was lower in Group H ( $n = 2, 3.1\%$ ,  $n = 22, 34.4\%$ ,  $p < 0.001$ , respectively).

The spinal needle thickness (Gauge) used in Groups N and H was no different ( $p > 0.05$ ). The

**Table 1.** Comparison of Demographic Characteristics, Preoperative Laboratory Parameters of Normotensive Patients (Group N) and Hypotensive Patients (Group H)

	Group N	Group H	Test Statistics	p
	Mean±SD Median (Min-Max)	Mean±SD Median (Min-Max)		
Age (years)	72.09±5.89 70 (65-88)	75.20±6.97 76 (65-89)	U=1526.5	<b>0.013</b>
Body Weight (kg)	75.61±13.99 73 (44-108)	76.28±13.71 75.5 (50-107)	t=-0.274	0.784
Height (cm)	172.06±7.70 172 (150-192)	168.22±7.97 169 (150-182)	t=2.773	<b>0.006</b>
BMI (kg/m <sup>2</sup> )	25.48±4.14 24.78 (15.22-40)	26.87±3.94 26.85 (18.73-35.36)	t=-1.944	0.054
Surgery time (minutes)	51.56±24.20 50 (20-120)	45.86±19.79 42.5 (20-115)	U=1771.0	0.184

DO SHOCK INDEX, MODIFIED SHOCK INDEX, AND SHOCK INDEX BY AGE HAVE A PREDICTIVE VALUE IN DETERMINING THE RISK OF POST-SPINAL HYPOTENSION IN ELDERLY PATIENTS?



Fasting time (hours)	10.81±2.06 10 (8-16)	11.02±1.92 10.5 (8-16)	U=1929.0	0.560
Charlson Index	1.5 (0-6)	2 (0-6)	U=1585.5	<b>0.023</b>
BUN (mg/dL)	47.72±22.26 44.5 (0.40-155)	43.98±17.19 42.5 (19-117)	U=1767.0	0.289
Creatinine (mg/dL)	1.08±0.52 0.93 (0.45-3.57)	1.06±0.33 0.98 (0.42-2.0)	U=1896.0	0.469
GFR (ml/min)	74.33±20.62 80 (16-113)	69.73±21.78 75 (30-129)	U=1723.5	0.122
AST (U/L)	19.90±12.79 17 (7-83)	21.57±9.04 20.5 (8-58)	U=1400.5	<b>0.026</b>
ALT (U/L)	20.86±12.22 19 (6-77)	22.37±13.07 19 (5-74)	U=1591.5	0.619
Hgb (g/dL)	13.18±2.03 13.15 (8.7-18.2)	13.00±2.16 13.2 (7-19.1)	t=0.497	0.620
Htc (%)	40.23±7.23 41.1 (3-56)	40.12±6.12 41.3 (21.6-56.3)	U=1992.0	0.790
WBC (μL/ml)	7.78±2.23 7.32 (4.51-17.31)	7.55±2.62 6.94 (2.15-17.61)	U=1868.0	0.391
SpO <sub>2</sub> (%)	95.17±2.05 95 (90-100)	94.73±1.93 95 (90-98)	U=1802.5	0.236
	n (%)	n (%)	Test Statistics	p
Gender				
Female	2 (3.1)	11 (17.2)	$\chi^2 = 6.935$	<b>0.008</b>
Male	62 (96.9)	53 (82.8)		
Type of surgery				
TUR-P	30 (46.9)	22 (34.4)	$\chi^2 = 2.073$	0.150
TUR-B	34 (53.1)	42 (65.6)		
ASA				
I	2 (3.1)	1 (1.6)	$\chi^2 = 13.147$	<b>0.001</b>
II	47 (73.4)	28 (43.8)		
III	15 (23.4)	35 (54.7)		

BMI; Body mass index, BUN; Blood urea nitrogen, GFR; Glomerular filtration rate; AST; Aspartate aminotransferase, ALT; Alanine aminotransferase, Hgb; Hemoglobin, Htc; Hematocrit, WBC; White blood cell, SpO<sub>2</sub>; Peripheral oxygen saturation, TUR-B; Transurethral resection of the bladder, TUR-P; Transurethral resection of the prostate, ASA; American Society of Anesthesiologists

rate of hypotension was higher in patients treated with 15 mg bupivacaine and lower in patients treated with 12.5 mg bupivacaine ( $p < 0.05$ ). In patients receiving i.v. midazolam for sedation, the rate of hypotension seen in those treated with 2 mg of midazolam was higher than those treated with 1 mg ( $p < 0.05$ ). The rate of hypotension was higher in patients whose block level was up to T8, and the rate of hypotension was lower in patients with sensory block levels of T10 and below ( $p < 0.01$ ) (Table 2).

Group H had slightly lower MSI values than Group N ( $p < 0.05$ ), while the SI and SIA values were identical between the groups (Table 3,  $p > 0.05$ ).

Though SI and SIA's success in separating hypotension was not significant ( $p > 0.05$ ), MSI's performance was significant ( $p < 0.05$ ), and the best cut-off point was 0.73 (Table 4).

The female gender raises the risk of developing hypotension 20.047 fold, a CCI scores increase of 1 point increases risk 2.058 fold, an application zone

**Table 2.** Comparison of Spinal Needle Thickness, Intrathecal Bupivacaine Dosage, Intravenous Midazolam and Fentanyl Dosages, and Spinal Anesthesia Sensory Block Levels of Normotensive Patients (Group N) and Hypotensive Patients (Group H)

	Group N		Group H		Test statistics	p
	n	%	N	%		
Spinal needle thickness						
25G	44	68.6	50	78.1	$\chi^2 = 2.350$	0.309
26G	16	25	13	20.3		
27G	4	6.2	1	1.6		
Bupivacaine dosage						
12.5 mg	41	64.1	29	45.3	$\chi^2 = 5.441$	<b>0.046</b>
15 mg	23	35.9	33	51.6		
12.5 +10 mcg fentanyl	0	0	2	3.1		
Midazolam dosage						
1 mg	37	90.2	32	72.7	$\chi^2 = 4.262$	<b>0.039</b>
2 mg	4	9.8	12	27.3		
Fentanyl dosage						
50 mcg	8	88.9	12	85	Comparison could not be made due to low number	
75 mcg	1	11.1	0	0		
100 mcg	0	0	2	14.3		
Sensory block level						
T6	0	0	4	6.2	$\chi^2 = 13.815$	<b>0.002</b>
T8	10	15.6	24	37.5		
T10	47	73.4	33	51.6		
T12	7	10.9	3	4.7		



**Table 3.** Comparison of Preoperative Shock Index, Modified Shock Index and Shock Index by Age Values of Normotensive Patients (Group N) and Hypotensive Patients (Group H)

Preoperative	Group N	Group H	Test Statistics	p
	Mean ± SD Median (Min-Max)	Mean ± SD Median (Min-Max)		
Shock Index (SI)	0.55±0.10 0.55 (0.39–1.02)	0.52±0.12 0.51 (0.31–0.81)	U=1730.0	0.129
Modified Shock Index (MSI)	0.78±0.13 0.78 (0.54–1.31)	0.73±0.17 0.71 (0.34–1.25)	U=1616.0	<b>0.039</b>
Shock index by Age (SIA)	40.28±8.34 39.38 (28.12–70.97)	39.20±8.44 40.11 (21.20–55.33)	U=2037.0	0.958

**Table 4.** Performance of Shock Index, Modified Shock Index, and Shock Index by Age Values in Distinguishing Between Hypotensive and Normotensive Patients\*

	AUC	95% CI	p	Threshold
Shock Index (SI)	0.578	0.478–0.677	0.130	-
Modified Shock Index (MSI)	0.605	0.507–0.704	0.040	<b>≤0.73</b>
Shock index by Age (SIA)	0.503	0.402–0.604	0.958	-

\*The power of Shock Index, Modified Shock Index, and Shock Index by Age values in discriminating between being hypotensive vs normotensive was evaluated via the area under the ROC curve (AUC). The best cut-off point was calculated using the Youden's Index.

level of L3-L4 increases risk by 199.594 fold as compared to L5-S1, and L4-L5 increases risk by 80.206 fold as compared to L5-S1 according to the logistic model developed with variables that influence the development of hypotension (Table 5).

In Group N, 9.4% of the patients (n = 6) and 20.3% of the patients in Group H (n = 13) were hospitalized in the PACU (p = 0.082). In terms of discharge time, there was no substantial difference between Groups N and H (3.55±5.34 and 4.59±6.48 respectively; p = 0.314).

The amount of intraoperative i.v. crystalloid administered and the amount of bladder irrigation fluids (mannitol, crystalloid) used did not vary be-

tween the groups, and no patients developed TUR syndrome (p = 0.810, p = 0.579 and p = 0.845, respectively).

Regarding preoperative patients with MSI values greater than or less than 0.73, there were no differences in PACU admission (n = 10, 15.3% and n = 9 14.5%, p = 0.920, respectively) or postoperative complication rates (n = 5, 7.6% and n = 2, 3.2%, p = 0.279, respectively). Acute renal dysfunction was observed in four patients in the postoperative period in the MSI>0.73 group; dyspnea and short-term desaturation were seen in two patients, and bladder perforation was seen in one patient in the MSI≤0.73 group.

**Table 5.** Outcome of Logistic Regression Model for Risk Factors Affecting Development of Hypotension

Variable	Regression Coefficient (SE)	OR	95% CI		p
Gender (Female)	2.998 (1.321)	20.047	1.506	266.917	0.023
Charlson Index	0.722 (0.209)	2.058	1.367	3.097	0.001
Level Application					0.000
L3-L4	5.296 (1.301)	199.594	15.578	2557.374	0.000
L4-L5	4.385 (1.273)	80.206	6.621	971.625	0.001

*\*In examining the risk factors affecting the development of hypotension, the independent variables found to be significant in the univariate analysis were included in the Multivariate Logistic regression analysis, and the result was a multivariate logistic regression model that included the **Backward LR** method.*

## DISCUSSION

This study found the incidence of postspinal hypotension after spinal anesthesia to be 50%, in patients over 65 years of age who underwent TUR-B and TUR-P surgery under spinal anesthesia. In the adult population, the incidence of hypotension after spinal anesthesia varies from 15% to 30% according to the literature (19). The differences in incidence are due to differences in the definition of hypotension used by the studies, as well as variations in the baseline threshold (20). Furthermore, the risk of hypotension increases with age, although the incidence differs depending on factors such as the type and dosage of local anesthetic used, the patients' comorbidities and anthropometric characteristics, and the level of spinal anesthesia (5). The ages of hypotensive patients were found to be higher than those of non-hypotensive patients in our study. Hypotensive patients were shorter in height, and their CCI and ASA scores were higher than those who were non-hypotensive. Patients with spinal application levels of L3-L4 and female gender were found to have higher levels of hypotension.

Most studies investigating hypotension in elderly patients following spinal anesthesia have focused on major and complicated operations, such as orthopedic surgery. For example, in elective ar-

throplastic operations performed under spinal anesthesia in patients >65 years of age, Jakobsson et al. discovered a rate of postspinal hypotension of 50% (21).

In line with the literature, our findings indicate that the incidence of postspinal hypotension in elective urological surgery is significantly higher.

During the aging period, the cardiovascular system undergoes several major changes. In elderly patients who arrive at the operating room, systemic vascular resistance (SVR) is usually high, but accompanying dehydration is a very common complication. Due to reduced stroke volume, SVR, and preload, these patients' hemodynamic status can be compromised during spinal anesthesia (2, 22). Intraoperative hypotension may develop following spinal anesthesia. Intraoperative hypotension can lead to severe complications, prolonging hospital stays, and significantly affecting mortality rates (23). Anticipating hypotension after spinal anesthesia can save time in terms of deciding on, preparing, and implementing preventive measures.

Non-invasive methods requiring advanced technology, such as invasive transthoracic echocardiography and the ultrasonic measurement of the inferior vena cava diameter, as well as the hypoten-



sion prediction index obtained from arterial pulse waveform analysis, are used to predict hypotension (22, 24). However, in routine anesthetic practice, these techniques cannot be used in every case. In this study, we investigated whether SI, MSI, and SIA have predictive value for post-spinal hypotension in elderly patients and found that MSI can be used as a practical bedside test to predict hypotension after spinal anesthesia. According to our review of the literature, studies of SI, MSI, and SIA concentrate on sepsis, trauma surgery, major orthopedic surgery, and obstetrics, and ours is the first study on this issue in elective minor urological surgery (9-18).

While SI and SIA were not found to be significant in predicting hypotension in our study, MSI was found to be significant in this regard. This index has a cut-off point of  $<0.73$ . Additionally, MSI reflects stroke volume and SVR. A high MSI ( $>1.3$ ) suggests a low stroke volume and a low SVR, both of which are indicators of hypodynamic circulation. These patients' decompensation was rapid, particularly in occult hemorrhagic situations. A low MSI ( $<0.7$ ) suggests a high SVR and a hyperdynamic state in the patient, which may indicate severe conditions. As a potential predictor of mortality, a high or low MSI is a stronger parameter than HR, SBP, DBP, and SI alone (10, 11). Except in the absence of severe hypovolemic or septic shock, we noticed that a cut-off point of  $<0.73$  is a strong indicator of hypotension due to spinal anesthesia in minor elective surgeries.

After neuraxial blockade, vasodilatory changes that may affect cardiac performance are dependent on the patient's initial sympathetic tone (a higher sympathetic tone equates to a greater hemodynamic change, particularly in the elderly) and the extent of sympathectomy (the level of the sensory block). The elderly have a different physiology than young patients regarding the hypotension caused by spinal anesthesia. Specifically, SVR drops by about 25%, central venous pressure drops by about 3 mmHg, and left ventricular end-diastolic pressure drops by about 20% at the T4-T6 sensory levels of

spinal anesthesia. Furthermore, elderly patients have a higher resting sympathetic tone than younger patients, which explains why SVR drops so dramatically after the sympathetic blockade (22). Given these physiological characteristics, it is reasonable to conclude that elderly patients with high SVR and low MSI values ( $<0.73$ ) due to preoperative hypertension are more susceptible to the risk of hypotension due to the effects of spinal anesthesia.

Increased block height is linked to advanced age. In elderly patients, the specific gravity of the cerebrospinal fluid increases as the volume of the fluid decreases. Furthermore, the nerve roots in the elderly tend to be more susceptible to local anesthesia (25). Patients with a sensory block level of T8 or higher and a bupivacaine dose of more than 12.5 mg had a higher incidence of hypotension in our study.

We reasoned that the SIA values in our sample were insignificant because the study population did not include all adult age groups and only minor age changes in patients above 65 years of age had no effect on the index.

In our study, postoperative complication rates, postoperative biochemical data, PACU hospitalization, and discharge time did not vary between hypotensive and normotensive patients. Long-term hypotension exposure is required for the development of postoperative adverse outcomes, according to the literature (3). It is possible that the lack of adverse outcomes in our study was due to effective fluid resuscitation and the use of necessary vasopressor therapy to avoid long-term hypotension.

One of our study's limitations was that patients of the female gender (10.2%) were quite uncommon because the male gender is more common in the patient population for urological surgery. Despite the fact that we achieved the target sample size, research with a greater number of patients and different minor surgeries performed under spinal anesthesia in elderly patients would be more reliable for the value of SI, SIA, and MSI in predicting hy-

potension. Similarly, the heterogeneity of the ratios of the spinal anesthesia administrations at different levels of the intervertebral space makes it difficult to discuss statistical significance. Moreover, our study design (being observational, not having a standardized anesthetic approach) was an other limitation itself.

## CONCLUSION

Aside from standard hemodynamic monitoring, non-invasive derivative monitoring methods such as SI, MSI, and SIA may predict hypotension in ger-

iatric patients due to their hemodynamically pathophysiological characteristics. In elderly patients, MSI based on MAP, which tests tissue perfusion, may be more significant in predicting hypotension.

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## RESEARCH

# RELATIONSHIP BETWEEN THE PROGNOSTIC NUTRITIONAL INDEX AND ALL-CAUSE MORTALITY IN ELDERLY PATIENTS WITH NON-ST SEGMENT ELEVATION MYOCARDIAL INFARCTION

## ABSTRACT

**Background:** Patients over 65 years of age with non-ST segment elevation myocardial infarction are at higher risk of mortality and morbidity than younger patients. The prognostic nutritional index is a combined immunological-nutritional status score based on serum albumin levels and lymphocyte values. We evaluated the association between prognostic nutritional index value and all-cause mortality in elderly patients with non-ST segment elevation myocardial infarction. The current study presents the first evaluation of prognostic nutritional index in elderly patients with non-ST segment elevation myocardial infarction.

**Methods:** This was a retrospective observational study. The study population was divided into two groups according to their admission prognostic nutritional index. A prognostic nutritional index of 46 was determined as the optimal cut-off value to predict the primary endpoint, which was all-cause death during the follow-up period.

**Results:** Compared to patients with a prognostic nutritional index  $\geq 46$ , those with a prognostic nutritional index  $< 46$  were older ( $p < 0.001$ ) and more often had a history of hypertension and known coronary artery disease ( $p = 0.001$ ). All-cause mortality was significantly higher in the group with lower prognostic nutritional index (12.5% vs 4.8%;  $p = 0.007$ ). The prognostic nutritional index predicted the primary endpoint, and this prediction was statistically significant (sensitivity 71%; specificity 67%). Univariate Cox regression analyses and multivariate Cox regression analyses showed that a cut-off level of prognostic nutritional index  $< 46$  was significantly associated with the primary endpoint.

**Conclusions:** The prognostic nutritional index score was associated with all-cause mortality in elderly patients.

**Keywords:** Mortality; Non-ST Elevated Myocardial Infarction; Nutrition Assessment.



## INTRODUCTION

The numbers and proportion of the population aged over 65 years are increasing due to extended lifespans, health improvements and decreasing birth rates (1). Of those who die from ischaemic heart disease, 83% are over the age of 65 years. Elderly patients with non-ST-segment elevation myocardial infarction (NSTEMI) are at higher risk of mortality and morbidity than younger patients (2). The current guidelines recommend evaluating invasive treatments and considering personal characteristics, such as estimated life expectancy, comorbidities, quality of life and patient preference, after a careful risk/benefit evaluation in elderly patients with NSTEMI (3). Therefore, clinical scores for risk assessment are of great importance in choosing the appropriate treatment and evaluating mortality and morbidity risk in elderly patients with NSTEMI.

Malnutrition is an important risk factor for cardiovascular disease (CVD) in the elderly population and has a known association with a prolonged hospital stay, increased mortality and reduced quality of life (4-6). Malnutrition has been shown to associate with poor prognosis and mortality in cardiovascular disease, such as ST-segment elevation myocardial infarction (STEMI) and heart failure (7,8). Therefore, routine screening of the elderly population in terms of nutrition has been suggested (9). Nevertheless, evaluating nutritional status is not simple, as different components of malnutrition need to be considered. The Prognostic Nutritional Index (PNI) reflects a combined score of an immunological nutritional status based on serum albumin levels and lymphocyte values (10). This index is easy to calculate, as it requires only simple blood parameters and is a cost-effective method. Recent studies have shown that nutritional status evaluated by PNI is an independent prognostic factor in patients with different CVD (7,8). However, the association of PNI with mortality has not been reported in elderly patients with NSTEMI. Therefore, in this study, we evaluated the association between the value of PNI and

all-cause mortality in elderly patients with NSTEMI. The current study presents the first evaluation of PNI in elderly patients with NSTEMI.

## METHODS

Between March 2019 and August 2020, 404 consecutively confirmed patients aged  $\geq 65$  with NSTEMI who were admitted to the emergency department of our institution were retrospectively evaluated. NSTEMI was determined by the appropriate guidelines (11). Patients with an active infection, a history of chronic inflammatory disease, a known neoplasm, severe hepatic disease, an advanced-stage renal disorder or missing clinical data, as well as individuals undergoing renal replacement therapy, were excluded from this study.

The PNI was calculated based on the serum albumin values and the total lymphocyte count obtained at admission:  $10 \times \text{albumin (g/dl)} + 0.005 \times \text{total lymphocyte count (permm}^3\text{)}$ . The PNI was calculated for each participant. The study population ( $n = 376$ ) was divided into two groups according to their admission PNI. The cut-off value of PNI to predict the primary endpoint was evaluated by receiver operating characteristic (ROC) curve analysis. A PNI of 46 was determined as an optimal cut-off value to predict the primary endpoint. The study population groups were organised accordingly: PNI  $< 46$  ( $n = 128$ ) and PNI  $\geq 46$  ( $n = 248$ ).

The study protocol was reviewed and approved by the University of Health Sciences, Ankara City Hospital Ethics Committee in accordance with the Declaration of Helsinki (approval no; E1/21/1487, date; 03 February 2021).

NSTEMI was defined as the presence of cardiac biomarkers, such as cardiomyocyte necrosis and increased troponin T (cTnT) with clinically concordant myocardial ischaemia and without ST segment elevation. The primary endpoint was all-cause death during the follow-up period. All-cause mortality was defined as death from any cause during hospitaliza-

tion or after discharge during the follow-up period. The mortality data of the participants were obtained by the medical records, while the details and the causes of death were obtained from the National Survival Registry. Cardiovascular death was defined as death due to myocardial infarction, death due to heart failure, death due to malignant arrhythmia or sudden cardiac arrest because of other or unknown causes during hospitalization and after discharge.

The baseline clinical and demographic characteristics of the patients were gathered from the hospital's medical database. Left ventricular ejection fraction (LVEF) was calculated using the modified Simpson method within 24 hours of admission (12). An electrocardiogram (ECG) was examined on admission in the emergency unit, after the procedure and daily during the hospital stay. Venous blood samples from the antecubital vein were obtained using standardized EDTA blood tubes within 10–30 minutes of admission to the hospital. A complete blood count including the white blood cell (WBC), haemoglobin and lymphocyte levels was measured using an automated haematology analyzer system (Beckman Coulter Ireland, Inc, Galway, Ireland). Albumin levels were measured using the photometric method (DC 800; Beckman Coulter, Dublin, Ireland).

According to the ESC guidelines, an immediate invasive strategy was performed on patients with at least one very-high-risk NSTEMI criteria (11); all the remaining patients underwent coronary angiography (CAG) within 48 hours after admission with a diagnosis of NSTEMI. The heart team determined the appropriate revascularization strategy (percutaneous coronary intervention or coronary artery bypass grafting) after CAG. For the patients whose coronary artery anatomy was not suitable for intervention treatment, pharmacological treatment was arranged. All the patients in the study received a loading dose of aspirin and a loading dose of P2Y12 receptor inhibitors on admission. The patients received 70–100 U/kg of intravenous unfractionated heparin before the procedure. The use of a glyco-

protein IIb/IIIa inhibitor (tirofiban) was at the discretion of the primary operator. Most of the percutaneous coronary intervention (PCI) procedures were performed using a transradial approach; a transfemoral approach was used on the patients who were not suitable for the transradial approach. The appropriate P2Y12 inhibitor therapy and 81–100mg aspirin per day were prescribed during the hospitalization and at discharge according to the current guidelines (11).

