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BG Katzung. Special Aspects of Geriatric Pharmacology, In:Bertram G. Katzung,Susan B. Masters, Anthony J. Trevor (Eds). Basic and Clinical Pharmacology. 10th edition, Lange, Mc Graw Hill, USA 2007, pp 983-90.

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# Contents



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On behalf of the Editorial Board members of Turkish Journal of Geriatrics, I cordailly wish to thank the following reviewers who have helped to maintain and improve the quality of our journal during 2023.

With their constructive criticism they contributed not only to the development of articles and our journal, but also to the researchers at the academic life as well.

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Yeşim GÖKÇE KUTSAL

ORIGINAL ARTICLE

# THE EFFECT OF FRAILTY AND SARCOPENIA ON PERIOPERATIVE COMPLICATIONS IN PATIENTS OVER 65 YEARS UNDERGOING ELECTIVE SURGERY, PROSPECTIVE-OBSERVATIONAL STUDY

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## Abstract

**Introduction:** With aging of population, frailty and sarcopenia have become very important issues. Therefore, we aimed to evaluate patients for frailty and sarcopenia preoperatively who aged 65≤ underwent elective surgical operation in university hospital and search complications intraoperatively and postoperatively.

**Materials and Method:** This prospective, cross-sectional study performed between November 2021 and May 2022 at university hospital and patients aged 65 years and older underwent elective surgery included. Patients scored with frailty index. Both thickness and cross-sectional area of rectus femoris muscle were measured by ultrasound for evaluating sarcopenia in all patients, preoperatively. Anesthetic management, surgical risks were determined. Intraoperative and postoperative complications recorded.

**Results:** Totally 1112 patients were assessed and 279 patients were included. According to the cross-sectional area 35.5%; according to rectus femoris thickness 32.2% and according to both of them 25.4% were detected as sarcopenia. While fragility was detected in 151(54.7%) patients which 112(74.2%) pre-frail, 39(25.8%) fragile. 176(63.8%) patients experienced intraoperative complications. Postoperative complications were detected in 115(41.7%). The sarcopenia, frailty, and higher surgical risk classifications are increased intraoperative and postoperative complications (4.7, 4.1, 4 and 3.7, 6.4, 3.9 fold, respectively). Length of stay hospital (6.5 and 5 days) and intensive care unit (21 and 19 days), intraoperative (91.4% and 100%) and postoperative complication (81.4% and 87.2%) was higher sarcopenia and frailty ($p<0.001$).

**Conclusion:** Intraoperative and postoperative complications were observed higher in frail and sarcopenic patients. Evaluation of frailty and sarcopenia in over 65 years at preoperative period can be helpful for prediction to risk of intraoperative and postoperative complications.

***Keywords:*** Intraoperative Complications; Frailty; Mortality; Postoperative Complications; Sarcopenia.

## INTRODUCTION

Due the aging of the population, the frequency of surgical interventions in the elderly population is increasing. People older than 65 years comprise the majority of healthcare expenditure, and more than 40% of all surgical procedures involve geriatric patients (1,2). The prevalence of frailty has been reported to be between 4% and 59% in elderly populations (3).

Fried et al. defined vulnerability as a clinical syndrome with a biological basis due to the depletion of physiological reserves of multiple organ systems with age (4,5). Frailty is commonly associated with physical inactivity, smoking, poverty, cardiovascular diseases, and cancer (4). Surgical procedures are a source of acute stress. Such stress can lead to complications in the elderly population. As a result, frail individuals have a high risk of perioperative complications and delayed recovery (4,6,7). Frailty can assess with Frailty index which is first described by Fried et al (5).

Sarcopenia, which may be the cause or result of frailty, refers to the progressive loss of muscle mass and strength. Frailty increases after the seventh decade due to inactivity and increased muscle mass loss, which is associated with the loss of functional independence in many cases. In addition to fragility, sarcopenia is associated with immobilization, trauma, decreased physical strength, a weakened immune system, postoperative morbidity, and an increased mortality risk (5, 8, 9). Sarcopenia can be diagnosed based on low muscle quality or quantity using a number of methods. These include a simple 5-item questionnaire (SARC-F) and grip strength, chair stand, and timed-up-and-go tests. Muscle quality and quantity can also be assessed using dual-energy X-ray absorptiometry, bioelectrical impedance analysis, ultrasound (USG), computer tomography, or magnetic resonance imaging (10). USG is a practical and non-invasive bedside technique for the assessment of muscle thickness, fascicle length, cross-sectional area, echogenicity, and pennation angle. A systematic review concluded that USG is a reliable method for assessing muscle size in elderly individuals and aids in the diagnosis of sarcopenia (11). The effect of sarcopenia on postoperative complications has presented as independent risk factor (11,12).

In this prospective observational study, we aimed to evaluate the association between fragility, sarcopenia and perioperative complications in an elderly population.