All the data were analysed using the SPSS 22.0 Statistical Package Program for Windows (SPSS; IBM, Armonk, New York, USA). A Kolmogorov–Smirnov test was utilized for the assessment of the normality of distribution. Continuous variables were presented as mean  $\pm$  standard deviation and median with interquartile ranges and categorical variables as the number of patients and percentages. A comparison between groups was made with a Student's t-test for normally distributed variables and a Mann–Whitney U test for variables without normal distribution. Categorical data from both groups were compared using the  $\chi^2$  or Fisher's exact test. Univariate and multivariate analyses with Cox proportional hazards regression were used to evaluate the association between PNI and all-cause mortality. Variables displaying  $p < 0.05$  in the univariable analysis were used in a multivariable logistic regression analysis. Survival estimates were calculated by the Kaplan–Meier method, and the log-rank tests were used for comparison. The ability of the PNI value to predict the primary endpoint was evaluated by ROC curve analysis and area under curve (AUC) values. The cut-off value was calculated according to the Youden index. A  $p$ -value  $< 0.05$  (using a two-sided test) was accepted as significant.

## RESULT

Initially, a total of 404 consecutive NSTEMI patients aged  $\geq 65$  were considered for the study; 28 patients were excluded because of having at least one of the exclusion criteria. Consequently, 376



patients were enrolled in the current study. In the study population, the mean age was  $73 \pm 7.1$  years, the male gender ratio was 60%, and the mean follow-up time was  $335 \pm 117$  days. The cut-off value of PNI for predicting the primary endpoint was 46 (sensitivity 71%, specificity = 67%) according to the Youden index. We divided the patients into two groups according to the PNI cut-off value; 128 patients had a PNI score  $< 46$ , and 248 patients had a PNI  $\geq 46$ . Demographic characteristics and clinical and laboratory values of the study population are presented in Table 1. Compared to the patients with PNI scores  $\geq 46$ , those with PNI scores  $< 46$  had an advanced age ( $p < 0.001$ ) and had a history of hypertension (HT) ( $p = 0.008$ ) and known coronary artery disease (CAD) ( $p = 0.001$ ) more often. However, the histories of the patients were similar in terms of diabetes mellitus (DM), hyperlipidemia (HPL), previous heart failure and stroke. The patients with a PNI score  $< 46$  had significantly lower

blood albumin ( $p < 0.001$ ), lower total cholesterol ( $p = 0.010$ ), a lower glomerular filtration rate ( $p < 0.001$ ), lower WBC counts ( $p = 0.012$ ), lower haemoglobin levels ( $p < 0.001$ ), lower lymphocyte counts ( $p < 0.001$ ) and higher C-reactive protein (CRP) levels ( $p = 0.011$ ) compared with those with a PNI score  $\geq 46$ . No significant differences were noted in systolic blood pressure (SBP), heart rate and LVEF at admission between the two groups. The patients in both groups had similar treatments with respect to aspirin, P2Y12 receptor inhibitors, B-blockers, statins and angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers. The ratio of diuretic therapy prescribed at discharge was higher in the low-PNI group ( $p = 0.009$ ).

The ratios of patients who underwent coronary artery bypass grafting as a revascularization strategy, who underwent PCI, and who were followed up medically without invasive intervention were similar in both groups (Table 1).

**Table 1.** Baseline clinical, echocardiographic, and laboratory characteristics of patients stratified by values of the prognostic nutritional index.

	Prognostic Nutritional Index		p value
	<46 (n=128)	$\geq 46$ (n=248)	
Age (year)	$78 \pm 12.7$	$70 \pm 7.0$	<0.001
Male, n (%)	68 (53.1)	160 (64.5)	0.032
Heart Rate, BPM	$78 \pm 11.0$	$78 \pm 21.0$	0.990
SBP, mmHg	$120 \pm 27.5$	$130 \pm 16.3$	0.062
LVEF, %	$45 \pm 10.0$	$45 \pm 15.0$	0.497
History, n (%)			
Diabetes mellitus	76 (59.3)	128 (51.6)	0.152
Hypertension	96 (75)	152 (61.2)	0.008
Hyperlipidemia	20 (16.6)	48 (19.3)	0.373
History of heart failure	48 (37.5)	96 (38.7)	0.332
Known coronary artery disease	44 (34.3)	120 (48.3)	0.001
History of Stroke	16 (12.5)	16 (6.4)	0.053

Admission Laboratory Variables			
Creatinine (mg/dl)	0.8 ± 0.3	0.8 ± 0.3	0.180
Albumin (g/dl)	37.0 ± 2.0	41.4 ± 4	<0.001
Total cholesterol (mg/dL)	165 ± 50	171 ± 62	0.010
LDL (mg/dL)	104 ± 39	104 ± 45	0.297
eGFR (ml/min/1.73m <sup>2</sup> )	74 ± 31	87 ± 29	<0.001
WBC (x10 <sup>3</sup> / μL)	8.6 ± 3.0	9.35 ± 3.44	0.012
Hemoglobin (mg/dL)	13.1 ± 2.1	13.5 ± 2.1	<0.001
Lymphocyte (x10 <sup>3</sup> / μl)	0.97 ± 0.39	1.90 ± 0.64	<0.001
CRP	8.23 ± 39.89	5.71 ± 6.90	0.011
Troponin T (ng/mL)	3.222 ± 9.672	2.433 ± 8.165	0.671
Coronary Artery Disease, n (%)			
Left Main	8 (6.2)	0	0.002
Left Anterior Descending	56 (43.7)	120 (48.3)	0.913
Left Circumflex	52 (40.6)	116 (46.7)	0.258
Right Coronary Artery	28 (21.8)	120 (48.3)	0.230
Angiographic Data, n (%)			
Syntax Score	10 ± 8.7	9 ± 9.7	0.674
TIMI Thrombus Grade	4.0 ± 2.0	3.0 ± 1.8	0.683
Selection Of Revascularization, n (%)			
Coronary Artery Bypass Grafting	8(6)	32(12.5)	0.128
Percutaneous Coronary Intervention	100(78.1)	188(75.8)	0.615
Non-Interventional Treatment	20(15)	32(12)	0.469
Medications At Discharge, n (%)			
Aspirin	127 (99.2)	244 (98.4)	0.505
B-blocker	116 (90.6)	228 (91.9)	0.328
Statins	120 (93.8)	236 (95.2)	0.180
ACEIs or ARBs	120 (93.8)	232 (93.5)	0.588
Diuretics	36 (28.1)	60 (24.2)	0.009
P2Y12 receptor inhibitors	125 (97.7)	242 (97.6)	0.964

SBP: Systolic Blood Pressure; LVEF: Left ventricular ejection fraction; LDL: Low-density lipoprotein cholesterol; eGFR: estimated glomerular filtration rate; WBC: White blood cell; CRP: C-reactive protein; Syntax: SYnergy between PCI with TAXUS and Cardiac Surgery; TIMI: Thrombolysis in Myocardial Infarction; ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin II receptor blockers



Table 2 presents the primary endpoint of the study according to the PNI values. During the follow-up period, all-cause death occurred in 28 of 376 subjects (7.4%). All-cause mortality was significantly higher in the group with lower PNI scores (12.5% vs. 4.8%;  $P = 0.007$ ). Although the incidence of cardiovascular death was higher in the low-PNI group, it was not statistically significant.

The ability of the PNI to predict the primary endpoint was evaluated by ROC curve analysis. The AUC value of this analysis is presented in Figure 1 (AUC = 0.636, 95% CI = 0.502–0.771,  $p = 0.016$ ). It was determined that the PNI predicted the primary endpoint, and this prediction was statistically significant (Sensitivity 71%, specificity = 67%).

The patients were followed up for a mean period of  $335 \pm 117$  days. The Kaplan–Meier analysis showed a significantly lower primary endpoint-free survival rate in patients with low PNI scores (log-rank,  $P = 0.008$ ) (Figure 2).

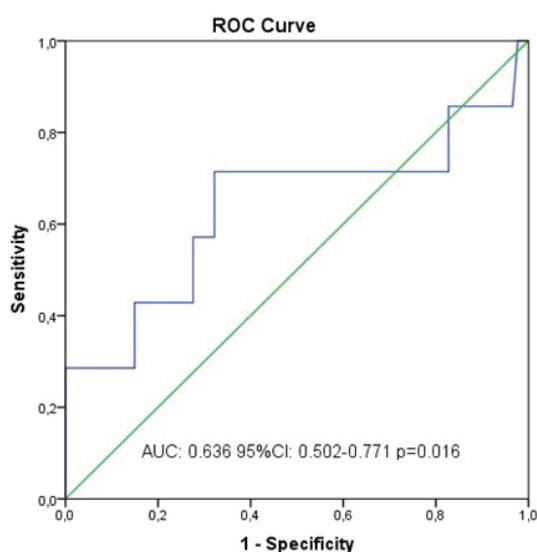
Univariate Cox regression analyses showed that the SYNTAX score, known CAD, admission heart

rate, SBP, WBC and a cut-off level of  $PNI < 46$  was significantly associated with the primary endpoint, as shown in Table 3. All-cause mortality had higher rates at lower PNI levels (hazard ratio: 0.328; 95% confidence interval 0.123–0.872;  $p = 0.025$ ). Other multivariate independent predictors of mortality were admission heart rate (hazard ratio, 1.060; 95% confidence interval, 1.029–1.093],  $P < 0.001$ ), LVEF (hazard ratio, 0.938; 95% confidence interval, 0.887–0.991,  $P = 0.022$ ) and WBC count (hazard ratio, 1.212; 95% confidence interval, 1.105–1.329,  $P < 0.001$ ) (Table 3).

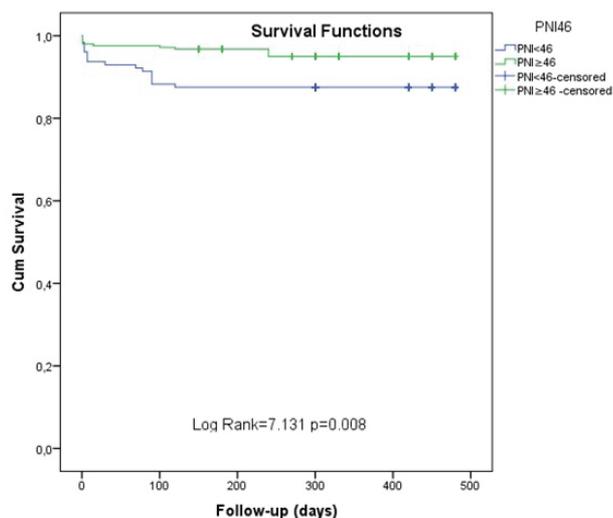
## DISCUSSION

To the best of our knowledge, this is the first study to investigate the prognostic value of PNI in patients aged  $\geq 65$  with NSTEMI. The major findings were as follows: the low PNI group had a higher all-cause mortality rate compared to the high-PNI group, even though both groups had similar medical histories, such as DM, heart failure, previous stroke and HPL. HT and known CAD were more common in

**Figure 1.** Receiver-operating characteristic curve of the PNI for predicting primary endpoint.



**Figure 2.** Kaplan–Meier curve analysis of the composite primary endpoint.



**Table 2.** The Primary Endpoint of patients classified by prognostic nutritional index

	PNI<46 (n=128)	PNI≥46 (n=248)	p value
All cause mortality	16(12.5)	12(4.8)	0.007
Cardiovascular death	8(6.2)	12(4.8)	0.563
Follow-up time, day	300±150	315±150	0.069

PNI: Prognostic Nutritional Index

**Table 3.** Univariate and Multivariate cox proportional hazard models for prediction of primary endpoint.

	HR (95% CI)	p value	HR (95% CI)	p value
SYNTAX Score	1.073 (1.037 – 1.111)	<0.001	1.046 (0.988 – 1.107)	0.121
Known coronary artery disease	0.303 (0.133 – 0.687)	0.004	0.902 (0.517 – 1.573)	0.717
Heart Rate, BPM	1.087 (1.062 – 1.113)	<0.001	1.060 (1.029 – 1.093)	<0.001
SBP, mmHg	0.928 (0.909 – 0.947)	<0.001	1.004 (0.974 – 1.035)	0.802
LVEF	0.916 (0.884 – 0.950)	<0.001	0.938 (0.887 – 0.991)	0.022
Creatinine (mg/dl)	3.030 (0.918 – 10.005)	0.069		
eGFR	0.987 (0.969 – 1.006)	0.176		
Total cholesterol (mg/dL)	1.000 (0.992 – 1.009)	0.923		
LDL (mg/dL)	1.002 (0.992 – 1.013)	0.681		
WBC (x10 <sup>3</sup> /ML)	1.214 (1.155 – 1.276)	<0.001	1.212 (1.105 – 1.329)	<0.001
Hemoglobin (mg/dL)	1.053 (0.868 – 1.277)	0.601		
CRP	1.011 (0.999 – 1.024)	0.075		
PNI<46	2.656 (1.256 – 5.614)	0.011	0.328 (0.123 – 0.872)	0.025

SYNTAX: SYnergy between PCI with TAXUS and Cardiac Surgery; SBP: Systolic Blood Pressure; LVEF: Left Ventricular Ejection Fraction; eGFR: Estimated Glomerular Filtration Rate; LDL: Low-density lipoprotein cholesterol; WBC: White blood cell; CRP: C-reactive protein; PNI: Prognostic Nutritional Index

the low-PNI group. The PNI value was a significant independent predictor of all-cause death. Cumulative survival was significantly lower for the patients in the low-PNI group (PNI < 46) relative to the patients in the high-PNI group (PNI ≥ 46). Thus, PNI on admission appears to be useful for risk stratification of elderly patients with NSTEMI.

It is known that elderly patients have an increased prevalence of poor prognostic factors, such as stroke, diabetes, congestive heart failure and HT

(13). In addition, elderly patients are often malnourished, and malnutrition contributes to poor prognosis by weakening the immune defences of elderly patients in the hospital (14). As a result of the increased risk profile, it may be useful to use different parameters in predicting prognosis.

PNI calculated with the albumin level and the lymphocyte count is used as an indicator of inflammation, immune function and nutritional level (15). Hypoalbuminemia is the result of inflammation, in-



adequate protein and calorie intake in people with chronic disease. Inflammation and malnutrition reduce the synthesis rate of albumin and increase the deterioration of albumin. Also, the transition of albumin into the extravascular space is increased. As a result, hypoalbuminemia is developed. The albumin level decreases the result of both inflammation and malnutrition in chronic diseases (16,17). Albumin increases the production of prostaglandin-D2 and indirectly causes the inhibition of platelet aggregation (18). Hypoalbuminemia increases blood viscosity and disrupts endothelial functions due to increased free lysophosphatidylcholine levels (19). Albumin is a commonly used measure for nutrition and has been demonstrated to relation with post-operative complications (20). Many reports have demonstrated an elevation of inflammatory markers in myocardial infarction (21) and there is increasing evidence that hypoalbuminemia on admission hospital is a powerful independent predictor of long-term mortality and acute heart failure development in STEMI patients (16).

The effects of malnutrition on the immune system are important. Malnourishment causes lymphatic tissues to develop atrophy, impairs cellular immunity and reduces bactericidal leukocyte activity. Interleukin (IL)-1 activity is suppressed in malnutrition. Impaired IL-1 activity leads to a decrease in the rate of lymphocyte generation (22). Lymphocytes have a crucial effect in regulating the inflammatory response at several stages of the atherosclerotic process (23). In acute coronary events, lymphocytopenia is observed secondary to increased corticosteroid level, and a higher lymphocyte count is considered a more suitable immune reaction and is seen as a stable inflammatory status (24). Lymphocytopenia has been independently associated with major adverse cardiac events and death after myocardial infarction (25). Therefore, a PNI that has been calculated from the serum albumin and lymphocyte counts can predict the nutritional, inflammatory and immune status of elderly patients with NSTEMI.

Long-term mortality rates of NSTEMI have reduced significantly in association with an increase in the frequency of care that includes early interventions (11). There are a few significantly accepted risk scores including TIMI risk score and GRACE score which present precious prognostic information. Age is a parameter for both the GRACE and TIMI risk score (26). Advanced age is accompanied by malnutrition and lower albumin level. A total of 945 elderly patients with STEMI were evaluated during a 2-year follow-up, and malnutrition was detected in approximately 55% of the participants (27). Therefore, considering that malnutrition increase with age, it can be expressed that data on the evaluation and importance of this in elderly patients with NSTEMI are limited. As presented in recent analyses, lower lymphocyte level is associated with higher mortality (28). PNI combines these two significant measurements and offers valuable prognostic information.

Initially, the PNI was presented to assess the immunological and nutritional aspects of malignancy patients (29). It has known that the PNI provides a stronger predictive power of mortality than do its components such as albumin and lymphocyte (30). Then, the PNI score was used as a predictive nutritional marker in patients with different cardiovascular diseases, such as heart failure and STEMI (7,8). Basta et al. demonstrated that in elderly patients with STEMI, a lower PNI level was significantly associated with poor prognosis (27). A recent retrospective observational study of patients with STEMI shown a significant relationship between PNI and inhospital and long-term mortality (7,8). However, the analysis has been made in elderly STEMI patients who underwent PCI (8). Therefore, this study has examined the association of PNI with all-cause mortality in elderly patients with NSTEMI.

In this study, we found that PNI was an independent predictor of mortality in elderly patients with NSTEMI. The current study has shown that the low PNI had a higher all-cause mortality rate compared to the high-PNI group, even though both groups

had similar medical histories, such as DM, heart failure, previous stroke and HPL. A large number of comorbidities are related to nutritional status, and patients in the low PNI group had a higher prevalence of known CAD and previous HT. In this study, patients with low PNI tended to be older, had a higher level of CRP. This partly explains that increased inflammatory activity and decreased serum albumin level may be two of the underlying mechanisms of mortality in elderly patients with NSTEMI. In patients with low PNI, higher CRP levels also confirmed a negative relationship between PNI and CRP levels in the present study. A previous study has presented that the PNI was independently associated with cardiovascular outcomes after adjusting for traditional risk factors (31). Multivariate Cox hazard models showed that the PNI was independently associated with all-cause mortality after adjusting for risk factors. Therefore, PNI is appropriate to be used in elderly patients with NSTEMI since it is easy and simple to calculate with available practical parameters and less likely to be affected by confounding clinical conditions in coronary artery disease patients such as statin use. Consistent with previous findings (27,30) that low PNI were related to poor prognosis in patients with CAD, the present study more enlarges this association to a particular cohort

such as elderly patients with NSTEMI.

As a result of multivariate Cox regression analysis, it was determined that low PNI and increased heart rate, high WBC, reduced LVEF were associated with the primary endpoint. It has been reported that higher WBC has been used in the estimation of major adverse cardiovascular events in elderly patients (32). In agreement with our study, the study by Kalyoncuoğlu et al. showed that reduced LVEF was an independent predictor of poor prognosis in elderly patients with NSTEMI (33).

This study had several limitations. The present study evaluated the PNI value at admission and did not assess its changes during the follow-up time. This was a retrospective, single-centre, observational study, in which information about the body mass index of patients was not obtained. The range of PNI values was relatively small. Additional assessments using nutritional indexes may supply beneficial information during the follow-up.

The PNI consists of simple objective measurements that can be easily obtained. Our findings suggest that the PNI score was found to be associated with all-cause mortality in elderly patients with NSTEMI.

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## RESEARCH

# SLEEP QUALITY IN PATIENTS OVER 65 YEARS OF AGE IN THE COVID-19 PANDEMIC

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### CORRESPONDANCE

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## ABSTRACT

**Introduction:** While Covid-19 affects people of all ages, elderly patients are at the highest risk. The Covid-19 pandemic has caused sleep disorders and mental health problems as well as physical symptoms.

**Materials and Methods:** A total of 142 patients, 71 Covid-19 patients hospitalized in the quarantine service and 71 non-covid, were included in the study. Patients were divided into groups of hospitalized in the COVID-19 and non-COVID-19 wards and by age (under 65 and over). The Pittsburg Sleep Quality Index was used to assess sleep quality, the Beck Depression Index to measure the level of depressive symptoms, and the Beck Anxiety Index to measure the level of anxiety symptoms.

**Results:** The sleep quality of those hospitalized in the COVID-19 ward was worse, and their anxiety and depression symptom scores were higher ( $p = 0.003$ ,  $p = 0.011$ , and  $p = 0.018$ ). The sleep quality of patients over 65 years of age was significantly worse than that of patients under 65 years of age ( $p < 0.001$ ), and anxiety and depression symptom scores of patients over 65 years of age were significantly higher than those of patients under 65 years of age ( $p < 0.01$ ,  $p < 0.01$ ).

**Conclusion:** During the COVID-19 pandemic, anxiety and depression symptoms were observed and sleep quality was deteriorated in patients aged  $>65$  years who were placed in quarantine. Hence, this group of patients should be closely monitored in terms of psychological disorders and sleep disorders. If necessary, psychological support and medical treatment should be provided.

**Keywords:** Covid-19; Pandemic; Anxiety; Depression; Sleep; Geriatrics.

## INTRODUCTION

Toward the end of 2019, a new coronavirus disease (COVID-19) pneumonia emerged in Wuhan, China, and spread rapidly all over the world. It was eventually announced a pandemic by the World Health Organization (WHO). COVID-19 causes physical and psychological problems due to the high risk of transmission and mortality, of the virus. While COVID-19 affects people of all ages, elderly patients are at the highest risk. Due to the COVID-19 pandemic, the mortality rate of those aged 80 years and above has increased five-fold compared to the global average (1). Therefore, health strategies, such as social distancing, are especially important for preventing the spread of the coronavirus (2, 3).

In many countries, patients infected with COVID-19 are treated in isolation wards under strict quarantine conditions. Due to social isolation, uncertainty, physical symptoms, side effects of drugs, fear of infecting others, death of a family member, and negative news on social media, patients with COVID-19 may experience loneliness, anger, anxiety, depression, insomnia, and post-traumatic stress disorder (PTSD) (4). In addition, SARS-CoV-2 can directly reach the brain, disrupt brain functions, and cause mental-psychological problems in patients (5). A recent study found that 96.2% of clinically stable COVID-19 patients experienced significant PTSD (6). Previous studies that followed patients infected with severe acute respiratory syndrome (SARS) in 2003 showed that the prevalence of PTSD among SARS survivors was 9.79% in the early recovery phase and 46.2% at 3 months after discharge, 38.8% at 12 months (7). Thus, post-pandemic mental distress may be persistent, even after the pandemic is over.

Many studies have reported that patients have negative changes in their sleep patterns and sleep quality due to quarantine (8, 9). Few studies have assessed depressive symptoms and impaired sleep quality, especially in elderly patients, during quarantine (10, 11). Some standardized questionnaires

are used to evaluate anxiety, depression, and sleep quality of patients. The most commonly used among these are the Beck Depression Index (BDI), Beck Anxiety Index (BAI), and Pittsburg Sleep Quality Index (PSQI) (9).

In our study, we aimed to examine to what extent the hospital quarantine applied during the Covid-19 pandemic affected the anxiety and depression symptoms and sleep quality of the patients and whether this effect changes with age.

## MATERIALS AND METHODS

This study was conducted on 71 patients diagnosed with COVID-19 and hospitalized in an isolated covid ward under quarantine conditions and 71 non-COVID-19 patients hospitalized in non-COVID-19 services, not under quarantine, in the Adana City Training and Research Hospital between February 15, 2021, and March 15, 2021. A total of 142 patients were enrolled in this study. Our study was approved by the ethics committee on January 13, 2021 (number 1256). Written consent was obtained from all patients.

Patients were divided into two groups, i.e., hospitalized in the COVID-19 and non-COVID-19 services, and evaluated them separately according to age (under and above 65 years of age). Patients in the COVID service consisted of stable patients with PCR (+) results, no respiratory distress, and under medical treatment. Patients hospitalized in non-COVID-19 services included stable patients who were deemed suitable for medical treatment. Sleep quality was evaluated using the PSQI, anxiety symptoms using the BAI, and depression symptoms using the BDI. Those younger than 18 years of age, those with previous psychiatric illnesses and sleep disorders, and those who could not complete their questionnaires in their entirety were excluded from the study.

The PSQI was used to evaluate the sleep quality of each patient over the last month, and consistent



and repeatable PSQI scores were used (12). The PSQI, which enables us to evaluate the sleep quality, as well as the amount, presence, and severity of sleep disorders in individuals through 19 questions, was filled out by the same physician using a one-on-one interview with the patients. The PSQI consists of seven items evaluating subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, and use of sleeping pills; the obtained global score ranges from 0 to 21, with higher values indicating poor sleep quality and high levels of sleep disturbance. A global score of 5 or above indicates that clinically, sleep quality is significantly worse. Its diagnostic sensitivity and specificity are 89.6% and 86.5%, respectively (12,13). Agargün et al. adapted the PSQI questionnaire for Turkish patients (13).

The BDI was developed to measure the risk of depression, the level of depressive symptoms, and the change in severity in adults (Beck 1961). The Turkish validity and reliability study was conducted by Hisli (1989). It measures the physical, emotional, and cognitive symptoms of depression. This scale includes 21 symptom categories with four options each. The total score obtained from the inventory indicates the following: 0–9, normal; 10–18, mild symptoms; 19–29, moderate symptoms; and 30–63, severe depression symptoms (14).

The BAI is a self-assessment scale developed by Beck et al. (1988) to determine the frequency of anxiety symptoms experienced by individuals. It evaluates the frequency of anxiety symptoms experienced by an individual. It is a self-rating scale, scored between 0 and 3, which consists of 21 items. The total score obtained from the inventory indicate the following: 0–7, normal state; 8–15, mild anxiety; 16–25, moderate anxiety; and 26–63, severe anxiety symptoms. Ulusoy et al. (1998) have conducted a Turkish validity and reliability study for this scale (15).

Statistical analyses were performed using SPSS 22.0. A chi-square test was used to compare the

findings according to sex. An independent sample t-test, chi-square test, Fisher's exact test, and Mann–Whitney U test were used to compare the findings of patients in COVID-19 and non-COVID-19 services and those under 65 years of age. A multiple linear regression analysis was performed to evaluate the relationship between PSQI, anxiety, and depression.

## RESULTS

A total of 142 patients, 71 hospitalized in the COVID-19 ward and 71 hospitalized in the non-COVID-19 ward were included in the study. A total of 88 patients were below 65 years of age, and 54 patients were above 65. There were 60 female and 82 male patients.

The sex distributions of the patients hospitalized in the COVID-19 and non-COVID-19 services were homogeneous according to the cut-odd of 65 years of age ( $p = 0.070$ ,  $p = 0.075$ ,  $p = 0.431$ ). There was no significant difference in terms of the mean age between those hospitalized in the COVID-19 ward ( $60.01 \pm 11.5$  (25–91)) and in the non-COVID-19 ward ( $60.46 \pm 11.39$  (28–86)) ( $p = 0.815$ ). Similarly, sex distribution was homogeneous ( $p = 1.00$ ) in patients hospitalized in the COVID-19 (female [30 (42.3)]) and non-COVID-19 wards (female [30 (42.3)]) (Table 1).

In those hospitalized in the COVID-19 service, individuals aged 65 years or older had a higher PSQI score (equal to or over 5), positive Beck anxiety score, and Beck depression symptoms than those aged <65 years ( $p = 0.026$ ,  $p < 0.001$ ,  $p = 0.005$ , respectively). No significant relationship was found in the PSQI among those hospitalized in the non-COVID-19 ward and those aged  $\geq 65$  and <65 years ( $p > 0.05$ ). In non-COVID-19 ward inpatients aged  $\geq 65$  years, the proportion of those with positive Beck anxiety symptoms and positive Beck depression symptoms was higher than in those aged <65 years ( $p < 0.001$ ,  $p < 0.001$ , respectively). The proportions of those aged  $\geq 65$  years, those with

**Table 1:** Sex and age distribution of patients hospitalized in Covid and non-Covid services,

	Covid services			Non-Covid services			Total			P <sub>group</sub>
	<65 age (n:44)	≥65 age (n:27)	Total (n:71)	<65 age (n:44)	≥65 age (n:27)	Total (n:71)	<65 age (n:88)	≥65 age (n:54)	Total (n:142)	
	Mean±SD (min-max)	Mean±SD (min-max)	Mean±SD (min-max)	Mean±SD (min-max)	Mean±SD (min-max)	Mean±SD (min-max)	Mean±SD (min-max)	Mean±SD (min-max)	Mean±SD (min-max)	
Age	53.23±8.14 (25-61)	71.07±6.41 (65-91)	60.01±11.5 (25-91)	53.68±8.13 (28-64)	71.52±5.93 (65-86)	60.46±11.39 (28-86)	53.46±8.09 (25-64)	71.30±6.12 (65-91)	60.24±11.40 (25-91)	0.815
Female	15 (34.1)	15 (55.6)	30 (42.3)	17 (38.6)	13 (48.1)	30 (42.3)	32 (36.4)	28 (51.9)	60 (42.3)	1.00
Male	29 (65.9)	12 (44.4)	41 (57.7)	27 (61.4)	14 (51.9)	41 (57.7)	56 (63.6)	26 (48.1)	82 (57.7)	
	p <sub>age</sub> =0.075			p <sub>age</sub> =0.431			p <sub>age</sub> =0.070			

Gender: Chi-Square test, Age:Independent Sample t test,

p<sub>age</sub>: Comparison of under 65 and over,

p<sub>group</sub>: Comparison of covid service and non-covid service

PSQI scores ≥5, and those with Beck anxiety and depression symptoms were higher than of those aged <65 years (p = 0.018, p <0.001, and p <0.001, respectively). Individuals under 65 years of age admitted in the COVID-19 and non-COVID-19 wards had similar PSQI and anxiety and depression symptoms (p > 0.05). The rate of PSQI values ≥5 was higher in those aged ≥65 years and those hospitalized in the COVID-19 ward than in those hospitalized in the non-COVID-19 ward (p = 0.011 and p = 0.028, respectively). Among individuals aged ≤65 years, the rates of anxiety and depression did not differ between those who were hospitalized in the COVID-19 and non-COVID-19 wards (p > 0.05 and p > 0.05, respectively) (Table 2).

Component 7 (daytime functions), PSQI, anxiety, and depression differed between individuals under 65 and over 65 years of age in the COVID-19 ward (p <0.05). The sleep quality of patients over 65 years of age hospitalized in the COVID-19 ward was significantly worse than that of patients under 65 years of age (p = 0.002). Anxiety and depression symptom scores of patients over 65 years of age hospitalized in the COVID-19 ward were significantly higher than

those of patients under 65 years of age (p <0.01 and p = 0.05). Component 2 (sleep latency), Component 3 (sleep time), Component 4 (sleep efficiency), PSQI, anxiety, and depression differed between individuals <65 years of age and ≥65 years of age with non-COVID cervicitis (p <0.05). The sleep quality of patients over 65 years of age hospitalized in a non-COVID service was significantly worse than that of patients under 65 years of age (p = 0.006). Anxiety and depression symptom scores of patients over 65 years of age hospitalized in the COVID-19 ward were significantly higher than those of patients under 65 years of age (p <0.01 and p <0.01).

Among those aged < 65 and ≥65 years, Component 1 (subjective sleep quality), Component 2 (sleep latency), Component 3 (sleep time), Component 4 (sleep efficiency), Component 5, (sleep disturbance), Component 7 (daytime functions), PSQI, anxiety, and depression were found to differ (p < 0.05). The sleep quality of patients over 65 years of age was significantly worse than that of patients under 65 years of age (p <0.001), and anxiety and depression symptom scores of patients over 65 years of age were significantly higher than those of



**Table 2:** Comparison of PSQI, anxiety and depression symptoms of patients under 65 and over 65 years of age in covid service and non-covid service

	Covid services						P <sub>age</sub>	Non-Covid services						P <sub>age</sub>	Total						P <sub>age</sub>	P <sub>age &lt;65; group</sub>	P <sub>age ≥65; group</sub>	P <sub>group</sub>
	<65 age		≥65 age		Total			<65 age		≥65 age		Total			<65 age		≥65 age		Total					
	n	%	n	%	n	%		n	%	n	%	N	%		n	%	n	%	n	%				
PSQI																								
<5	25	56.8	8	29.6	33	46.5	0.026	32	72.7	16	59.3	48	67.6	0.239	57	64.8	24	44.4	81	57.0	0.018	0.118	0.028	0.011
≥5	19	43.2	19	70.4	38	53.5		12	27.3	11	40.7	23	32.4		31	35.2	30	55.6	61	43.0				
Beck anxiety Index																								
anxiety symptoms -	22	50.0	2	7.4	24	33.8	<0.001	29	65.9	5	18.5	34	47.9	<0.001	51	58.0	7	13.0	58	40.8	<0.001	0.131	0.420	0.088
anxiety symptoms +	22	50.0	25	9.6	47	66.2		15	34.1	22	81.5	37	52.1		37	42.0	47	87.0	84	59.2				
Beck depression Index																								
depression symptom -	22	50.0	4	1.8	26	6.6	0.005	29	65.9	6	22.2	35	49.3	<0.001	51	58.0	10	18.5	61	43.0	<0.001	0.131	0.728	0.127
depression symptom +	22	50.0	23	8.2	45	63.4		15	34.1	21	77.8	36	50.7		37	42.0	44	81.5	81	57.0				

Chi-Square test, Fisher Exact test, p<sub>age</sub>: Comparison of under 65 and over 65, p<sub>age <65; group</sub>: Comparison of covid service and non-covid service under 65, p<sub>age ≥65; group</sub>: Comparison of covid service and non-covid service aged 65 and above, p<sub>group</sub>: Comparison of covid service and non-covid service, PSQI: Pittsburgh Sleep Quality Index

patients under 65 years of age (p <0.01, p <0.01). Among those under 65 years old who were hospitalized in the COVID-19 ward and those who were hospitalized in the non-COVID-19 wards, Component 2 (sleep latency), Component 3 (sleep time), Component 5 (sleep disturbance), PSQI, anxiety, and depression differed significantly (p <0.05). Sleep quality was worse in patients under 65 years of age, and anxiety and depression symptoms in the COVID ward scores were higher (p = 0.030, p = 0.011, p = 0.008). Component 5 (sleep disturbance), Component 7 (daytime functions), and PSQI differed between those hospitalized in the COVID-19 ward and those hospitalized in the non-COVID-19 ward among individuals aged 65 years and older (p <0.05). Sleep quality was worse in those aged 65 years and older who were hospitalized in the COVID-19 ward (p = 0.010). When all patients were evaluated, component 2 (sleep latency), Component

3 (sleep time), Component 5 (sleep disturbance), PSQI, anxiety, and depression differed between those hospitalized in the COVID-19 ward and those hospitalized in the non-COVID-19 wards (p <0.05). The sleep quality of those hospitalized in the COVID-19 ward was worse, and their anxiety and depression symptom scores were higher (p = 0.003, p = 0.011, and p = 0.018, respectively) (Table 3).

For the PSQI, when sleeping in the COVID-19 ward, age, sex, anxiety, and depression were assessed together, stay in the non-COVID-19 ward decreased the PSQI score. An increase in the depression score in patients aged of 65 years and above also increased the PSQI (p <0.05). These variables accounted for 30.9% of the PSQI (p <0.001).

Increased depression scores were accompanied by increased anxiety scores (p <0.05). This variable accounted for 55.8% of the anxiety scores (p <0.001).

**Table 3:** Comparison of PSQI components, total PSQI scores, anxiety and depression scores of patients under the age of 65 and over from Covid service and non-covid service

	Covid services				p <sub>age</sub>	Non-Covid services				p <sub>age</sub>	Total				p <sub>age&lt;65group</sub>	p <sub>age≥65group</sub>	p <sub>group</sub>			
	<65 age	≥65 age	Total			<65 age	≥65 age	Total			<65 age	≥65 age	Total							
	Mean±SD (min-max)	Median [IQR]	Mean±SD (min-max)	Median [IQR]	Mean±SD (min-max)	Median [IQR]	Mean±SD (min-max)	Median [IQR]	Mean±SD (min-max)	Median [IQR]	Mean±SD (min-max)	Median [IQR]	Mean±SD (min-max)	Median [IQR]	Mean±SD (min-max)	Median [IQR]	Page	Page<65group	Page≥65group	Page
Component 1: subjective sleep quality	0.98±0.76 (0-3)	1 [0-1]	1.37±0.84 (0-3)	1 [1-2]	1.13±0.81 (0-3)	1 [1-2]	0.061	0.91±0.8 (0-3)	1 [0-1]	1.15±0.77 (0-3)	1 [1-2]	0.168	0.94±0.78 (0-3)	1 [0-1]	1.26±0.81 (0-3)	1 [1-2]	<b>0.022</b>	0.586	0.365	0.338
Component 2: Sleep latency	1.07±0.82 (0-3)	1 [0.25-2]	1.41±0.89 (0-3)	1 [1-2]	1.2±0.86 (0-3)	1 [1-2]	0.110	0.68±0.71 (0-2)	1 [0-1]	1.04±0.65 (0-2)	1 [1-1]	<b>0.032</b>	0.88±0.79 (0-3)	1 [0-1]	1.22±0.79 (0-3)	1 [1-2]	<b>0.012</b>	<b>0.025</b>	0.108	<b>0.008</b>
Component 3: sleep time	0.45±0.66 (0-2)	0 [0-1]	0.89±1.05 (0-3)	1 [0-2]	0.62±0.85 (0-3)	0 [0-1]	0.092	0.18±0.45 (0-2)	0 [0-0]	0.41±0.57 (0-2)	0 [0-1]	<b>0.048</b>	0.32±0.58 (0-2)	0 [0-1]	0.65±0.87 (0-3)	0 [0-1]	<b>0.016</b>	<b>0.026</b>	0.107	<b>0.009</b>
Component 4: sleep efficiency	0.45±0.66 (0-3)	0 [0-1]	0.74±0.94 (0-3)	1 [0-1]	0.56±0.79 (0-3)	0 [0-1]	0.217	0.27±0.5 (0-2)	0 [0-0.75]	0.63±0.69 (0-2)	1 [0-1]	<b>0.017</b>	0.36±0.59 (0-3)	0 [0-1]	0.69±0.82 (0-3)	1 [0-1]	<b>0.011</b>	0.166	0.932	0.294
Component 5: Sleep disturbance	1.39±0.89 (0-3)	2 [1-2]	1.78±0.8 (0-3)	2 [1-2]	1.54±0.88 (0-3)	2 [1-2]	0.100	1±0.75 (0-3)	1 [0.25-1]	1.3±0.82 (0-3)	1 [1-2]	0.167	1.19±0.84 (0-3)	1 [1-2]	1.54±0.84 (0-3)	1 [1-2]	<b>0.035</b>	<b>0.026</b>	<b>0.024</b>	<b>0.002</b>
Component 6: drug use	0.34±0.83 (0-3)	0 [0-0]	0.48±1.01 (0-3)	0 [0-0]	0.39±0.9 (0-3)	0 [0-0]	0.633	0.18±0.45 (0-2)	0 [0-0]	0.74±1.99 (0-10)	0 [0-1]	0.138	0.26±0.67 (0-3)	0 [0-0]	0.61±1.57 (0-10)	0 [0-1]	0.166	0.669	0.637	0.988
Component 7: daytime functions	0.77±1.46 (0-6)	0 [0-1]	2±1.92 (0-6)	1 [0-4]	1.24±1.74 (0-6)	0 [0-2]	<b>0.001</b>	0.86±1.19 (0-4)	0 [0-2]	1±1.59 (0-6)	1 [0-1]	0.673	0.82±1.33 (0-6)	0 [0-1]	1.5±1.82 (0-6)	1 [0-2]	<b>0.004</b>	0.423	<b>0.030</b>	0.527
PSQI	5.48±3.39 (0-18)	5 [3-7.75]	8.44±4.25 (1-18)	9 [5-10]	6.61±3.98 (0-18)	6 [4-9]	<b>0.002</b>	4.05±2.93 (0-10)	3 [1.25-6]	5.93±2.93 (3-13)	5 [4-8]	<b>0.006</b>	4.76±3.23 (0-18)	4 [2-7]	7.19±3.84 (1-18)	6 [4-10]	<b>&lt;0.001</b>	<b>0.030</b>	<b>0.010</b>	<b>0.003</b>
Anxiety	11.5±10.86 (0-54)	7.5 [5-15]	21.67±15.55 (5-63)	15 [9-28]	15.37±13.68 (0-63)	11 [6-19]	<b>&lt;0.001</b>	6.95±8.28 (0-50)	5 [2-9]	16.59±11.39 (0-46)	15 [10-22]	<b>&lt;0.001</b>	9.23±9.87 (0-54)	6 [3-11]	19.13±13.74 (0-63)	15 [9.75-24.25]	<b>&lt;0.001</b>	<b>0.011</b>	0.372	<b>0.011</b>
Depression	12.27±7.17 (2-27)	9.5 [7-19.25]	18.52±9.94 (5-46)	18 [12-22]	14.65±8.81 (2-46)	12 [8-22]	<b>0.005</b>	8.45±6.92 (0-31)	7.5 [3-10.75]	16.44±8.27 (3-35)	17 [11-21]	<b>&lt;0.001</b>	10.36±7.27 (0-31)	8 [5-13.75]	17.48±9.12 (3-46)	13.07±8.71 (0-46)	<b>&lt;0.001</b>	<b>0.008</b>	0.556	<b>0.018</b>

Mann Whitney U test, p<sub>age</sub>: comparison of under 65 and over,

p<sub>age<65group</sub>: Comparison of covid service and non-covid service under 65, p<sub>age≥65group</sub>: Comparison of covid service and non-covid service aged 65 and above, p<sub>group</sub>: Comparison of covid service and non-covid service PSQI: Pittsburg Sleep Quality Index.



Increased PSQI and anxiety scores also increased the depression score ( $p < 0.05$ ). These variables accounted for 56.9% of the depression scores ( $p < 0.001$ ) (Table 4).

## DISCUSSION

While medical complications are generally noted during the COVID-19 epidemic, the effects of SARS-CoV-2 on mental health and sleep quality should not be ignored. Considering that many psychiatric disorders were noted after the SARS-CoV-1 epidemic in 2002–2003, the effects of the SARS-CoV-2 epi-

demio on the mental health should be examined. In our study, we found that patients over 65 years of age generally had worse sleep quality and higher anxiety and depression symptom scores. Being in the COVID-19 ward directly affected sleep quality negatively, especially in patients over the age of 65 years, and caused sleep disturbances. In addition, we found that the anxiety and depression symptoms of the patients in the COVID-19 ward were significantly higher than of those in the non-COVID-19 ward, especially in those aged  $>65$  years.

In a meta-analysis on the effects of the COV-

**Table 4:** The relationship between PSQI, anxiety and depression scores, age, gender, service and each other

		Unstandardized Coefficients		Standardized Coefficients	t	p
		B	Std. Error	Beta		
PSQI R <sup>2</sup> :0,309 p<0,001	(Constant)	3.903	0.603		6.472	<b>&lt;0.001</b>
	Non-covid services	-1.237	0.533	-0.170	-2.321	<b>0.022</b>
	Age ( $\geq 65$ )	1.188	0.596	0.158	1.993	<b>0.048</b>
	Sex (female)	-0.644	0.539	-0.087	-1.194	0.235
	Anxiety	0.045	0.031	0.154	1.444	0.151
	Depression	0.125	0.044	0.297	2.815	<b>0.006</b>
Anxiety R <sup>2</sup> :0,558 p<0,001	(Constant)	-1.806	1.868		-0.967	0.335
	Non-covid services	-1.363	1.472	-0.055	-0.926	0.356
	Age ( $\geq 65$ )	2.409	1.630	0.094	1.478	0.142
	Sex (female)	2.842	1.453	0.113	1.956	0.053
	Depression	0.877	0.098	0.615	8.908	<b>&lt;0.001</b>
	PSQI	0,334	0.231	0.098	1.444	0.151
Depression R <sup>2</sup> :0,569 p<0,001	(Constant)	4.707	1.233		3.819	<b>&lt;0.001</b>
	Non-covid services	-0.347	1.021	-0.020	-0.340	0.734
	Age ( $\geq 65$ )	1.952	1.124	0.109	1.736	0.085
	Sex (female)	-0.402	1.019	-0.023	-0.394	0.694
	PSQI	0.441	0.157	0.185	2.815	<b>0.006</b>
	Anxiety	0.420	0.047	0.599	8.908	<b>&lt;0.001</b>

p: Multiple Linear Regression

PSQI: Pittsburgh Sleep Quality Index,

ID-19 pandemic on mental health, 43 studies were examined, and only two of them evaluated patients infected with COVID -19. Of these 43 studies, 41 were conducted on healthcare workers and the general population. In the two studies on COVID-19 patients, high levels of post-traumatic stress symptoms (PTSS) (96.2%) and significantly higher depressive symptoms ( $p = 0.016$ ) were observed (16).

In a study by Zhang et al. in COVID-19 patients, 20.9% and 18.6% had symptoms of anxiety and depression, respectively. In Guo et al.'s study, 38.8%, 45.9%, and 54.1% of patients had symptoms of anxiety, depression, and a sleep disorder, respectively. Finally, Dai et al. found symptoms of anxiety and depression and poor sleep quality in 18.6%, 13.4%, and 84.7% of patients, respectively (17, 8, 9). Female sex, having colleagues infected with COVID-19, poor sleep quality, more than two physical symptoms of anxiety, having a family member infected with COVID-19, and more than two physical symptoms of Covid-19 were identified as the greatest risk factors for depression (9, 17). In addition, the quarantine period and some inflammatory markers may affect these parameters (17). In our study, 66.2%, 63.4%, and 53.3% of patients in the COVID-19 ward had symptoms of anxiety, depression, and sleep disturbances, respectively. Thus, the results of these studies on anxiety and depression and the factors affecting them are discrepant. In our study, being in quarantine and being over 65 years of age increased the symptoms of anxiety and depression and negatively affected the sleep quality. Our study was conducted in patients hospitalized in isolated COVID-19 wards. Patients were kept in quarantine in single rooms for an average of 10–14 days until their treatment was completed, and nobody could enter or leave the room except for the medical staff. In addition, communication was facilitated through room phones. There was only one companion allowed, especially for elderly patients who could not perform self-care. The patients remained secluded from their relatives, friends, and social circles dur-

ing their hospitalization periods. It is impossible for social isolation not to adversely affect the mental health of patients (18). Many studies have reported that curfew, quarantine, and isolation conditions increase the symptoms of anxiety and depression (18).

A previous study reported that COVID-19 patients hospitalized with mild symptoms showed higher levels of depression, anxiety, and PTSS than non-COVID-19 controls (8). In our study, patients hospitalized in the COVID-19 ward showed a significantly higher rate of anxiety and depression symptoms than those hospitalized in non-COVID-19 wards; in addition, their sleep quality was worse. In our study, we did not assess PTSS but evaluated the sleep quality of the patients according to seven components of the PSQI and the total PSQI score. We found that the sleep quality of patients hospitalized in the COVID-19 ward, especially those over 65 years of age, was worse. We found that these patients had worse daytime functions. Moreover, they had difficulty staying awake during daily activities such as drinking, eating, and socializing; they also had reluctance in doing these activities regularly.

It was observed that COVID-19 patients showed higher symptoms of anxiety and depression in the first week of hospitalization, and that these symptoms decreased 1 month following hospitalization (19). Some studies have reported mental health problems and changes in sleep quality, even after hospital discharge (20). Some studies have emphasized the importance of social support after discharge, as well as during hospitalization (20). We followed the patients during hospitalization and did not assess them after discharge. COVID-19 patients should be followed up even after discharge, and if necessary, the duration of psychological support should be extended.

Bao et al, 49.8% of patients reported that psycho-education services provided in the hospital were useful (6). Given the detrimental impact of PTSS, appropriate psychological interventions and



long-term follow-up evaluations for COVID-19 patients should be urgently initiated. Healthcare professionals, particularly clinical nurses, should be aware of the psychological state of COVID-19 patients and promote resilience to improve their mental health. Mental and physical health in the elderly is adversely affected by social isolation. Therefore, a multi-component program that includes exercise and psychological strategies is highly recommended for this population during quarantine. In our study, psychiatric consultation was requested for patients with clinical psychological disturbances, and medical treatment was initiated if necessary. However, these were not recorded during the study and were excluded. Further studies are needed on patients aged >65 years who are admitted in the COVID-19 ward and need psychological support.

Ozamis et al. measured anxiety, stress, and depression levels in a sample of 976 adults using the Depression Anxiety and Stress Scale (DASS) during the COVID-19 pandemic. They observed higher levels of anxiety, depression, and stress, especially in people under 60 years of age and in those with chronic conditions (18). They also stated that the anxiety and depression symptoms of the patients increased after the quarantine order was given. The authors recommend psychological support to alleviate the psychological effects of the pandemic. Similarly, we found that quarantine conditions increased the symptoms of anxiety and depression in our study. In our study, unlike the Ozamycin study,

anxiety and depression symptoms were found to be higher in the geriatric population. These differences may be due to the study population, age of the patients, presence of chronic disease, quarantine status, hospitalization, and COVID-19 positivity.

This study had several limitations. We did not assess patients' comorbid diseases and quarantine periods. In addition, we did not record anxiety and depression symptoms or the sleep quality of the patients after discharge. Our study was conducted in a small population, and more extensive studies in larger populations may yield more robust conclusions.

## CONCLUSION

During the COVID-19 pandemic, anxiety and depression symptoms were observed and sleep quality was deteriorated in patients aged >65 years who were placed in quarantine. Hence, this group of patients should be closely monitored in terms of psychological disorders and sleep disorders. If necessary, psychological support and medical treatment should be provided.

**CONFLICT OF INTEREST STATEMENT:** None

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## RESEARCH

# VALUATION OF THE RELATIONSHIP BETWEEN THE END OF LIFE HOSPITALIZATION NEEDS AND EARLY PRESENTING TO PALLIATIVE CARE

## ABSTRACT

**Background:** For a number of reasons, hospitalizations, and the need for intensive care increases during the last months of life in patients with life-threatening illnesses. We aimed to investigate the impact of the timing of presenting to palliative care on hospitalization (intensive care unit, palliative care and other departments inpatient services) during the end-of-life period and finally places of the death.

**Methods:** We conducted a retrospective analysis of the hospitalization data of adult patients who were treated in the Tokat Gaziosmanpaşa University Palliative Care Center and died between January 1, 2019, and June 30, 2020. Data that included the duration of time spent in inpatient care and the intensive care units at the end of life and the place of death were compared in relationship to their time of presentation to palliative care. Presentation timing was evaluated as early (>90 days before death) or late (<90 days before death) period.

**Results:** A total of 146 patients were included: 66.4% applied to the palliative care center in the late period and 33.6% in the early period. Their mean age was 67.4 years. The patients in the early-presenting group were found to have been hospitalized for less statistically significant time during the last six weeks of their lives ( $p = 0.002$ ). However, the data do not show a statistically significant difference between the groups in terms of length of stay in the intensive care unit.

**Conclusion:** For cancer patients, earlier palliative care provides improvement in symptom control, increases their quality of life, decreases unnecessary hospitalizations.

**Keywords:** Palliative Care; Terminal Care; Hospitalization; Intensive Care Units; Death.

## INTRODUCTION

The number of patients in need of palliative care is increasing both in our country and throughout the world. This is a consequence of the prolongation of life expectancy alongside increasing developments in medical practice and the increase in the incidence of neurological diseases and cancer. The general principle of palliative care involves the rapid and holistic assessment of patients, including their physical, social, and spiritual needs, and treatment in order to higher life quality. Studies have demonstrated that earlier palliative care consulting increase the quality of life of the patients and reduce the need for hospitalization and intensive care at the end of life as well (1).

Studies evaluating the early application of palliative care reported that patients were more satisfied with the care and that they referred to emergency room care, hospitalization, and time in the intensive care unit (ICU) less frequently. On the other hand the fact that patients have additionally been shown to have better mood and quality of life and less depression was emphasized in the same study (2). These studies also accentuated that patients who are able to use palliative care services more effectively are more likely to die at home rather than in hospital (1,2). Another study showed that the quality of life increased the most in cancer patients who started earlier palliative care (3).

The retrospective evaluation of subjects such as palliative care access timing, hospitalization periods in follow-up, intensive care needs, and the place of death are beginning to find a place in the literature. In this study, we aim to contribute to the literature by evaluating the impact of the timing of presenting to palliative care on total hospitalization (intensive care unit, palliative care and other departments inpatient services) during the end-of-life period and places of the death.

## MATERIAL AND METHODS

The Tokat Gaziosmanpaşa University Palliative Care Center provides holistic treatment services, including both outpatient and inpatient. The adult terminal stage cancer patients who were treated in our palliative care center (inpatient or outpatient) and who died between January 1, 2019, and June 30, 2020, constituted the universe of our study. There were 213 patients who met these criteria; 67 who had missing data in their patient records were excluded from the study. Our study was conducted using the data obtained by a retrospective scanning of 146 patient records whose information was accessed completely. The patients in our study were examined in two groups: an early-presenting group (>90 days before death) and a late-presenting group (<90 days before death), based on the date of death. The 90-day limit was determined according to the definition of early palliative care specified in similar studies in the literature (4, 5). The groups were analyzed in relationship to the variables of age, gender, and hospitalization in the palliative care service, other department inpatient services, intensive care unit during the last six weeks of their lives and the places of death. In the comparative analysis, the length of stay in the hospital was evaluated as "never," "short," between one and 10 days, and "long" for more than 10 days.

Ethical approval for our study was obtained from the Tokat Gaziosmanpaşa University Ethics Committee (20-KAEK-252).

The research data were analyzed with the SPSS v20 ready-made package program. Descriptive statistics (percentage, mean, and standard deviation) were used in the evaluation of the demographic data. The Chi-square test was used for comparisons between groups. The statistical significance level was accepted as  $p < 0.05$ .



## FINDINGS

In our study, 98 (67.1%) of the patients were male and 48 (32.9%) were female. Their mean age was  $67.4 \pm 11.8$  years. (Table 1) When evaluated according to the time of the first application to palliative care, 97 (66.4%) patients were found to have applied during the late period and 49 (33.6%) applied in the early period. In the late-presenting patient group, the average hospital stay was  $6.79 \pm 8.92$  days, and the average intensive care stay was  $2.06 \pm 5.15$  days. In the early-presenting group, the mean hospital stay was  $5.32 \pm 7.21$  days, and the average intensive care stay was  $2.12 \pm 4.18$  days.

Regarding the comparisons of the hospitalizations in the last six weeks of their lives, the patients in the early-presenting group were hospitalized for less statistically significant time ( $p = 0.002$ ). When the total hospitalization stays were compared, it was seen that 38.8% of the patients in the early-presenting patients group had no hospitalization at all, and this rate was 15.5% in the late-presenting patients group. It was observed that the long-term (>10 days) total hospitalization rate was significantly higher in the late-presenting patients group. In terms of inpatient treatment in palliative care and other clinical inpatient services, the patients in the early-presenting group were found to have had less statistically significant need for treatment ( $p < 0.001$ ). Similar to the total hospitalization rates, in the comparison of inpatient service stays, the rate of no hospitalization was higher in the early admission group (55.1%) than the late admission group (24.7%), and the long-term

hospitalization rate was found to be lower. Regarding comparison of palliative care inpatient service stay duration, it is seen that hospitalizations of the patients in the early-presenting group were shorter statistically significantly ( $p < 0.05$ ). However, the data do not show a statistically significant difference between the groups in terms of length of stay in the ICU. Information regarding the hospitalizations of the groups is summarized in Table 2.

When the patients' places of death were examined, no statistically significant difference was found between the patient groups. However, although approximately half (46.9%) of the patients in the early-presenting group died at home, it is noteworthy that this rate remained at 35% in the late-presenting group. The data regarding the place of death of the patients are summarized in Table 3.

## DISCUSSION

In our study which we investigated the impact of presenting timing to the palliative care center on hospitalization status in the end of life and places of death, the patients who present to palliative care center in the early period were found to have been hospitalized for less statistically significant time during the last six weeks of their lives. However, the data showed that there was no statistically significant difference between the groups in terms of length of stay in the intensive care unit. Similarly, a statistically significant difference was not found between the patient groups regarding places of death.

**Table 1.** Gender and age data of patients

Variables		Early-presenting Patients Group	Late-presenting Patients Group	Total
Gender	Male n (%)	37 (37.8)	61 (62.2)	98 (100)
	Female n (%)	12 (25)	36 (75)	48 (100)
Age (Mean $\pm$ SD)		$67.8 \pm 12.9$	$67.2 \pm 12.3$	$67.4 \pm 11.8$

**Table 2.** Hospitalization data

Hospitalization		Early-presenting Patients Group n (%)	Late-presenting Patients Group n (%)	p
Inpatient Service Stay	Never (0 day)	27 (55.1)	24 (24.7)	<b>&lt;0.001</b>
	Short (0-10 day)	19 (38.7)	44 (45.3)	
	Long (>10 day)	3 (6.1)	29 (29.9)	
	Total	49 (100)	97 (100)	
Palliative Care Inpatient Service Stay	Never (0 day)	31 (63.3)	40 (41.2)	<b>&lt;0.05</b>
	Short (0-10 day)	15 (30.6)	45 (46.4)	
	Long (>10 day)	3 (6.1)	12 (12.4)	
	Total	49 (100)	97 (100)	
ICU Stay	Never (0 day)	34 (69.4)	73 (75.2)	0.488
	Short (0-10 day)	12 (24.5)	16 (16.5)	
	Long (>10 day)	3 (6.1)	8 (8.2)	
	Total	49 (100)	97 (100)	
Total Hospitalization Stay	Never (0 day)	19 (38.8)	15 (15.5)	<b>0.002</b>
	Short (0-10 day)	21 (42.8)	44 (45.3)	
	Long (>10 day)	9 (18.3)	38 (39.1)	
	Total	49 (100)	97 (100)	

\*The Chi-square test was used

**Table 3.** Places of Death Data

Groups	Place of Death n (%)			p
	Home	Inpatient Services	ICU	
Early-presenting Patients Group	23 (46.9)	11 (22.4)	15 (30.6)	0.09
Late-presenting Patients Group	34 (35)	42 (43.3)	21 (21.6)	



Due to a decrease in performance capacity and increased symptom burden in the last six months of life, hospital admissions are frequent in palliative care patients. For various reasons such as emergency room applications, hospitalizations, and the need for intensive care, the time spent in a hospital increases during the last months of life. Researchers are endeavoring to reduce this time. In the literature, there is tremendous interest in studies directed toward reducing aggressive treatment approaches and hospitalization costs (6, 7). Hospitals and intensive care units, in particular, are not desirable places to die. Because of both the uneasiness that they feel regarding the discontinuation of treatment for the primary diagnosis and for a range of social and cultural reasons, patients and caregivers do not tend to prefer the palliative approach, consequently, intensive care admissions increase at the end of life (8). Even so, studies have shown that the early initiation of palliative care relieves symptom burden and leads to fewer hospital admissions during the end-of-life period (9, 10).

In investigating the influence of palliative care timing on the hospitalization of our patients in the last six weeks of their lives, in our study, we observed that there were statistically significantly fewer hospitalizations into inpatient services and total hospitalizations (inpatient service + intensive care) in the patient group receiving palliative care during the early period. There was no significant difference between the two groups when considering the length of the stay in the intensive care unit in the last six weeks. Although no statistically significant difference was observed, when the patients' places of death were evaluated, the rate of dying at home was found to be higher in the early palliative group in comparison to the late period group.

The study that Temel et al. (11) conducted in 2010 with patients with newly diagnosed metastatic non-small-cell lung cancer brought the timing of palliative care to the agenda. In this study, two patient groups were compared who had been referred

to palliative care at the time of diagnosis and continued with standard oncological treatment. Randomly assigned patients' clinic data were recorded for three years. The patients who received palliative care concomitantly with the cancer diagnosis were hospitalized less, received less chemotherapy, and had a higher quality of life at the end of their lives. In the same study, the palliative care group was found to have lived four months longer than the control group (11). In their study with advanced cancer patients, especially in their investigation of the effectiveness and timing of outpatient palliative care treatment, Blackhall et al. (9) showed that, although they applied to their centers in the last three to four months of their lives, the patients needed less hospitalization. The results of our study as earlier palliative care decrease hospitalization at the end of life, are similar to those of others in the literature.

The Robbins et al. (4) in retrospective cohort study utilizing hospital and hospice administrative databases study, which investigated the effects of palliative care consultation timing, found that early stage patients whose palliative care admissions were 90 days before death had fewer hospitalizations and that their intensive care needs especially decreased. In a retrospective cohort study by Romano et al. (2), patients with advanced stage cancer were examined in two groups: those receiving early palliative care and those receiving standard oncological treatment. These authors found that the control group had more statistically significant intensive care hospitalizations than the palliative care group. However, there was no difference between the groups when the duration of the intensive care stays and the intensive care procedures were evaluated (2). In our study, no statistically significant difference was observed between the early and the late palliative care patient groups in the evaluation of the length of stay in the intensive care unit. The reason for this may be the low number of patients and variety of diagnosis of our patients.

Most individuals with life-threatening illnesses want to die at home rather than in a hospital. In this

respect, the place of death can be considered as one of the quality indicators of end-of-life care (12). The Blackhall et al. (9) study found that the control group died in a hospital at a higher rate in comparison to the palliative care group. Similarly, the study by Romano et al. (2) found that the death rate in the hospital and intensive care units was reported to be lower in the patient group receiving early palliative care. Although no statistically significant difference was found between the early and the late palliative patient groups in our study, the rate of death at home was higher in the early-presenting palliative patient group in comparison to the late-presenting patient group.

The limitations of our study include the fact that our study was conducted in a single center, a small number of patients were included in the study.

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## CONCLUSION

The findings in our study emphasized that, for terminal stage cancer patients who need frequent hospital referrals and hospitalizations due to severe symptom burden and deterioration in the quality of life, early contact with palliative care will result in improvement in symptom control, in a decrease in unnecessary hospital and intensive care hospitalizations, an increase in the patient's quality of life, and a decrease in medical expenses. These findings are in concurrence with those of the literature. Therefore, we feel that it is important that palliative care centers become widespread and that the number of competent palliative care teams be increased.



## RESEARCH

# DEPRESSION AND ANXIETY LEVELS IN A GROUP OF ELDERLY WITH TEMPOROMANDIBULAR DISORDERS

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### ABSTRACT

**Introduction:** The objective of this study was to assess stress and anxiety in a sample of elderly patients suffering from temporomandibular joint disorders who did not have previously diagnosed emotional disturbances. It is well known that patients presenting with temporomandibular joint disorders are more commonly affected by anxiety and depression. However, there is a lack of data regarding the prevalence of undiagnosed anxiety and emotional stress disorders among elderly patients with temporomandibular joint disorders.

**Materials and Method:** Clinical examination was performed using Research Diagnostic Criteria (Axis I). Patients with previously diagnosed and managed psychiatric and psychological disorders were excluded. Magnetic resonance imaging findings were also used to confirm the diagnosis. Beck Depression Inventory and Beck Anxiety Inventory forms were obtained to assess stress and anxiety levels.

**Results:** A total of 125 patients (103 [82.4%] women and 22 [17.6%] men) aged 60 to 87 ( $71.89 \pm 10.39$ ) years were included. The highest depression and anxiety scores were found among patients suffering from bruxism, followed by those with disc displacement without reduction and myofascial pain syndrome. All the patients showed significantly elevated depression levels.

**Conclusion:** The emotional health status of elderly patients with intra- and extra-articular temporomandibular joint disorders should be attentively assessed.

**Key words:** Anxiety; Depression; Temporomandibular Joint Disorder.

## INTRODUCTION

Temporomandibular joint disorders (TMDs) are fundamentally painful, affecting the temporomandibular joint (TMJ) together with the masticatory system and innervation of the head and neck (1), and they are detected at an incidence rate of about 25% in general society (1). Considering the complex modality of the TMJ, the symptoms can be variable, including local or spreading pain in the TMJ or masticatory muscles, crepitation, dislocation, or clicking on the movement of the TMJ, severe headache in the temporal region, and tinnitus (2). Even though TMD symptoms were seen in each age group and affect 90% of the general population at one or another life stage (3), TMDs were mostly determined between the third and fifth decades of life (4). However, studies focusing on TMDs in elderly patients are limited (5).

The aetiological factors of TMDs could be biological, environmental, social, emotional, and/or cognitive. Moreover, the effects of emotional status on the symptoms and prognosis of TMDs have been widely discussed and several studies have also shown that parafunctional habits, muscle hyperactivity, and micro-occlusal trauma could result from emotional stress disorders; thus, elevated stress, anxiety, and/or depression levels could correlate with TMD-related signs and symptoms (6).

The classification of TMDs was described at the International Research Diagnostic Criteria for Temporomandibular Dysfunction Consortium Network in 2013 (7) the Validation Project determined that the RDC/TMD Axis I validity was below the target sensitivity of  $\geq 0.70$  and specificity of  $\geq 0.95$ . Consequently, these empirical results supported the development of revised RDC/TMD Axis I diagnostic algorithms that were subsequently demonstrated to be valid for the most common pain-related TMD and for one temporomandibular joint (TMJ). TMDs were mainly subdivided into intra- and ex-

tra-articular pathologies. Among extra-articular manifestations, myofascial pain syndrome has been shown to be the most frequent cause of orofacial pain (42.0%), whereas disc displacement without reduction (32.1%) is the most common painful intra-articular pathology (7) the Validation Project determined that the RDC/TMD Axis I validity was below the target sensitivity of  $\geq 0.70$  and specificity of  $\geq 0.95$ . Consequently, these empirical results supported the development of revised RDC/TMD Axis I diagnostic algorithms that were subsequently demonstrated to be valid for the most common pain-related TMD and for one temporomandibular joint (TMJ). Besides, osteoarthritis is suggested to be the magnetic resonance characteristic of TMJ disc displacement in elderly patients (5).

Over the last decades, the correlation between TMDs and emotional status has been widely studied (6,8). It is well known that patients presenting with TMDs are more commonly affected by anxiety and depression (6). However, there seems to be a lack of data on the prevalence of undiagnosed anxiety and emotional stress disorders among elderly patients with TMDs. Therefore, the objective of this study was to assess the level and prevalence of stress and anxiety in a sample of patients suffering from TMDs.

## MATERIALS AND METHODS

This study was conducted in accordance with the Helsinki Declaration. Ethical approval was obtained from the Committee of Non-invasive Clinical Studies (03 January 2018, 1/17). The patients were informed, and written consent forms were obtained.

### Study Design

This study was conducted between April and December 2020; the study groups consisted of patients who were referred to the Department of Oral



and Maxillofacial Surgery with complaints of TMDs. The Research Diagnostic Criteria for TMDs (RDC/TMD) Axis I was applied to identify TMDs (7) the Validation Project determined that the RDC/TMD Axis I validity was below the target sensitivity of  $\geq 0.70$  and specificity of  $\geq 0.95$ . Consequently, these empirical results supported the development of revised RDC/TMD Axis I diagnostic algorithms that were subsequently demonstrated to be valid for the most common pain-related TMD and for one temporomandibular joint (TMJ). According to The Research Diagnostic Criteria for TMDs (RDC/TMD) Axis I (7);

Group I: Muscle Disorders

- I. a. Myofascial Pain
- I. b. Myofascial Pain with Limited Opening
- I. c. Myofascial Pain with Referral
- I. d. Temporalis Tendonitis

Group II: Disc Displacements

- II. a. Disc Displacement with Reduction
- II. b. Disc Displacement without Reduction without Limited Opening
- II. c. Disc Internal Derangement with Reduction with Transient Limited Opening
- II. d. Disc Internal Derangement without Reduction with Limited Opening

Group III: Arthralgia/Arthritis/Arthrosis

- III. a. Arthralgia /Arthritis
- III. b. Osteoarthritis /Degenerative Joint Disease
- III. c. Osteoarthrosis /Degenerative Joint Disease

Group IV: Temporomandibular Joint Hypermobility

- IV. a. Subluxation/Luxation

Group V: Tension-type Headache with Temporalis Muscle Tenderness

- V. a. Infrequent Episodic Tension-type Headache Involving the Temporalis Muscle

- V. b. Frequent Episodic Tension-type Headache Involving the Temporalis Muscle
- V. c. Chronic Tension-type Headache Involving the Temporalis Muscle

Magnetic resonance imaging (MRI) findings were also used to confirm the diagnosis. The patients were subdivided into five groups according to their diagnosis:

- Group I: Anterior disc displacement with reduction
- Group II: Anterior disc displacement without reduction
- Group III: Bruxism
- Group IV: Myofascial pain syndrome
- Group V: Control group (patients who presented with complaints other than TMDs)

Patients with previously diagnosed and managed psychiatric and psychological disorders such as depression, anxiety, and personality disorders, neurological disorders, Eagle syndrome, rheumatologic disorders affecting the TMJ, and acute TMD symptoms and those younger than 60 years were excluded. Their socio-demographic data and Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) forms were obtained.

Briefly, the BDI consists of 21 questions quantified by summing the scores between 0 and 3 obtained for each answer, which defines the depression level (9). Values 0–9 are determined as normal, 10–18 mild, 19–29 moderate, and 30–63 severe depression. Similarly, the BAI is a Likert-type scale scored between 0 and 3, which consists of 21 items and is used to determine the frequency and level of anxiety symptoms (10). Values 0–7 are considered normal, 8–15 mild, 16–25 moderate, and 26–63 severe anxiety.

According to the answers and scores obtained from the forms and scales, the relationship determinants of anxiety and depression and parameters such as the classification of TMDs into two groups

and their age and gender distributions were comparatively assessed.

### Statistical Analysis

Study data were analysed using Minitab 17 (Minitab Inc., State College, PA, USA). The Shapiro–Wilk test was run to analyse the normality of the parameters. In descriptive statistical evaluation, one-way analysis of variance, chi-squared test, and Bonferroni corrections were used to compare the groups. The Mann–Whitney *U* test was used to evaluate parameters which did not show normal distribution. Statistical results were evaluated at a 95% confidence interval and  $p < 0.001$  and  $<0.05$  significance level.

### RESULTS

A total of 125 patients (103 [82.4%] women and 22 [17.6%] men) aged 60–87 ( $71.89 \pm 10.39$ ) years were included. The statistical differences in terms of age ( $p = 0.141$ ,  $>0.05$ ) were insignificant (Table

1). The mean age of the patients with anterior disc displacement with reduction was higher than that of the other groups (Table 1). There was no statistically significant difference in terms of the gender distribution among the subgroups ( $p = 0.143$ ,  $>0.05$ ; Table 1). However, the number of women was significantly higher in total.

A statistically significant difference was seen in depression scores between the patients with TMDs and the control group ( $p = 0.000^*$ ,  $<0.001$ ; Table 2). The highest depression scores were noted in the bruxism and disc displacement without reduction subgroups ( $p = 0.000^*$ ; Table 3). A statistically significant difference was also observed in the assessment of anxiety scores between the groups ( $p = 0.000^*$ ,  $<0.001$ ). The highest anxiety scores were found in the bruxism and myofascial pain syndrome groups (Table 3). However, a comparative analysis of the subgroups revealed that the patients with bruxism and disc displacement without reduction showed the highest differences compared to the control group, and both differences were also nearly equal (Table 4).

**Table 1.** Evaluation of demographic data between subgroups.

Classification of TMD	Age	Gender	
		♀ (n)	♂ (n)
Disc Displacement with Reduction	67.30±6.90	21	4
Disc Displacement without Reduction	71.88±11.77	20	5
Bruxism	73.85±12.32	21	4
Myofascial Pain Syndrome	74.93±11.96	20	5
Control	69.25±7.71	21	4
p	<sup>1</sup> p=0.141	<sup>2</sup> p=0.143	

The number of women was relatively higher in all groups. (TMD: temporomandibular disorder)



**Table 2.** Evaluation of depression scores according to the Beck depression inventory.

Classification of TMD	BDS	Evaluation of BDS	
Disc Displacement with Reduction	9.75 ±7.70	Mild depression	<b>p: 0.000*</b>
Disc Displacement without Reduction	12.40 ±7.90	Mild depression	
Bruxism	16.60 ±12.00	Mild depression	
Myofascial Pain Syndrome	11.28 ±8.39	Mild depression	
Control	5.675 ±3.892	Normal	

All patients showed mild depression scores, which were also significantly higher compared to the control group. (TMD: temporomandibular disorder, BDS: Beck Depression Score)

**Table 3.** Comparison of Beck Depression Scores between subgroups.

Comparison of Beck Depression Scores	p
Disc Displacement with vs without Reduction	0.079
Bruxism vs Disc Displacement with Reduction	0.011*
Disc Displacement with Reduction vs Myofascial Pain Syndrome	0.511
Disc Displacement with Reduction vs Control	0.020*
Disc Displacement without Reduction vs Bruxism	0.188
Disc Displacement without Reduction vs Myofascial Pain Syndrome	0.625
Disc Displacement without Reduction vs Control	0.000*
Bruxism vs Myofascial Pain Syndrome	0.042*
Bruxism vs Control	0.000*
Myofascial Pain Syndrome vs Control	0.007*

\*\*\* showing the significant differences. All subgroups showed significantly higher values compared to the control group. Patients with Bruxism and disc displacement without reduction showed the highest values, followed by the myofascial pain syndrome.

**Table 4.** Evaluation of anxiety scores between subgroups according to the Beck anxiety inventory.

Classification of TMD	BAS	Evaluation of BAS	
Disc Displacement with Reduction	11.28 ±9.74	Mild anxiety	<b>p: 0.000*</b>
Disc Displacement without Reduction	14.03 ±8.71	Mild anxiety	
Bruxism	22.65 ±13.50	Moderate anxiety	
Myofascial Pain Syndrome	16.23 ±14.70	Moderate anxiety	
Control	6.125 ±4.900	Normal	

Elevated anxiety scores were observed in all subgroup, whereas the patients with disc displacements showed mild and bruxism and myofascial pain syndrome patients showed moderate anxiety scores respectively. (TMD: temporomandibular disorder, BAS: Beck Anxiety Score)

**Table 5.** Comparison of Beck Anxiety Scores between subgroups.

Comparison of Beck Anxiety Scores	p
Disc Displacement with vs without Reduction	0.091
Bruxism vs Disc Displacement with Reduction	0.002*
Disc Displacement with Reduction vs Myofascial Pain Syndrome	0.209
Disc Displacement with Reduction vs Control	0.021*
Disc Displacement without Reduction vs Bruxism	0.004*
Disc Displacement without Reduction vs Myofascial Pain Syndrome	0.699
Disc Displacement without Reduction vs Control	0.000*
Bruxism vs Myofascial Pain Syndrome	0.039*
Bruxism vs Control	0.000*
Myofascial Pain Syndrome vs Control	0.001*

“\*\*” showing the significant differences. All subgroups showed significantly higher values compared to the control group. Patients with Bruxism and disc displacement without reduction showed the highest differences compared to the control group and both differences were also nearly equal.



All the TMD subgroups showed significantly higher depression and anxiety levels compared to the control group. The depression and anxiety scores among the subgroups revealed that the patients with bruxism had the highest scores. Those with bruxism and disc displacement without reduction showed the highest differences compared to the control group in the assessment of both depression and anxiety levels ( $p = 0.000^*$ ).

## DISCUSSION

The role of psychological factors in the aetiology of TMDs cannot be ignored, as they play a great role in many painful conditions and parafunctional habits of the human body (11). Psychological disorders have also been defined as key factors in the development of TMDs by some authors (12). Therefore, the prevalence of anxiety and stress in patients with TMDs has been studied in the literature (13). However, most studies have only focused on the prevalence of psychological disorders among patients with TMDs. The strength of this research, this is the first study to focus on undiagnosed stress and anxiety disturbances in elderly patients with TMDs, our knowledge.

Saeed and Riaz (14) TMD symptoms may be caused by different physiological and/or psychosocial factors. The purpose of this study is to determine the level of depression in patients with TMD. These findings can guide the diagnosis, prevention, and treatment of TMDs. In a prospective study, participants were screened and underwent a baseline physical examination of the head and neck, conducted according to the protocol of Research Diagnostic Criteria Axis I for Temporomandibular Disorders (RDC/TMD) to determine the depression levels in patients with TMDs and stated that moderate depression was more frequent in these patients (i.e. 30.7%), followed by severe depression (22.0%), extreme depression (16.0%), and borderline clinical depression (10.0%). Bertoli and de Leeuw (15) reported elevated suicidal ideation, depression, and

anxiety levels among patients with TMDs, especially in those with chronic muscle pain, compared to the general population. The current study results showed that patients with intra- and extra-articular TMJ pathologies presented with mild depression levels. Additionally, the assessment of anxiety levels revealed that the patients with intra-articular pathologies showed mild elevated anxiety levels, whereas those with extra-articular pathologies such as bruxism and myofascial pain syndrome showed moderate levels. Generally, both elevated stress and anxiety levels were in accordance with the existing literature (16).

Surprisingly, a comparative analysis of both the anxiety and depression scores of patients suffering from TMDs with disc displacement without reduction and the control group revealed nearly equal differences with the bruxism group. In the literature, an association between disc displacement with reduction and quality of life has been stated previously (17) 43 were included in the present study. Fonseca's anamnestic index was used for initial screening while axis I of the Research Diagnostic Criteria for Temporomandibular Disorders (RDC-TMD). However, studies focusing on the relation between TMJ disc displacement without reduction and elevated anxiety and/or depression levels are limited in terms of case studies (18). Considering the prevalence of the condition, this phenomenon might warrant further research.

Ogura et al (5) evaluated the magnetic resonance characteristics of TMJ disc displacement in elderly patients and stated that the incidence of disc displacement with osteoarthritis was significantly high (41.9%). In the current study, to avoid undiagnosed rheumatologic conditions which could mimic TMD symptoms and obscure the perceptions of the patients, those with osteoarthritis of the TMJ were excluded from the study.

The BDI and BAI scales were developed by Beck et al (9) and are used to quantify depression and determine the frequency and level of anxiety

symptoms (10). In the literature, the validity of both methods has been approved by several studies (19,20) pain threshold at pressure, pain vigilance, oral health-related quality of life (OHRQoL. In a recent study, Maślak-Bereś et al (20) as described by the Beck's Depression Inventory (BDI) have assessed the relationships between TMD/RDC clinical diagnoses and psycho-emotional status via the BDI and Perceived Stress Scale (PSS-10) and observed that in those with pain, the mean values on the BDI and PSS-10 scales were higher than those pain-free. Because of the complex modality of the TMJ region, MRI is the gold standard for assessing the internal derangements of the TMJ. Therefore, the results of TMD studies based solely on RDC and clinical findings could be controversial. In the current study, the intra-articular derangements of the TMJ were also confirmed via MRI.

Another point to discuss is the similarities in the need for treatment of both TMD and psychological disturbances. TMD-related problems occur in 90% of the population at least once in a lifetime; however, the need for treatment depends mainly on the pain perception and/or functional disturbances of a patient. Similarly, undiagnosed depression or elevated stress levels are common mental disorders with a prevalence varying from 20% to 53% in different decades of life (21), which could have a considerable effect on the health-related quality of life and satisfaction levels of patients. Additionally, it has also been proclaimed that there could be a significant delay in seeking treatment for the mental health of patients with TMD symptoms (22). Like patients with TMDs, not all elderly patients with undiagnosed depression or elevated stress levels need psychological evaluation and management; however, it should be kept in mind that undiagnosed depression could also lead to several outcomes if not managed properly.

It is also well known that because of the ongoing COVID-19 pandemic, most elderly people are in social isolation, which could be a "serious public

health concern" because of their heightened risk of cardiovascular, autoimmune, neurocognitive, and mental health problems (23). Moreover, recent studies have shown that social disconnection puts elderly people at greater risk of depression and anxiety (24) but less is known about the distinct contributions of different aspects of isolation. We aimed to distinguish the pathways through which social disconnectedness (eg, small social network, infrequent social interaction). As observed in the current study, the elevated anxiety and stress levels among elderly patients with TMDs might be related to their social disconnection due to the ongoing COVID-19 pandemic; however, further comparative studies with long-term results are necessary to determine the exact relation.

This study has clearly shown that bruxism is the main condition, which might be correlated to elevated anxiety and stress levels and requires multidisciplinary management. Many patients suffering from bruxism are also primarily seeking treatment from neurologists and/or psychiatrists. In the management of bruxism, selective serotonin reuptake inhibitors (SSRIs) could be a feasible option to overcome elevated stress and anxiety levels. However, at this point, a well-described (still underreported) condition should be highlighted. SSRI-associated bruxism, which could occur as an adverse reaction to antidepressant therapy, is a rare entity which neurologists, psychiatrists, and dentists should be aware of. Besides, increased blood pressure and sleep-related bruxism warrant further research; thus, the relationship between sleep apnoea and hypertension has not yet been well documented. Considering that systemic diseases and medication needs increase with age, dentists should properly review the medication of elderly patients with TMDs.

One might suggest that complete denture wearers are more likely to develop TMD symptoms; however, no robust association between prosthetic factors and TMD was found in the literature (25). Because of the controversies surrounding the asso-



ciation between TMD symptoms and edentulism, complete denture wearers were excluded from the study.

Patients with both intra- and extra-articular TMJ pathologies presented with elevated depression and anxiety levels, whereas those with bruxism, disc displacement without reduction, and myofascial

pain syndrome showed significantly higher anxiety and depression levels.

The literature is remarkably deficient in the evaluation of the relationship between TMD and the undiagnosed psychological status of a patient. Despite the limitations, the current study has confirmed that this relation warrants further research.

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## RESEARCH

# RELATIONSHIPS BETWEEN PARKINSON'S DISEASE DEMENTIA AND 25-HYDROXY VITAMIN D AND BRAIN-DERIVED NEUROTROPHIC FACTOR LEVELS

## ABSTRACT

**Introduction:** Parkinson's disease dementia is an important condition that worsens the quality of life in approximately 30% of parkinson disease patients. Vitamin D deficiency and brain-derived neurotrophic factor have been implicated in the pathogenesis of alzheimer type dementia, parkinson's disease, and many neurodegenerative diseases. The aim of this study was to investigate the relationship between cognitive impairment and 25-hydroxy vitamin D and brain-derived neurotrophic factor levels in parkinson's disease dementia patients.

**Materials and Method:** 25-hydroxy vitamin D and brain-derived neurotrophic factor serum levels were evaluated in patients with parkinson's disease dementia (n = 63) and healthy controls (n = 33). Brain-derived neurotrophic factor and vitamin D levels were examined using one sample t-tests, and multiple comparisons among independent groups were done using ANOVA post hoc Tukey's test analysis. Wechsler Memory Scale and Mini-Mental State Examination were used to evaluate the cognitive functions of the groups. The disease levels of the patients were determined using the Hoehn and Yahr scale and the Unified Parkinson's Disease Rating Scale.

**Results:** There was a significant negative correlation between the worsening of dementia and vitamin D levels ( $p = 0.009$ ). However, there were significant negative correlations between the unified parkinson's disease rating scale daily living activity and Hoehn and Yahr scales and vitamin D levels. No significant relationship was found between brain-derived neurotrophic factor and parkinson's disease dementia ( $p = 0.983$ ).

**Conclusions:** Vitamin D deficiency plays a role in cognitive loss in parkinson's disease dementia. Vitamin D replacement can be used in dementia support treatment.

**Keywords:** Parkinson Disease; Dementia; Vitamin D; Brain-Derived Neurotrophic Factor.

## INTRODUCTION

Idiopathic Parkinson's disease (IPD) is a progressive neurodegenerative disease that is accompanied by resting tremors, bradykinesia, rigidity, and postural disorders (1). Non-motor signs are also common in IPD but are mostly ignored. The incidence of IPD in all age groups ranges from 4.5 to 9 per 100,000 (2). Cognitive loss and dementia develop over the course of IPD in 30% of patients (3,4). Parkinson's disease dementia (PDD) constitutes 0.5% of all dementia cases in people over the age of 65 and 3–4% of the dementia cases in all age groups (5,6). Symptoms like rigidity and akinesia, recurring falls, and severe gait disorders are significant risk factors for slow-onset, severe cognitive deterioration (7). Frontal executive function disorders and memory errors are the main characteristics of the disease (7).

Vitamin D is a neuro-steroid hormone that has important roles in bone mineralization and the regulation of the calcium-phosphorus balance (8). Vitamin D has significant effects on the brain and has various roles in the central nervous system, in cell proliferation and differentiation, neurotransmission, and neuroplasticity as well as neuroprotection (9).

Brain-derived neurotrophic factor (BDNF) is a member of the neurotrophin family and is found in several brain regions (10). BDNF mainly affects neuron development and regeneration and the structural health of major neural pathways and their functioning. A correlation has been found between low BDNF levels and Alzheimer's disease (11,12). It is believed that BDNF is also associated with other neurodegenerative diseases, including IPD (13).

The aim of this study was to investigate the relationship between cognitive impairment and 25-hydroxy vitamin D (25 (OH) vitamin D) and BDNF levels in PDD patients.

## MATERIALS AND METHODS

### Patient Selection

The study included 63 patients with IPD who were followed up in the Movement Disorders Clinic of the Department of Neurology, Inonu University, and 33 healthy individuals of similar age and education level without any neurological disease. There were no patients diagnosed with osteoporosis in either group. Individuals were diagnosed using their files and clinical evaluations. None of the participants were using vitamin D, multivitamins, or calcium or phosphate group drugs.

The specimens for measuring the BDNF levels of 13 patients had deteriorated, and these patients were excluded. Subjects who were on any vitamin replacement treatment, those with a bone metabolism disease, such as osteoporosis, or a chronic systemic disease, were excluded. All subjects provided informed consent before participating in the study, which was approved with a protocol code of 2016/23 by the Malatya Clinical Research Ethics Committee.

The personal and actual knowledge and long-term memory of all subjects were assessed using the Wechsler Memory Scale (WMS) 1; orientation was assessed with WMS 2; mental control and the ability to sustain attention were assessed with WMS 3; logical memory (momentary and long-term remembering test) was assessed with WMS 4; and WMS R was used to assess simple and complex attention based on numbers and visual range. Proverb interpretation and similarity tests were used to assess abstract thinking (abstraction); planning skills were assessed by drawing clocks; structuring was assessed by shape copying; concentric circles were drawn to evaluate constructional praxis; and verbal conciseness functions were examined via word finding. For the patients who could not perform these tests due to cognitive loss, the Mini-Mental State



Examination (MMSE) was administered. In this test, participants answer 11 questions and can obtain a maximum of 30 points; scores of 20–24 points indicate mild cognitive disorder, 10–19 indicate moderate dementia, and less than 10 points, severe dementia. For the patients whose clinical dementia scores were calculated, orientation, memory, attention, calculation, recall, language, motor function and perception, and visuospatial capacities were evaluated.

After undergoing the neurological examinations, the patients' disease levels were determined using the Hoehn and Yahr (H&Y) scale and the Unified Parkinson's Disease Rating Scale (UPDRS).

### **Blood Samples**

Fasting blood samples were collected in vacutainers and centrifuged at 3000 rpm for 10 min to obtain serum. The serum samples were frozen at  $-70^{\circ}\text{C}$  until the BDNF and 25 (OH) Vitamin D levels were measured. Before the analysis, the frozen serum samples were slowly brought to room temperature and stirred gently. The BDNF and 25(OH) vitamin D analyses were performed on the same day.

### **Biochemical Analysis of Serum BDNF**

The serum BDNF levels of both groups were measured using a commercial enzyme-linked immunosorbent assay (ELISA) kit (Boster Biological Technology, Pleasanton, CA, USA) based on the manufacturer's instructions. This analysis is based on the ELISA method. The serum and standard samples were added to wells that were precoated with human BDNF monoclonal antibodies and incubated for 90 min at  $37^{\circ}\text{C}$ . After incubation, the contents of the wells were removed by overturning the plate on a paper towel. After this, biotinylated polyclonal detection antibodies were added to each well and incubated for 60 min at  $37^{\circ}\text{C}$ . After incubation, the wells were washed three times to extract unbound biotinylated polyclonal antibodies. After this, an avi-

din-biotin-peroxidase complex was added to each well and incubated for 30 min at  $37^{\circ}\text{C}$ . After incubation, the wells were washed three times to extract the unbound avidin-biotin-peroxidase complex. A tetramethylbenzidine (TMB) solution (chromogen) was then added to each well and incubated in the dark for 25–30 min at  $37^{\circ}\text{C}$ , and thus, the color of the fluid in the wells turned blue. The reaction was ended by adding a TMB stop solution (acidic stop solution), and the blue color finally turned yellow. The absorbance values of the yellow fluid were measured at 450 nm using a microplate reader (Synergy H1 Hybrid Multi-Mode Reader; BioTek Instruments, Inc., Winooski, VT). The absorbance of the yellow color that was obtained was proportional to the level of human BDNF found in the serum. The results are reported in units of pg/mL. The intra-assay and inter-assay coefficient of variation values of the test were  $< 4.5\%$  and  $< 7.5\%$ , respectively.

### **Biochemical Analysis of Serum Vitamin D**

The serum vitamin D levels were analyzed using high-performance liquid chromatography (HPLC) with a Shimadzu LC-10ADVP HPLC system (Shimadzu Corporation, Kyoto, Japan), Immuchrom vitamin D3 controls, and an HPLC kit (Immuchrom GmbH, Heppenheim, Germany) while measuring the serum 25(OH) vitamin D levels. In summary, this method is based on subjecting samples to precipitation and extraction before they are injected into the HPLC system. The HPLC separation process was carried out with a 'reverse phase' C18,  $150 \times 4.6$  mm particle-size column (VertiSep GES; Vertical Chromatography Co., Ltd., Thailand) at  $30^{\circ}\text{C}$  at a 1 mL/min flow rate and using acetonitrile-water (99:1, v/v) as the mobile phase. The volume of the injected samples was 50  $\mu\text{l}$ , and the HPLC separation process lasted for 15 min. Chromatograms were determined using a UV detector at 264 nm. The results were calculated with the 'in-house standard method' via the integration of the peak regions. The results are reported as nmol/L. The coefficient of variation values

of the test were < 2.5% and < 4.0% for intra-assay and inter-assay, respectively.

### Statistical Analysis

Statistical analysis was performed using SPSS v.17 software (SPSS Inc., Chicago, IL, USA). The data were analyzed using SPSS, and  $p < 0.05$  was considered significant. The differences between the groups in terms of age, education level, disease duration, age of disease onset, and 25(OH) vitamin D and BDNF levels were examined using a t-test. The differences in the gender ratios between the groups were calculated using the chi-square test. Analysis of variance (ANOVA) and the post hoc Tukey's test were used for multiple comparisons among independent groups, while the cognitive levels and H&Y stages of the groups were compared using the Pearson's chi-square test. The Pearson's correlation test was used to determine the correlation between the UPDRS score and 25(OH) vitamin D and BDNF levels.

### RESULTS

The mean age of the patients was  $65.54 \pm 7.07$  years versus  $66.88 \pm 5.37$  years for the controls ( $p = 0.097$ ).

There was no significant gender difference between the groups ( $p = 0.101$ ). The normal range of the 25(OH) vitamin D levels for both groups was accepted as 75–250 nmol/L. The mean 25(OH) vitamin D level was  $240.55 \pm 89.01$  nmol/L for the patients and  $217.03 \pm 68.71$  nmol/L for the controls ( $p = 0.146$ ). Similarly, there was no significant difference in the BDNF levels of the two groups ( $p = 0.604$ ) (Table 1).

For the patients, the mean disease duration was  $5.32 \pm 3.75$  years, and the mean age of disease onset was  $60.13 \pm 7.12$  years. Comparing the cognitive levels of the patients and UPDRS scores, the UPDRS-cognitive function score was significantly correlated with the stage of dementia ( $p < 0.001$ ) (Table 2).

In PDD patients, there was a strong correlation between the worsening of cognitive function and a reduction in 25(OH) vitamin D levels ( $p = 0.009$ , Table 3). However, no significant relationship was found between the BDNF levels and cognitive levels of the patients ( $p = 0.983$ , Table 3).

There was also an inverse correlation between worsening H&Y stage and 25(OH) vitamin D levels ( $p = 0.046$ , Table 4). There was no significant relationship between BDNF level and H&Y stage ( $p =$

**Table 1.** Comparison of age, gender, 25(OH) vitamin D, and BDNF levels between patient and control groups

	Patient group (n = 63)	Control group (n = 33)	F	p
Age (years)	$65.54 \pm 7.07$	$66.88 \pm 5.37$	2.808	0.097*
Vitamin D (nmol/L)	$240.55 \pm 89.01$	$217.03 \pm 68.71$	2.147	0.146*
BDNF (pg/mL)	$137.80 \pm 12.08$	$137.22 \pm 16.67$	0.271	0.604*
Gender				
Female	29 (%58.0)	21 (%42.0)	2.689	0.101 <sup>†</sup>
Male	34 (%73.9)	12 (%26.1)		

\*t-test, <sup>†</sup>chi-square test



**Table 2.** Comparison of the patients' UPDRS scores and cognitive levels

	MCI (n = 36) X ± SD	Mild Dementia (n = 19) X ± SD	Moderate Dementia (n = 8) X ± SD	Test and Significance
UPDRS-Motor	22.47 ± 13.23	25.94 ± 12.43	32.62 ± 12.92	F = 2.112 p = 0.130
UPDRS-Daily Life Action	8.41 ± 5.88	9.68 ± 5.18	13.62 ± 6.78	F = 2.662 p = 0.078
UPDRS-Cognitive Function	3.16 ± 1.63	4.21 ± 1.03	6.25 ± 1.66	F = 14.885 <b>p &lt; 0.001</b>
UPDRS-Treatment Complication	8.75 ± 5.26	8.15 ± 4.98	11.37 ± 6.04	F = 1.082 p = 0.345
UPDRS-Total	42.80 ± 23.47	48.00 ± 21.7	63.87 ± 24.13	F = 2.756 p = 0.072

**Table 3.** Comparison of cognitive functions and 25-OH vitamin D and BDNF levels in patient group

	25-OH vitamin D (nmol/L)	F	p
MCI (n = 36)	269.63 ± 89.50	5.166	<b>0.009<sup>β</sup></b>
Mild Dementia (n = 19)	205.94 ± 76.39		
Moderate Dementia (n = 8)	191.87 ± 69.33		
Total (n = 63)	240.55 ± 89.01		
	BDNF (pg/mL)	F	p
MCI (n = 29)	139.90 ± 113.06	0.017	0.983 <sup>γ</sup>
Mild Dementia(n = 16)	133.10 ± 148.63		
Moderate Dementia(n = 5)	140.64 ± 80.76		
Total (n = 50)	137.80 ± 12.08		

<sup>γ</sup>ANOVA Post-Hoc Tukey test

**Table 4.** Comparison of H&Y stages and 25-OH vitamin D levels in patient group

	25-OH vitamin D (nmol/L)	F	p
H&Y Stage 1 (n = 18)	267.05 ± 88.35	3.247	<b>0.046<sup>μ</sup></b>
H&Y Stage 2 (n = 31)	247.38 ± 88.22		
H&Y Stage 3 (n = 14)	191.35 ± 76.97		
Total (n = 63)	240.55 ± 89.01		

<sup>μ</sup>ANOVA Post-Hoc Tukey test

**Table 5.** Correlation analysis of patients' UPDRS scores with vitamin D and BDNF levels

	25-OH Vitamin D (nmol/L)	BDNF (pg/ml)	UPDRS-Motor	UPDRS-Daily Life Activity	UPDRS-Cognitive Function	UPDRS-Treatment Complication	UPDRS-Total
25-OH Vitamin D (nmol/L)	1						
BDNF (pg/ml)	0,016** (p = 0,912)	1					
UPDRS-Motor	-0,164** (p = 0,200)	-0,117** (p = 0,417)	1				
UPDRS-Daily Life Activity	-0,310** <b>(p = 0,014)</b>	-0,161** (p = 0,265)	0,823** (p < 0,001)	1			
UPDRS-Cognitive Function	-0,156** (p = 0,222)	-0,051** (p = 0,723)	0,602** (p < 0,001)	0,624** (p < 0,001)	1		
UPDRS-Treatment Complication	-0,157** (p = 0,219)	-0,081** (p = 0,575)	0,721** (p < 0,001)	0,658** (p < 0,001)	0,451** (p < 0,001)	1	
UPDRS-Total	-0,216** (p = 0,090)	-0,128** (p = 0,375)	0,969** (p < 0,001)	0,903** (p < 0,001)	0,667** (p < 0,001)	0,823** (p < 0,001)	1

\*\* Pearson correlation test

0.375). When the UPDRS subscale scores of the patients and their 25(OH) vitamin D and BDNF levels were compared, an inverse correlation was found between their daily life activities and vitamin D levels ( $p = 0.014$ , Table 5), while there was no significant relationship between the vitamin D and BDNF

levels and the other subscales. Accordingly, the relationship between low vitamin D levels and H&Y stage was stronger than low vitamin D levels relationship with the UPDRS subscales, except for the daily life activities subscale.



## DISCUSSION

Vitamin D is a secosteroid that plays a role in the regulation of bone health physiology and calcium-phosphorus homeostasis (14). Vitamin D levels were determined by measuring serum levels of 25(OH) vitamin D. In our study, we tried to obtain reliable results by examining the 25(OH) vitamin D levels, which has a half-life that can be extended when blood samples are taken under protection from light. Statistically, there was no significant difference between the 25(OH) vitamin D levels of the patients and those of the controls in this study. Both groups had mean 25(OH) vitamin D levels in the normal reference range. The lack of a difference between our two groups might be explained by the fact that most of our patients lived in rural areas, were sufficiently exposed to sunlight, and consumed mostly organic foods, unlike individuals in developed countries or urban areas.

Vitamin D is a neurosteroid, and its deficiency has been the subject of research in the pathogenesis of many neurological diseases. There are many studies that examine the relationship between cognitive loss and vitamin D deficiency, especially in alzheimer's disease. In a study of 412 Korean patients, Ahn et al. found a positive correlation between vitamin D levels and MMSE scores (15). They also showed that physical activity affected vitamin D levels, and independence in physical activity might indirectly affect MMSE scores (15). Llewellyn et al. examined cognitive function in elderly individuals and reported a 0.3-point loss per year in the MMSE scores of those with vitamin D deficiencies (16). Peterson et al. obtained similar results, finding positive correlations between vitamin D levels and verbal conciseness and verbal memory (17). These studies have suggested that vitamin D has a positive effect on cognitive function. There are few studies that examine the relationship between PDD and vitamin D. In this study, our patients were divided into three groups according to their MMSE scores: mild cognitive impairment, mild dementia, and

moderate dementia. A positive correlation was observed between the MMSE scores of PDD patients and vitamin D deficiency. Although vitamin D levels were still in the normal reference range, a decrease in these levels might have contributed to the development of cognitive loss or dementia in PDD.

The relationship between the motor symptoms of parkinson's disease and vitamin D has recently been a subject of research. It has been thought that there may be many factors affecting vitamin D deficiency in parkinson's disease. Knekt et al. found a significant relationship between parkinson's disease and vitamin D levels, which was affected by age, sex, marital status, education level, alcohol consumption, physical activity, smoking, and body mass index (18). In another study, Evatt et al. examined the vitamin D levels of parkinson's patients and healthy individuals and found that the vitamin D levels of parkinson's patients were significantly lower (19).

Suzuki et al. also found significant correlations between the H&Y and UPDRS total and motor scores of individuals with a diagnosis of parkinson's and the vitamin D receptor Fok1 genotype and low vitamin D levels (20). Similarly, in our study, there was a relationship between the H&Y and UPDRS-daily life activity scores of the patients and low vitamin D levels. We found a significant negative correlation between PDD and 25(OH) vitamin D levels and a negative correlation between the patients' H&Y stages and their 25(OH) vitamin D levels. However, the only relationship between the UPDRS scores and 25(OH) vitamin D levels was for the daily life activities subscale.

In a meta-analysis, Zhou et al. stated that low vitamin D levels may contribute to the development of parkinson's disease, but vitamin replacement does not have a significant effect on motor function (21). However, Llewellyn et al. showed that early stage vitamin D replacement therapy is important in improving MMSE scores in elderly individuals (16). Accordingly, we think that although the measured 25(OH) vitamin D levels were in the normal range,

supplementary treatment should be started when these scales worsen, which might slow the progression of dementia rather than motor symptoms.

BDNF is a neurotrophin that contributes to the development and regeneration of neurons in the central and peripheral nervous systems (10). Howells et al. determined that BDNF expression was decreased in alzheimer's, parkinson's, and huntington's disease, amyotrophic lateral sclerosis, and multiple sclerosis (13). Also, Laske et al. compared the serum and cerebrospinal fluid BDNF levels of patients with alzheimer's disease, normal-pressure hydrocephaly, and healthy individuals and found that the BDNF levels were significantly lower in both disease groups compared to the healthy individuals (22). In another study, researchers examined 47 parkinson's patients and 23 healthy individuals and found that the serum BDNF levels were significantly lower in the patients (23). By contrast, Faria et al. examined 50 Alzheimer's patients, 37 mild cognitive disorder patients, and 56 healthy individuals and found that the plasma BDNF levels were significantly higher in the alzheimer's group (24). Hence, different results have been found regarding BDNF levels in various neurodegenerative diseases. In our study, there was no significant relationship between BDNF and PDD or disease stages. According to our current knowledge, BDNF is not suitable for predicting the course of neurodegenerative diseases. However, this needs to be clarified with larger, more comprehensive studies. When evaluating the differences in the results of the different studies, we should note that neurotrophin synthesis is influenced by genetic, environmental, and infectious factors.

This study has some limitations. We had a low number of patients and controls. Our results should

be supported by studies with a larger number of patients. The absence of any severe dementia in our study may affect the results.

In conclusion, a negative correlation was found between the H&Y stages, UPDRS-daily living activities and PDD dementia levels and vitamin D levels. These results suggest that vitamin D has an important role in cognitive functions in PDD. However, no significant difference was found in the BDNF levels between the PDD and healthy groups or based on the dementia stages of the PDD group. In this study, the idea that vitamin D affects dementia pathogenesis and cognitive degeneration is supported, and early vitamin D replacement can contribute to dementia prevention. More comprehensive studies are needed on this subject.

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### **Conflicts of interest**

There are no conflicts of interest.

### **Ethical approval**

This study, with a protocol code of 2016/23, was approved by the Malatya Clinical Research Ethics Committee.

### **Informed consent**

Written informed consent was obtained from all individual participants included in the study.



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## RESEARCH

# USING THE ROTTERDAM CT SCORE TO PREDICT OUTCOMES OF HEAD INJURIES IN THE GERIATRIC POPULATION

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## ABSTRACT

**Introduction:** Managing head traumas are quite different in the geriatric population than in other age groups due to patient comorbidities, decreased cerebral compliance, and antithrombotic use. The aim of this study was to examine head injuries in geriatric patients and investigate the effectiveness of the Rotterdam CT score in diagnosing and treating patients at the time of admission to facilitate head trauma management.

**Methods:** Demographic, clinical, and radiological data from head trauma cases in geriatric patients, along with each patient's latest status, if our clinic followed up with them, were studied retrospectively.

**Results:** The mean admission Glasgow Coma Scale score was  $12.89 \pm 3.134$ . Patients who had experienced a fall had a higher mean age ( $p=.004$ ), while patients who had fallen from a height had a lower Glasgow Coma Scale score at the time of admission ( $p=.000$ ) but higher mortality ( $p=.018$ ). Patients had a mean Rotterdam CT score of  $1.514 \pm 1.153$  at the time of admission. Mean Rotterdam CT scores were higher in patients who were hospitalized in the intensive care unit ( $p=.000$ ), had a history of falling from a height ( $p=.000$ ), and required surgery in the acute period ( $p=.005$ ). Patients with comorbidity had longer hospitalization times ( $p=.042$ ), while patients with high Rotterdam CT scores had low modified Glasgow outcome scores ( $p=.000$ ).

**Conclusion:** We determined that the need for rehabilitation and long-term care and the possibility of mortality increase after head traumas in the geriatric population and Rotterdam CT score were a good indicator of the clinical situation and final status.

**Keywords:** Craniocerebral Trauma; Glasgow Outcome Scale; Brain Injuries, Traumatic.

## CORRESPONDANCE

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## INTRODUCTION

Advanced age increases the risk of complications and mortality from trauma due to increased comorbidity and immobility (1). However, the risk of developing intracranial events also increases even in minor traumas due to physiological changes in the brain, especially in the elderly (2–5).

The Glasgow coma scale (GCS) is a quick way to obtain information about a patient's clinical condition. However, such clinical scales may not provide sufficient information in the presence of diseases such as dementia and delirium, which are common in the elderly (6). This requires new methods for patient management and outcome estimation.

Managing developing intracranial pathology is quite different in geriatric populations due to patient comorbidities, decreased cerebral compliance, and antithrombotic use. Neurological diseases can also affect the patient's examination at the time of admission and can make it difficult to effectively manage treatment, follow-up, and imaging findings. The aim of this study was to examine cases of head trauma in geriatric patients to facilitate trauma management. We also aimed to investigate the effectiveness of the Rotterdam CT score in diagnosing and treating patients at the time of admission.

## METHOD

This study was approved by the non-interventional clinical research ethics committee of the University of Health Sciences, Gazi Yasargil Education and Research Hospital, under number 514 on July 24, 2020. Informed written consent was obtained from all patients, and the principles of the Declaration of Helsinki were followed.

The study included 142 patients over age 65 admitted to the emergency department of our hospital between January 2017 and July 2020 after a

head trauma and who had undergone a computed tomography (CT) scan of the brain. We evaluated the relationship in geriatric patients between the Rotterdam CT score at the time of admission and the modified Glasgow outcome scores (mGOS) of the patient's final status and attempted to determine the factors affecting final status.

We recorded the patients' age, sex, GCS at the time of admission, hospitalization services (clinic/intensive care), type of trauma, pathology detected in the CT, Rotterdam CT score at the time of admission, surgeries, accompanying traumas, chronic subdural hematoma (cSDH), Markwalder score in patients with cSDH, comorbidities, antiaggregant/anticoagulant use, length of hospital stay, mGOS, and final status.

## Statistical analysis

The data were evaluated in terms of averages, numbers and percentages, and minima-maxima. We used bivariate correlations (Pearson's R, Spearman's correlation, one-way ANOVA) to evaluate the correlation between data. Groups were analyzed primarily in terms of their suitability of normal distribution. Analyses were performed using the Kolmogorov-Smirnov normal distribution test, and we made graphs of conformity to normal distribution. Student's t-test was used to compare normally distributed variables, and the Mann-Whitney U test was used to analyze independent data that did not conform to a normal distribution. The chi-squared test was used for categorical data. SPSS for Windows (version 20.0) was used for analysis. A p-value of less than .05 was considered significant.

## RESULTS

### Demographics

Of the patients in the study, 61.3% (87) were male and 38.7% (55) were female. The youngest patient

was 65 years old, the oldest was 98, and the mean age was  $74.25 \pm 7.014$ . When patients were compared by sex, it was found that females had a higher average age, but this was not statistically significant ( $p = .079$ ) (Table 1).

### Clinical characteristics

The mean GCS score of patients at the time of admission was 12.89 points (3–15 points,  $\pm 3.134$ ). Males had a lower GCS score at the time of admission ( $p = .024$ ) (Table 1). In terms of hospitalization, 53.5% (76) were hospitalized in the clinic and 46.5% (66) in the intensive care unit.

### Trauma type

There were multiple causes of traumas: falls (68.3%), traffic accidents (26.1%), falls from a height (4.2%), and assault (1.4%). Although it was thought that effective randomization could not be achieved due to the low number of patients who had been assaulted and who had been followed up with, it was found that patients involved in traffic accidents and who had fallen from a height could develop multi-trauma that required intensive care more often ( $p = .000$  and  $p = .000$ , respectively). Patients who had fallen had a higher mean age ( $p = 0.004$ ), and patients who had fallen from a height had lower GCS scores at the time of admission and higher mortality ( $p = .000$  and  $p = .018$ , respectively). Although patients who had experienced falls have a greater need for surgery due to cSDH at the time of admis-

sion ( $p = .674$ ) and afterwards ( $p = .055$ ), it was not statistically significant. Patients developed cSDH more often after a fall than after a traffic accident or falling from a height, but it was not statistically significant ( $p = .055$ ). It appears that the development of cSDH in both patients who had been assaulted affected the statistical data (Table 2).

### Radiological evaluation

No pathology was found in CT scans in 42.3% (60) of patients imaged at the time of first admission. No pathology was found in CT scans taken at the time of admission in 52.7% of females and 35.6% of males. Subarachnoid hemorrhages were found in 29.5% (42) of patients, subdural hematoma in 20.4% (29), intracerebral hematoma in 6.4% (9), epidural hematoma in 5.6% (8), intraventricular hemorrhage in 2.8% (4), and pneumocephalus in 1.4% (2). More than one pathology was found in 8.4% (12) of patients. Subdural hematomas were most common in males (23.0%), whereas subarachnoid hemorrhage was the most common (23.6%) in females. No statistical significance was found between sex and diagnosis at presentation ( $p = .061$ ). The mean Rotterdam CT score at the time of admission was  $1.514 \pm 1.153$ . Mean Rotterdam CT scores were higher in patients hospitalized in the intensive care unit ( $p = .000$ ), who had fallen from a height ( $p = .000$ ), and who required surgery in the acute period ( $p = .005$ ). Although Rotterdam CT scores were higher in males ( $p = .433$ ) and in patients using antiaggregants ( $p = .547$ ), it was not statistically significant. Mean Rotter-

**Table 1.** Comparison of patient characteristics according to gender

Gender	Age	GCS	Surgery	Multitrauma	cSDH	cSDH-S	Mortality
M (61.3%)	73.43±6.40	12.4±3.6	8.0%	20.7%	37.9%	57.6%	16.1%
F (38.7%)	75.55±7.76	13.6±2.1	5.5%	36.4%	14.5%	37.5%	10.9%
<b>p value</b>	.079	.024	.410	.040	.002	.006	.272



**Table 2.** Comparison of trauma type and patient characteristics

Trauma Type	Assault (n=2)	Falls (n=97)	Traffic accidents (n=37)	Falls from height (n=6)	p value
Age	65.0±0.0	75.4±2.1	71.3±5.8	75.0±5.8	.004
Gender (M/F)	50%/50%	59.8%/40.2%	64.9%/35.1%	66.7%/33.3%	.925
GCS	13.0±0.0	13.7±6.7	11.05±4.1	10.8±4.7	.000
ICU	100 %	34.0 %	73.0 %	66.7 %	.000
Surgery	0.0 %	8.2 %	5.4 %	0.0 %	.674
cSDH	100 %	32.0 %	18.9 %	16.7 %	.055
cSDH-Surgery	100 %	18.6 %	5.4 %	0.0 %	.000
Multitrauma	100 %	16.5 %	48.6 %	33.3 %	.000
Mortality	0.0 %	8.2 %	27.0 %	33.3 %	.018

dam CT scores were lower at the time of admission in patients who developed cSDH ( $p = .075$ ) and in those who required surgery ( $p = .004$ ) (Table 3).

### Comorbidity and multitrauma

One to four comorbidities were detected in 77.5% of patients. The average number of comorbidities across all patients was  $1.317 \pm 0.970$ . The most common one was hypertension (59.2%, or 84 patients), followed by diabetes mellitus (20.4%, or 29 patients), respiratory tract diseases (asthma, COPD, etc.) (12.6%, or 18 patients), neurological diseases (cerebrovascular diseases, dementia, Parkinson's, etc.) (11.2%, or 16 patients), cardiac diseases other than hypertension (atrial fibrillation, heart failure, valvular heart diseases) (11.2%, or 16 patients), and other diseases (psychiatric, hematological, urinary, endocrine, and malignancy) (13.3%, or 19 patients). The most common comorbidity in both sexes was hypertension. Comorbidities were found in 89.1% of females and 70.1% of males, which was statistically significant ( $p = .006$ ). Diabetes mellitus occurred more often in females, and neurological, cardiovascular, and urogenital system diseases occurred more often in males and were statistically

significant ( $p = .043$ ). Patients with comorbidities had longer hospitalization times ( $p = .042$ ). No relationship was found between comorbidity and age, final patient status, GCS score, Rotterdam CT score, needing surgery, mGOS score, or cSDH development ( $p > .05$ ). A total of 31.7% (45) of patients used antithrombotics.

The use of antithrombotics had no effect on mortality or mGOS score ( $p > .05$ ). Furthermore, 26.8% (38) of patients had trauma to another system. Additional trauma was found in 36.4% of females and 20.7% of males and was statistically more common in females ( $p = .040$ ). The most common additional trauma for both sexes was to the spine (13.4%, or 19 patients), followed by trauma to the extremities (6.3%, or 9 patients), thorax (5.6%, or 8 patients), and abdomen or maxillofacial area (1.4%, or 2 patients) (Table 1). The second most common trauma was to the extremities in females and to the thorax in males. Two additional traumas were found in 1.4% of patients.

The incidence of additional trauma was higher in patients presenting after a traffic accident ( $p = .000$ ), and patients with additional trauma had longer hospitalization times ( $p = .006$ ) and a higher chance of

**Table 3.** Rotterdam CT score evaluation according to patient characteristics

Rotterdam CT score (mean)					
<b>Gender</b> female male	1.41 ± 0.95 1.57 ± 1.26	<b>Unit</b> clinic ICU	1.06 ± 0.52 2.03 ± 1.43	<b>Trauma type</b> assault fall traffic accident falls from height	1.21 ± 0.98 2.24 ± 1.21 2.17 ± 1.47 3.15 ± 1.69
p = .433		p = .000		p = .000	
<b>Final situation</b> discharge mortality	1.24 ± 0.76 3.15 ± 1.69	<b>Surgery</b> yes no	2.50 ± 1.84 1.43 ± 1.05	<b>cSDH</b> yes no	1.24 ± 0.83 1.62 ± 1.24
p = .000		p = .005		p = .075	
<b>cSDH-S</b> yes no	0.86 ± 0.46 1.63 ± 1.20	<b>Antiagg.</b> yes no	1.60 ± 1.43 1.47 ± 1.00	<b>Comorbidity</b> yes no	1.50 ± 1.20 1.53 ± 0.94
p = .004		p = .547		p = .924	

pathologies revealed in cranial imaging at the time of presentation ( $p = .026$ ). However, the presence of additional trauma did not have an effect on mortality or mGOS score.

### Surgery

At the time of admission, 7.0% (10) of patients had undergone surgery. Although males required surgery more often and had a higher mortality rate in the acute period after trauma, it was not statistically significant (Table 1). In 28.9% (41) of patients, cSDH developed in the first three months after trauma, and 53.7% of those needed surgery. The clinical conditions of patients who developed cSDH were evaluated using the Markwalder grading scale (MGS). The clinical conditions of patients who developed cSDH ranged from grade 0 (normal neurological picture) to grade 3 (stupor and hemiplegia); the mean was  $0.854 \pm 0.910$ . Males developed cSDH more frequently ( $p = .002$ ) and needed surgery for cSDH hematomas more often ( $p = .006$ ) (Table 1).

### Hospitalization and mortality

Patients were hospitalized for 1 to 209 days; the average was  $10.47 \pm 21.621$  days. Patients' final sta-

tuses, as assessed by mGOS, ranged from 1 to 8 points ( $\pm 2.495$ ), with an average of 6.19. A total of 14.1% (20) of patients died during hospitalization. No statistically significant relationship was found between comorbidity and mortality ( $p = .365$ ). Patients with a higher Rotterdam CT score had a significantly increased risk of mortality ( $p = .000$ ) (Table 3), and also patients with high Rotterdam CT scores had low mGOS scores ( $p = .000$ ).

**Table 4.** Comparison of Rotterdam CT Scale and mGOS

mGOS score	Number of patients	Rotterdam CT score (mean)
1	21	$3.143 \pm 1.65$
2	3	$2.333 \pm 1.52$
3	2	$1.000 \pm 1.41$
4	1	3.000
5	6	$1.500 \pm 1.37$
6	13	$1.692 \pm 0.85$
7	34	$1.324 \pm 0.68$
8	62	$0.984 \pm 0.46$
p = .000		



## DISCUSSION

Certain physiological changes that develop with age can cause hemorrhagic complications in head trauma, including cerebral atrophy (increased wall tension in the brain), hypertension (increased wall tension), reduced cerebral blood flow resulting in hypoxic brain injury, cerebrovascular atherosclerosis, reduced cerebrovascular autoregulation, and increased superoxide production (2). Major complications also increase with age, even in minor traumas (7–9). Although country-based studies of head trauma in the geriatric population in America (10) and Europe (11) have shown that head injuries are more common in females, our study was majority male. This is thought to be related to sociocultural restrictions on participation by females in social life as they age.

Nearly 80% of all traumas in the geriatric population are mild head traumas (GCS score 13–15), but the geriatric population has a higher morbidity and mortality than young people do for both cranial traumas and other types (12). In our study, the average GCS score was 12.89 points (3–15 points,  $\pm 3.134$ ) and 76.1% of cases were mild head traumas. Of the head traumas, 10.5% were moderate and 13.4% were severe. Studies have shown that even in mild head injuries, both neurobehavioral and functional outcomes are affected (12). Also, elderly patients have a greater need for rehabilitation and long-term care and a higher mortality rate from mild to moderate head trauma compared to younger patients (13). While up to 60% of young people have a good outcome with mild to moderate head traumas, the rate for the elderly is only 20% (14). In our study, patients had good outcomes (as defined by their mGOS) more frequently (43.6%) than in the literature.

As patients age, they are at greater risk of developing complications from minor traumas (15). Studies have shown that the most common cause of head trauma in the elderly is falls (falling down, tripping, etc.), followed by traffic accidents (16).

Although our study supports the literature when it comes to trauma type, it also found a higher mean age for patients who had experienced a fall ( $p = .004$ ), which supports the potential of low-energy traumas to cause damage as age increases. However, mortality was higher in high-energy traumas (most commonly falls from heights, followed by traffic accidents). An increased subdural distance in geriatric patients increases the risk of developing subdural hematoma by up to 45% (16). Although subdural hematomas were most commonly found in men in our study, the most common radiological finding was subarachnoid hemorrhage.

When evaluated radiologically, the mean Rotterdam CT score was  $1.514 \pm 1.153$ . Mean Rotterdam CT scores were higher in patients hospitalized in the intensive care unit ( $p = .000$ ), who had fallen from a height ( $p = .000$ ), and who required surgery in the acute period ( $p = .005$ ), suggesting that the Rotterdam CT score might be more effective than GCS scores, as it is a radiological parameter that offers clinical clues and indications of final statuses in geriatric patients. It might also be used to support neurological findings in clinical evaluations of patients with conditions such as dementia who cannot be examined effectively. In a study evaluating the effectiveness of the Rotterdam CT score in all age groups, it was found that the score correlated with trauma severity and outcome in the elderly (17). In our study, the Rotterdam CT score was found to be highly correlated with outcome (as defined by their mGOS) in the geriatric population ( $p = .000$ ).

Comorbid diseases and medications used by the aged may increase the risk of falls (7), make it difficult to manage treatment after trauma, and cause prolonged hospitalizations (18). In particular, the use of antithrombotics are associated with an increased risk of hemorrhagic complications (16). Of our patients, 77.5% had at least one comorbidity, and 31.7% took an antithrombotic. Our study also found that comorbidity was more common in female patients, and hospital stays were longer when

comorbidities were present.

One study of head and other traumas in the geriatric population found that the most common extremity fractures and subsequent head traumas were observed in the geriatric population. The study stated that fragility increased with age and that all traumas were more common in females (11). Our study found that the incidence of additional trauma was higher in females, with spinal trauma being the most common additional trauma in both sexes, suggesting that osteoporosis, the risk of which increases with age, may increase susceptibility to spinal trauma.

Although very few patients (7.0%) required surgery at the time of presentation, a relatively large number developed cSDH and required surgery (28.9%–53.7%). However, fewer patients needed surgery at the time of admission than suggested by the literature (16). Patients had a higher risk of developing cSDH if they had experienced a fall, which was thought to be related to the fact that patients involved in traffic accidents or falls present with a worse clinical picture in the acute period and a higher mortality rate in the following period.

One study found similarities in demographics, injury mechanism and severity, and comorbidity but showed that the risk of death was four times higher in the elderly than in young adults (11). In our study, in high-energy traumas, the presence of ICH/IVH in the CT scan at the time of admission, a low GCS score, and a high Rotterdam CT score were all found to be associated with mortality. The risk of mortality also increased in those whose pathologies required surgery. On the other hand, low-energy traumas, high GCS scores, low Rotterdam CT scores, normal CTs or SAH at the time of admission, and an absence of comorbidity were found to be

associated with good outcomes.

## **CONCLUSION**

The geriatric population has a greater need for rehabilitation and long-term care and higher mortality after head traumas. The Rotterdam CT score is a radiological parameter that offers indications of the clinical picture in elderly people with dementia and similar neurological problems and can help predict final outcomes. Concomitant diseases and medications used by the elderly may increase the risk of falls, make it difficult to manage treatment after trauma, and cause prolonged hospitalizations. All in all, we concluded that diagnoses and treatment of head trauma in the geriatric population should be evaluated and followed up more closely and for a longer time than in other age groups.

## **Acknowledgement**

Statement of Ethics

The study was approved by the Ethics Committee of University of Health Sciences, Diyarbakır Gazi Yasargil Education and Research Hospital. The study complied with the Declaration of Helsinki.

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The authors have no conflicts of interest to declare.

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## RESEARCH

# RELATIONSHIP OF DAILY TIME SPENT OUTDOORS WITH SLEEP QUALITY AND EMOTIONAL WELL-BEING AMONG COMMUNITY-DWELLING OLDER ADULTS DURING COVID-19 RESTRICTIONS

## ABSTRACT

**Introduction:** Given the recent constraints imposed due to the ongoing COVID-19 pandemic and the importance of the daily light-dark cycle for entraining the human circadian system, it is possible to state that the elderly are likely to be at serious risk of experiencing sleep-related problems. Whilst reduced or limited time outdoors, and thus, exposure to diurnal bright light appear to be detrimental to sleep and emotional well-being in old age, further research is required to confirm this relationship.

**Materials and Method:** To build on earlier work, a two-week study was conducted in a sample of 79 community-dwelling older adults recruited by using snowball sampling method. Throughout the study, the participants were allowed to be outdoors from 10.00 a.m. to 1.00 p.m. on weekdays. Whilst the participants were performing their daily habitual activities, they were asked to keep an activity diary and report on their sleep quality and emotional well-being using two questionnaires.

**Results:** The results demonstrated that participants' daily time spent outdoors (49.13 minutes on average) positively correlated with their perceived sleep quality and emotional well-being at various — but significant — levels ( $p < 0.05$ ). Moreover, significant negative correlations were identified between participants' sleep quality and experienced emotional disturbances ( $p < 0.001$ ).

**Conclusion:** Based on the research findings, it is reasonable to conclude that spending momentary periods outdoors may have adverse consequences for the elderly. To maintain a healthy sleep-wake cycle and alleviate related emotional problems in old age, increasing outdoor time and diurnal bright light exposure should be encouraged.

**Keywords:** Aged; COVID-19; Emotions; Photoperiod; Sleep; Social Isolation.



## INTRODUCTION

In industrialised nations, urban adult populations spend a substantial portion (approximately 90%) of their day in buildings and other enclosed spaces, as evidenced by research on human activity patterns (1, 2). Inevitably, this type of lifestyle has led many people to perform most of their daily activities in dimly and artificially lit environments. Studies on diurnal light exposure patterns have provided empirical evidence that the daily duration of exposure to outdoor light levels  $>1,000$  lx is about 90 minutes in young and middle-aged adults (3) and can be as short as 3 minutes in the institutionalised elderly (4). Given the COVID-19-related preventive measures, such as precautionary self-isolation and lockdown globally taken to mitigate the ongoing outbreak, it seems reasonable to expect that the elderly are likely more at risk of beginning to spend less time outdoors and being confined to indoor spaces that lack daylight. Thus, the question arises as to whether these recent changes are inflicting an extra burden on the systemic health and well-being of the elderly.

Sleep is a biological need; it plays a major role in maintaining good health, including immunologic health, and quality of life (5). Elderly individuals with sleep problems are more prone to depression, cardiovascular diseases, cerebrovascular diseases, and hypertension (6). In humans, sleep is regulated by the reciprocal interaction between the homeostatic sleep drive, which tracks the amount of prior sleep, and the circadian system, which synchronises bodily processes with the 24-hour solar day (7). Whilst light is the most important exogenous stimulus for entraining the circadian system (8), its potency dramatically decreases with age. It has been demonstrated that the steady decline in both crystalline lens transmittance and pupil area reduces the circadian photoreception of a 65-year-old adult to roughly one-third of the amount in a young adult aged 25 (9). As light exposure becomes more criti-

cal to a healthy sleep-wake cycle, and thus, general well-being in old age, it is plausible to assume that the precautions against the COVID-19 pandemic and, unavoidably, reduced or limited diurnal light exposure outdoors may lead to serious sleep and sleep-related health problems in the elderly.

A critical review of the existing literature on this subject reveals that inconsistent or equivocal results have been reported thus far. On one hand, several studies provide empirical evidence to discredit the assumption made about the inadequacy of light exposure and its implications. For example, Noi and colleagues (4) observed that, despite the significant difference between the length of morning exposure to illuminances  $>1,000$  lx in summer and winter, the actigraphic sleep metrics, subjective sleep quality, and emotional well-being of a small group of nursing home residents did not vary considerably with the season. On the other hand, other studies indicate that spending time outdoors and being exposed to daylight are of benefit to the elderly (10–13). The issue with these latter studies is that the optimal duration or frequency of outdoor exposure cannot be determined. In a recent study, Corley and colleagues (10) demonstrated that using home gardens more often during lockdown, compared to the pre-lockdown period, was significantly associated with better sleep quality and mental health amongst a sample of community-dwelling elderly adults. Whilst this finding is in support of a previous study suggesting that increasing the daily duration of exposure to high illuminances is related to ameliorated sleep and depression in old age (11), it is not in complete accord with the results of two similar studies (12, 13). Unlike the others, these two studies, conducted in long-term care facilities, showed that being outdoors and exposed to daylight for only 30-40 minutes in the morning was potent enough to improve sleep quality and that longer or more frequent light exposure might not be required.

Due to the lack of available evidence in the existing literature, it is still unsafe to reach any conclusions on the possible link between low daily doses of light and experiencing sleep-related problems. Before we can achieve a more detailed understanding of the influence of light on the sleep-wake cycle of older adults, there is a necessity for additional research studies to yield more conclusive results. Therefore, to build on earlier work, the present study was conducted by recruiting a sample of community-dwelling adults aged  $\geq 65$  over a two-week period. This paper reports the results of our study to test the following hypotheses:

Hypothesis 1. Older individuals spend only brief periods outdoors.

Hypothesis 2. Limited time outdoors, and thus, less exposure to daylight have an inverse relationship with initiating and maintaining nocturnal sleep and, as a direct consequence, perceived sleep quality.

Hypothesis 3. Experiencing sleep difficulties is accompanied by emotional disturbance(s).

## **MATERIALS AND METHOD**

### **Participants**

To minimise contact with the elderly as much as possible during the COVID-19 pandemic, the researchers utilised the snowball sampling method; this yielded a total of 98 community-dwelling elders residing in ten different cities in Turkey. Among them, nine volunteers failed to meet the inclusion criteria. Additionally, ten volunteers had difficulties in following the study protocol and withdrew from the study. The remaining participants, whose descriptive characteristics are given in Table 1, were:

a) aged  $\geq 65$ ;

b) literate;

c) cognitively intact. Approximately two weeks prior to the study, the cognitive functioning of the elderly volunteers was assessed by administering

a Turkish version of the Standardised Mini-Mental State Examination (SMMSE-T). The SMMSE-T, translated and validated by Gungen and colleagues (14), is composed of various questions and tests to measure performance across different cognitive ability domains. A SMMSE-T score of 30 indicates no impairment; a score of 23/24 is considered to be the cut-off for the diagnosis of mild dementia in the Turkish population. Volunteers who scored  $< 24$  were excluded to screen out individuals with dementia;

d) not concurrently using more than five prescribed medications or any medication for sleep and depression;

e) not in poor health, based on scores from a general health profile. For profiling purposes, all volunteers reported on their physical and mental health status by completing a Turkish version of the Short Form 36 (SF-36T). The SF-36T, reported to be valid and reliable by Pinar (15), is a 36-item, self-administered questionnaire assessing perceived changes in health and general health across eight domains. For each domain, raw item scores are converted, summed, and then transformed into a single score ranging from zero (the worst possible health state) to 100 (the best possible health state). Participants' SF-36T scores were comparable to the normative data of Demiral and colleagues (16) for Turkish adults aged  $\geq 65$ . The domains for which relatively low scores were obtained were social functioning (62.50 vs. 83.70) and role emotional (62.02 vs. 86.50); and

f) thoroughly informed about the study. As per the ethical clearance granted by Yaşar University Ethics Committee, written informed consent was obtained from each participant.

### **Sleep Quality**

A Turkish version of the Richards-Campbell Sleep Questionnaire (RCSQ-T), shown to be reliable and valid by Özlü and Özer (17), was also com-



**Table 1.** Descriptive characteristics of the participants (n=79)

Variable		n	%			
Gender	Female	44	55.7			
	Male	35	44.3			
Education Status	Literate	5	6.3			
	Primary school	22	27.8			
	Secondary school	4	5.1			
	High school	4	5.1			
	Graduate	32	40.5			
	Postgraduate	12	15.2			
Chronic Illness	Yes	55	69.6			
	No	24	30.4			
Variable		Mean	SD	Median	Minimum	Maximum
Age (years)		71.62	4.90	71	65	92
Body Mass Index (kg/m <sup>2</sup> )		26.78	3.56	26.43	20.96	34.37
SMMT-T Score		27.76	1.96	28	24	30
SF-36T Score	Physical functioning	75.88	20.44	80	0	100
	Role physical	57.59	42.24	75	0	100
	Bodily pain	61.44	25.83	62	0	100
	General health	61.81	20.33	62	0	100
	Vitality	59.93	19.00	60	10	100
	Social functioning	62.50	31.39	62.50	0	100
	Role emotional	62.02	41.93	66.66	0	100
	Mental health	67.69	16.68	72	24	100

SMMT-T: Standardised Mini-Mental Test; SF-36T: Short Form 36; SD: Standard deviation

pleted daily by the participants to evaluate previous night's sleep. The RCSQ-T is a five-item, visual analogue scale measuring perceived sleep depth, latency, efficiency, and overall sleep quality. A total score, ranging from 0–100, is obtained by calculating the mean score for all items. A high total score represents a high level of sleep satisfaction.

### Daily Activity

To measure time spent outdoors during daylight hours, the participants kept a daily activity diary devised by the authors. The diary comprises a table in which all activities performed over a day are reported. In each row of the table, information on activity definition, time, duration, and place is required.

Based on the contemporaneous sunrise and sunset hours at the activity location, the amount of outdoor time for all daytime activities was calculated and used to obtain the cumulative total for a single day or daily time spent outdoors (DTSO).

### Emotional Well-Being

A Turkish version of the Depression Anxiety Stress Scale (DASS-42T), translated and demonstrated to be psychometrically sound by Uncu and colleagues (18), was used to assess participants' emotional well-being. The DASS-42T is a self-administered instrument that is composed of three subscales measuring the negative emotional states of depression, anxiety and stress over the last seven days. Each subscale consists of 14 items rated on a four-point scale of severity. Subscale scores, varying between 0–42, are obtained by adding the scores for each subscale item. Scores greater than nine, seven, and 14 were reported to be indicative of depression, anxiety and stress, respectively.

### Procedure

From 1–7 February 2021, the cognitive functioning and perceived health status of the consenting volunteers were evaluated by administering the SMMSE-T and SF-36T in person or online. Moreover, data on volunteers' sociodemographic characteristics, body weight, height, chronic illnesses, and medication use were also gathered in this period. Following the screening for participation, a bound folder containing the daily activity diary, RCSQ-T, and DASS-42T was posted to each participant. All participants were thoroughly informed about how to use the folder during the week prior to the study.

The study was conducted between 15 February–1 March 2021. During this period, due to the precautions against the spread of COVID-19 and the related restrictions, adults aged  $\geq 65$  were only allowed to be outdoors from 10.00 a.m. to 1.00 p.m. on weekdays. This two-week period was considered

to be long enough to understand the possible effects of imposed restrictions without jeopardising participant adherence, and, thus, it was employed for data collection. Throughout the study, the participants updated the activity diary daily from 15–28 February 2021 and filled in the RCSQ-T each morning between the second and last day of the study. On the eighth and last day, the DASS-42T was self-administered to gain an insight into participants' emotional well-being over the first and second weeks of the study. Following the completion of the study, participants either sent back the folders by post or scanned them to transfer their data electronically. Official permission was granted by the Republic of Turkey Ministry of Health for the study and its procedure (Application No: 2021-01-25T16\_04\_06).

### Statistical Analysis

The Kolmogorov-Smirnov test and normality plots were used to assess the normality of the data. Continuous variables were reported by using means, standard deviations, medians, minimum values, and maximum values. Categorical variables were presented by using absolute and relative frequencies. Spearman's correlation coefficients were calculated to determine the relationships between participants' self-reported data obtained over two weeks. According to Pallant's (19) definition, the strength of these relationships was considered to be *small*, *medium*, and *large* for the ranges of 0.10–0.29, 0.30–0.49, and 0.50–1, respectively. All statistical analyses were carried out by using the Statistical Package for the Social Sciences (version 22.0; SPSS Inc., Chicago, IL, USA). The level of significance was set at  $p < 0.05$ .

### RESULTS

Participants' cumulative DTSO, RCSQ-T, and DASS-42T scores were calculated (see Table 2). It was evident from the results that the average DTSO was



**Table 2.** Participants' DTSO, RCSQ-T scores and DASS-42T scores (n=79)

Variable	Mean	SD	Median	Minimum	Maximum
DTSO (minutes)	49.13	36.08	42.85	0	171.43
RCSQ-T Score	71.52	14.26	70	42.43	100
Depression Score	12.74	9.93	10.5	0	40
Anxiety Score	10.81	10.30	6.5	0	41.50
Stress Score	15.15	9.42	14	0	40

DTSO: Daily time spent outdoors; RCSQT: Richards-Campbell Sleep Questionnaire; DASS-42T: Depression Anxiety Stress Scale; SD: Standard deviation

only 49.13 minutes; this was in support of Hypothesis 1. Whilst the participants did not report experiencing major sleep disturbances based on their RCSQ-T scores, they were mildly depressed, moderately anxious, and mildly stressed, according to their scores on the DASS-42T.

To test Hypothesis 2, the correlation of participants' DTSO scores with their RCSQ-T scores was also computed over the overall study period. The results were in support of the second hypotheses (Table 3). There was a weak — but significant —

positive correlation between their DTSO scores and perceived sleep quality ( $p < 0.05$ ). In addition, it was further identified that participants' DTSO was found to inversely correlate with their depression, anxiety, and stress scores at various — yet significant — levels ( $p < 0.05$ ). Moreover, participants' RCSQ-T and DASS-42T scores significantly and negatively correlated with each other at moderate or high levels ( $p < 0.001$ ). These results were consistent with Hypothesis 3.

**Table 3.** Correlations among participants' DTSO, RCSQ-T scores and DASS-42T scores (n=79)

Variable		DTSO	RCSQ-T Score	Depression Score	Anxiety Score	Stress Score
DTSO	r	1.000	0.288	-0.322	-0.370	-0.250
	p	-	<b>0.010</b>	<b>0.004</b>	<b>0.001</b>	<b>0.026</b>
RCSQ-T Score	r	0.288	1.000	-0.527	-0.475	-0.427
	p	<b>0.010</b>	-	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>
Depression Score	r	-0.322	-0.527	1.000	0.856	0.853
	p	<b>0.004</b>	<b>&lt;0.001</b>	-	<b>&lt;0.001</b>	<b>&lt;0.001</b>
Anxiety Score	r	-0.370	-0.475	0.856	1.000	0.836
	p	<b>0.001</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>	-	<b>&lt;0.001</b>
Stress Score	r	-0.250	-0.427	0.853	0.836	1.000
	p	<b>0.026</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>	-

DTSO: Daily time spent outdoors; RCSQ-T: Richards-Campbell Sleep Questionnaire; DASS-42T: Depression Anxiety Stress Scale; r: Spearman's rho

## DISCUSSION

One of the aims of our study was to determine the time that the elderly participants spent outdoors to estimate the duration of their outdoor daylight exposure during the ongoing COVID-19 restrictions. It was shown that the average DTSO was approximately 49 minutes during daylight hours — in other words, on average, our sample spent only 3.4% of a day in outdoor light levels. This finding is consistent with those of other researchers; for example, Obayashi and colleagues (20) demonstrated that the duration of daytime light exposure to illuminances  $>1,000$  lx was 50.3 minutes per day in a large sample of home-dwelling older adults. Given the importance of light to entrain the circadian system in humans, it is possible to expect that this limited exposure can induce or aggravate sleep disturbances and produce sleep-related emotional problems in the elderly.

The question of whether there is a link between daily light exposure and sleep-related problems in the elderly remains unresolved. However, our results indicate that there may be a significant association between these variables, which is well worth considering. Even though our sample reported fewer difficulties with sleep initiation and maintenance than their peers living independently and in long-term care facilities (21), the participants' DTSO significantly correlated with their sleep quality and their emotional state. Moreover, there were significant negative correlations between the RCSQ-T and DASS-42T scores. These results confirm the findings of other studies (10, 11), which suggest that increased time spent outdoors and bright natural light exposure is beneficial to nocturnal sleep, and thus, emotional well-being in community-dwelling elders.

Although it is possible to state that a brief exposure period  $<1$  hour can be potent enough to elicit a significant circadian response based on our results and those of other studies (12, 13), it is too soon to reach a conclusion about the optimal duration

of DTSO. Despite the relationship of participants' DTSO with their sleep quality and DASS-42 scores, it is not possible to state with certainty whether increasing the length of exposure will yield much better results due to the correlational nature of this study. In this regard, the literature provides unclear evidence to confirm or refute this assertion. Whilst it has been demonstrated that there may be an upper efficacious limit for daylight exposure (12), it has also been suggested that longer exposure periods are likely to be more effective (11, 22).

A major strength or contribution of this study is that it addresses an important gap in our knowledge by gathering data from elderly adults living in different regions of Turkey during the restrictions imposed on adults aged  $\geq 65$  due to COVID-19 pandemic. Moreover, it assesses not only sleep but also emotional well-being of the participants. In addition to these strengths, it should also be noted here that, in interpreting the above-mentioned results, two inherent weaknesses, or at least limitations, warrant consideration. Firstly, because of the ongoing pandemic and its impact on participant recruitment, the study population did not truly represent the entire age spectrum of elderly adults. Only two participants were older than 80 years at the time of data collection. Therefore, it is unclear to what extent our results are valid for those in extreme old age. Secondly, approximately 70% of the sample had chronic diseases associated with old age and were on medication for these diseases. Whilst the participants were not using any antidepressants or sleep aids, they were taking medications such as  $\beta$ -blockers, which interfere with nocturnal sleep (23). Apart from its weaknesses or limitations, it is important to note here that employing actigraphy can also be considered for objectively delineating both sleep and light exposure patterns (24) in future studies and comparing their results with our RCSQ-T and DTSO results.

Even though further interdisciplinary research is required to fully apprehend the effects of time



spent outdoors on the older population, one can safely draw two main conclusions from the results discussed above. Firstly, it is reasonable to conclude that spending only brief periods outdoors is likely to be detrimental to sleep and emotional well-being in the elderly. Before it was feasible to use electric lighting to compensate for the lack of daylight in buildings and enable living indoors, the sun had been our primary source of light. Therefore, from an evolutionary perspective, older adults should be encouraged to spend more time outdoors to reduce the extra burden on their health imposed by the

COVID-19 pandemic and the related precautions (i.e. social isolation). Secondly, given that spending time outdoors and being exposed to bright diurnal light may greatly benefit the elderly, we can be fairly certain that the successful incorporation of daylight into the built-environment is crucial for older adults, especially for those with mobility impairments.

### Conflict of Interest

The authors declare no conflicts of interest.

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## RESEARCH

# SEXUAL ATTITUDE SCALE FOR ELDERLY PEOPLE: A RELIABILITY AND VALIDITY STUDY IN TURKEY

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## ABSTRACT

**Introduction:** The purposes of this study were to translate the Sexual Attitude Scale for Elderly People into Turkish and determine its psychometric characteristics.

**Materials and Method:** A total of 127 people aged between 60 and 86 years participated in this study. Participants completed Turkish versions of the Sexual Attitude Scale for Elderly People, Aging Sexuality Knowledge and Attitudes Scale, and Socio-demographic Information Form. Exploratory and confirmatory factor analyses were then conducted to investigate the construct validity. In addition, the relationship between the total score of the Sexual Attitude Scale for Elderly People and attitude sub-dimension of the Aging Sexuality Knowledge and Attitudes Scale was examined for concurrent validity. Finally, discriminant validity was assessed by investigating the effect of gender and active sex-life on the total score.

**Results:** Similar to the original structure, both the exploratory and confirmatory factor analyses revealed a 4-factor solution: volunteerism, significance, closeness, and communication. There was a significant relationship between the total score of the Sexual Attitude Scale for Elderly People and attitude sub-dimension of the Aging Sexuality Knowledge and Attitudes Scale. Further, a series of independent sample t-tests indicated significant differences in terms of gender and active sex-life. The Cronbach alpha coefficients were .95 for the total score and between .86 and .90 for the sub-dimensions.

**Conclusion:** The findings of this study indicated that the scale can be used as a reliable and valid measure in Turkey.

**Key words:** Aged; Sexuality; Factor Analysis, Statistical; Attitude.

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## INTRODUCTION

Similar to other developmental stages, aging is a period characterized by physiological, behavioral, psychological, and social changes (1). Further, it is known that changes occurring during this period affect sexuality related to the psychological well-being of the elderly. Because sexuality is an essential dimension of human life and a right for every person, it is important to understand that sexuality does not end in old age and continues to be important for elderly people (2). However, it is generally assumed (due to various sexual myths) that the majority of elderly people have lost their sexual desire or cannot perform physically (3). Today, it remains common for the elderly to be defined as lacking in sexual attraction and desire and for their sexuality to be seen as taboo (4, 5). In a study conducted in Turkey, these sexual myths were investigated, with one of the most widely held being "it is not appropriate for the elderly to have sexual intercourse." (3). Other myths include female sexuality ending after the menopause and sexuality only being for young people (6).

Especially in cultures where sexual myths are common, it is known that knowledge and attitudes towards sexuality (which are directly related to an active sex-life) are also affected (7). When the attitudes of elderly people towards their sexuality were examined, they were found to be generally positive. Further, elderly who had more positive attitudes tended to continue their sexual life actively (8). In their study on elderly people, Walker and Ephross found that the majority were tolerant of sexuality. Similarly, 80% of the participants stated that masturbation is an acceptable sexual activity for elderly women. It is also noteworthy that there is a consistent gender difference in the attitudes of the elderly towards their sexuality (9). For example, in a study conducted by Træen, Carvalheira, Hald, Lange, and Kvaem in Norway, Denmark, Belgium, and Portugal, elderly women were found to be more conservative compared to elderly men (10). Similarly, Waite,

Laumann, Das, and Schumm found that elderly men have a more positive attitude towards their sexuality (11). Although there are some studies on attitudes towards the sexuality of the elderly, there is a lack of literature on this subject in Turkey. Moreover, in the few studies conducted on the sexuality of the elderly, the attitudes of health personnel, students studying in health-related departments, and family members of the elderly were frequently studied rather than the attitudes of elderly people themselves (12). Considering the perspectives of the elderly and trying to understand their views and needs about their sexuality will provide an opportunity to shape the services to be provided to the elderly and increase many positive developmental outcomes (13).

The Aging Sexuality Knowledge and Attitudes Scale (ASKAS) is frequently used in the literature to measure the attitudes of elderly people towards sexuality (14). However, it would be necessary to adapt this scale for a Turkish audience, since the scale is only translated and is used without investigating its validity and reliability. Because ASKAS includes a large number of scale items, the Sexual Attitude Scale for Elderly People has emerged as an expedient and practical scale for both elderly people and researchers. Instead of evaluating attitudes as a single dimension, it is thought that evaluating the volunteering, meaningfulness, closeness, and communication dimensions will provide more information. Therefore, the aim of this study is to adapt the Sexual Attitude Scale for Elderly People scale developed by Park, Shin, and Cha for a Turkish audience and examine its psychometric properties (15).

## MATERIALS AND METHODS

### Sample

The study sample consisted of 127 elderly people (aged  $\geq 60$  years) living in Izmir and Ankara. Participants who provide valid informed consent and understand the purpose of the study were included in the study. The participants were recruited from



the community; therefore, hospitalized older adults and nursing home residents were not included in the study.

### Measures

**Socio-demographic Information Form:** This form was prepared by researchers to obtain the following socio-demographic information: marital status, educational status, perceived socioeconomic level, chronic diseases, and sex-life.

**ASKAS:** This is used to evaluate the knowledge and attitudes of individuals towards sexuality of the elderly and was translated into Turkish by Doğan, Demir, Eker, and Karim (16). The scale has two sub-dimensions (knowledge and attitude) and 61 items in total. The first 35 knowledge questions gather basic information and are coded as “yes”, “no”, and “don’t know”, whereas the attitude questions are evaluated using a 7-point Likert type. Low scores in the knowledge dimension indicate that individuals have a high level of knowledge about the sexuality of elderly people, while low scores in the attitude dimension suggest that individuals have a more permissive attitude in terms of attitudes towards the sexuality of the elderly. It is known that this scale is commonly used to evaluate knowledge and attitudes in our country (16, 17). In this study, the Cronbach’s alpha internal consistency coefficients for the knowledge and attitude sub-dimensions were .91 and .92, respectively.

**Sexual Attitude Scale for Elderly People:** This scale was developed by Park, Shin, and Cha (15) to measure the attitudes of the elderly towards sexuality, which was then adapted into Turkish within the scope of this study. The scale consists of 18 items and is evaluated using a 5-point Likert scale (1 = Strongly disagree to 5 = Strongly agree). This scale has four sub-dimensions: volunteerism (6 items), significance (4 items), closeness (5 items), and communication (3 items). In the original study, the Cronbach alpha coefficient was calculated as .93.

### Procedure

Participants were recruited using an appropriate sampling method and snowball sampling, which are both non-random sampling methods. Data were collected between January 2019 and June 2019. After the purpose of the study was explained to the participants, their written informed consent was obtained. The scales were delivered to the participants in an envelope to reduce bias and took between 20 and 25 minutes to complete.

### Translation of The Sexual Attitude Scale for Elderly People into Turkish

After obtaining the necessary permissions from the authors who developed the scale for the adaptation study, the items of the scale were translated into Turkish by three research assistants who have command of English and Turkish. These translations were reviewed by another faculty member and translated back into English. Finally, to examine the comprehensibility of the scale, the scale was applied to some elderly people, the incomprehensible items were reorganized, and the scale was finalized.

### Data Analysis

The first task was to examine whether missing data were randomly distributed. According to Little’s MCAR test, it was found that the missing data (chi-square = 6160.362, df = 6887,  $p > .05$ ) were randomly distributed. Therefore, an average score was assigned to the missing data. The construct validity of the scale was then examined by exploratory and confirmatory factor analyses. Subsequently, a correlation analysis was performed to determine concurrent validity and the relationship of the scale with ASKAS scores was examined. To evaluate the discriminant validity, t-test analyses were performed and gender and active sex-life differences were examined. Finally, Cronbach alpha coefficients were used to evaluate the internal consistency of the adapted scale. All analyses were performed using SPSS 22.00 and LISREL 8.80 programs.

### Ethical Issues

Permission for the study was obtained from the Ufuk University Social and Human Sciences Scientific Research and Publication Ethics Committee (reference number: 2018-50).

## RESULTS

### Characteristics of the Sample

The age range of participants was 60–86 years ( $\bar{x}$  = 68.42,  $SD$  = 5.7), of which 61.4% ( $n$  = 78) were female and 38.6% were male. Further, 74% ( $n$  = 94) of the sample were married. Other demographic information about the sample is provided in Table 1.

### Construct Validity

The construct validity of the Sexual Attitude Scale for Elderly Individuals was first evaluated by exploratory factor analysis. The Kaiser–Meyer–Olkin (KMO) coefficient and Bartlett Sphericity tests were then conducted to examine whether the data were suitable for conducting an exploratory factor analysis. The KMO coefficient of the scale was .93 and the Barlett Sphericity test was found to be significant at  $p < .001$ . Because the KMO coefficient was  $> .50$  and the Barlett test was significant, this indicated the data set was suitable for conducting an exploratory factor analysis (18). Similar to the original structure of the scale, the number of factors was limited to four and equamax rotation was performed. The 4-factor structure explained 67.10% of the total variance. Within the scope of this study (as in the original scale), the first factor was voluntariness and the factor loads of the items ranged from .79 to .24. The factor loads of the items in the second factor (significance) varied between .74 and .30, while those in the third factor (intimacy) varied between .63 and .44. The factor loadings of the items in the final factor (communication) varied between .88 and .57.

The construct validity of the adapted scale was examined by second-order confirmatory factor

analysis (CFA). In the first stage, first-order CFA was applied to the model, which consisted of 4 latent and 18 observed variables, as in the original. As a result of the first-order CFA, it was observed that the  $t$  values obtained for the factor loads of all items and the relationship between latent variables were statistically significant. In addition, the first-order CFA results indicated an acceptable model fit ( $\chi^2$  = 189.57,  $p$  = .00,  $\chi^2/df$  = 1.50, RMSEA = .063, NFI = .96, NNFI = .98, CFI = .99, IFI = .99, and SRMR =

**Table 1.** Sociodemographic characteristics of the sample ( $N$  = 127)

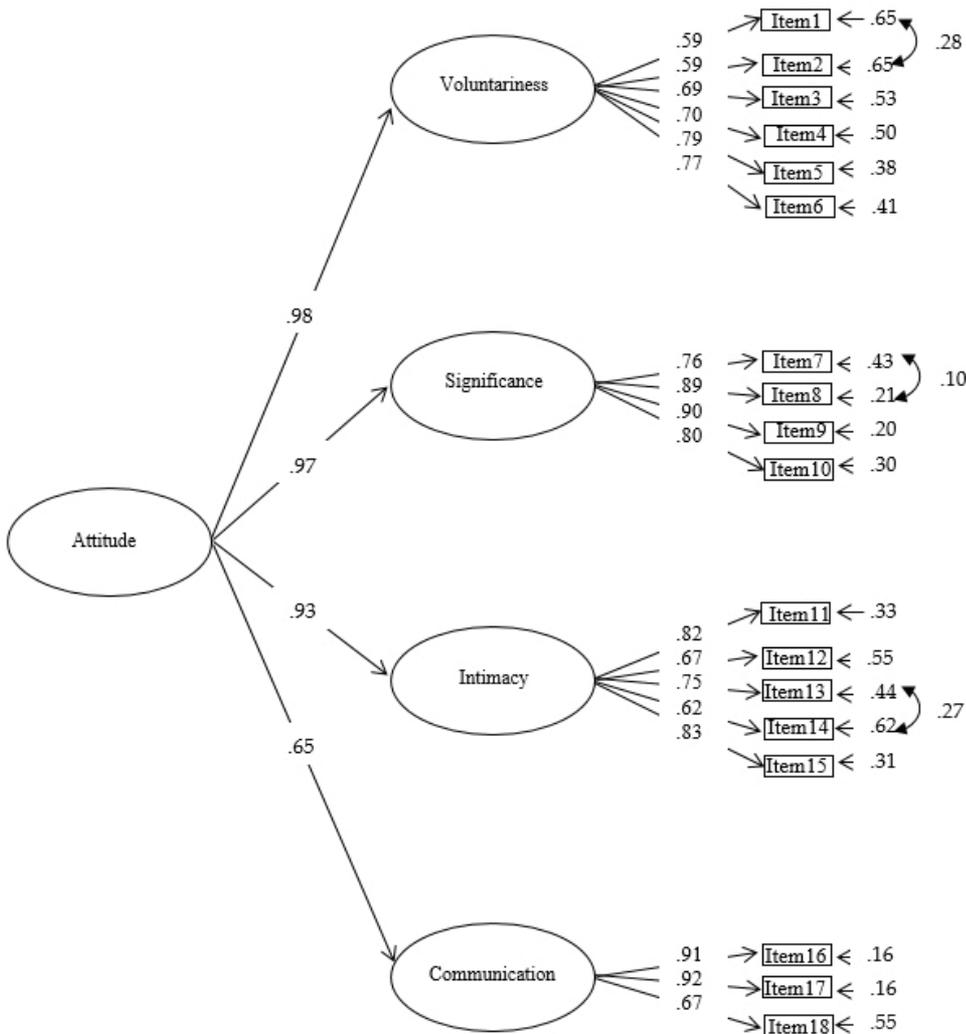
Variable	Frequency	%
Education level		
Literate / Primary School	55	43.2
Secondary / High School	45	35.5
College and above	27	21.3
Perceived SES		
Low	28	22
Middle	73	57.5
High	26	20.5
Chronic disease		
Yes	66	52
No	61	48
Active sex-life		
Yes	73	57.5
No	54	42.5
Frequency of sexual intercourse		
2-3 times a week	5	3.9
1 time per week	18	14.2
Once in 2 weeks	21	16.5
1 per month	8	6.3
Several times a year	8	6.3
No	54	42.5



.075). In the second-order CFA, the voluntariness, significance, intimacy, and communication dimensions of the scale were tested as components of the latent variable. As a result of the second-order CFA, it was observed that the t values were statistically significant for all variables. The second-order CFA results also indicated an acceptable model fit ( $\chi^2 = 227.68$ ,  $p = .00$ ,  $\chi^2/df = 1.78$ ,  $RMSEA = .079$ ,  $NFI =$

.96,  $NNFI = .98$ ,  $CFI = .98$ , and  $IFI = .98$ ). The ratio of  $\chi^2/df$  was found to be lower than the value of 5 recommended in the literature. Furthermore, the CFI, NFI, NNFI, and IFI values were higher than the .95 suggested in the literature (19). Finally,  $SRMR < .08$  and  $RMSEA$  were both indicators that the model data fit was acceptable (20). The values obtained as a result of second-order DFA are given in Figure 1.

Figure 1. Results of CFA of the Sexual Attitude Scale for Elderly People



### Concurrent Validity

To investigate the concurrent validity of the scale, the relationship between the attitude dimension of ASKAS (which measures a similar structure) and Sexual Attitude Scale for Elderly People was investigated. It was found that the concurrent validity was at an acceptable level and significant ( $r = -.57$ ,  $p < .01$ ).

### Discriminant Validity

For evidence of the discriminant validity of the adapted scale, it was examined whether attitudes towards sexuality of the elderly differed according to gender. A significant difference was found according to gender in terms of attitude ( $t = -3.94$ ,  $p < .001$ ). The scores for attitude of men ( $\bar{x} = 68.71$ ;  $SD = 12.93$ ) were higher than for women ( $\bar{x} = 58.31$ ;  $SD = 15.40$ ). Accordingly, it can be stated that elderly men are more permissive in terms of attitudes towards sexuality. In addition, it was found that attitudes towards sexuality also differed according to whether participants had an active sex-life ( $t = 2.84$ ,  $p < .01$ ). Further, attitude scores for those who continue to have an active sex-life ( $\bar{x} = 65.55$ ;  $SD = 14.92$ ) were higher than for those who did not continue to have an active sex-life ( $\bar{x} = 57.96$ ;  $SD = 14.87$ ). In other words, it can be said that elderly people who continue with an active sex-life are more permissive compared to those who do not continue with an active sex-life in terms of attitudes towards sexuality.

### Reliability

To determine the reliability of the adapted scale, the Cronbach alpha internal consistency coefficient was calculated. Accordingly, the Cronbach alpha internal consistency coefficient for the whole scale was found to be .95. In addition, the values were calculated as .86 for voluntariness, .90 for significance, .87 for intimacy, and .87 for communication.

### DISCUSSION

The aims of this study were to translate the Sexual Attitude Scale for Elderly People developed by Park, Shin, and Cha (15) into Turkish and determine its psychometric properties. First, exploratory and confirmatory factor analyses were conducted to examine the construct validity of the scale. From these analyses, it was found that the scale preserved the 4-factor structure in our country in a similar way to the original study. In addition, it is thought that the relationship validity is acceptable since there is a statistically significant relationship between scale scores and the attitude sub-dimension of ASKAS. It is also assumed that the scale has concurrent validity when the relationship between scales that evaluate similar structures is high (21). Because there were significant differences of attitudes towards sexuality in terms of gender (16, 22) and active sex-life (23), discriminant validity was evaluated by demonstrating the effect of gender and active sex-life on attitudes towards sexuality based on these findings in the literature. The results indicate that attitude scores obtained from the scale differ significantly according to gender and active sex-life. Thus, the scale is thought to have discriminant validity. To determine the reliability of the adapted scale, the Cronbach alpha internal consistency coefficient was calculated. Accordingly, it is possible to say that the Sexual Attitude Scale for Elderly People is a reliable measurement tool for an elderly sample, since the Cronbach alpha internal consistency coefficients for both the scale and its sub-dimensions were  $>.70$  (21).

In conclusion, the scale adapted within the scope of this study has sufficient psychometric properties for an elderly sample. Furthermore, adaptation of this scale is thought to be important in terms of contributing to studies on the sexuality of the elderly in our country. Although this study makes important contributions to the literature, there are some limitations. First, the number of participants was low



and they were only recruited from Ankara and Izmir. Hence, the generalizability of the findings is limited due to these sampling characteristics. It is suggested that working with a higher sample size and participants from different cities in future studies would contribute more to the literature. The second limitation of this study was collecting information from elderly people through self-report questionnaires. Considering this topic is taboo in our country, it should be remembered that participants might have provided biased (socially acceptable) answers. Finally, there is a need for studies that re-evaluate

the relationships between variables related to attitudes towards elderly sexuality using the adapted scale.

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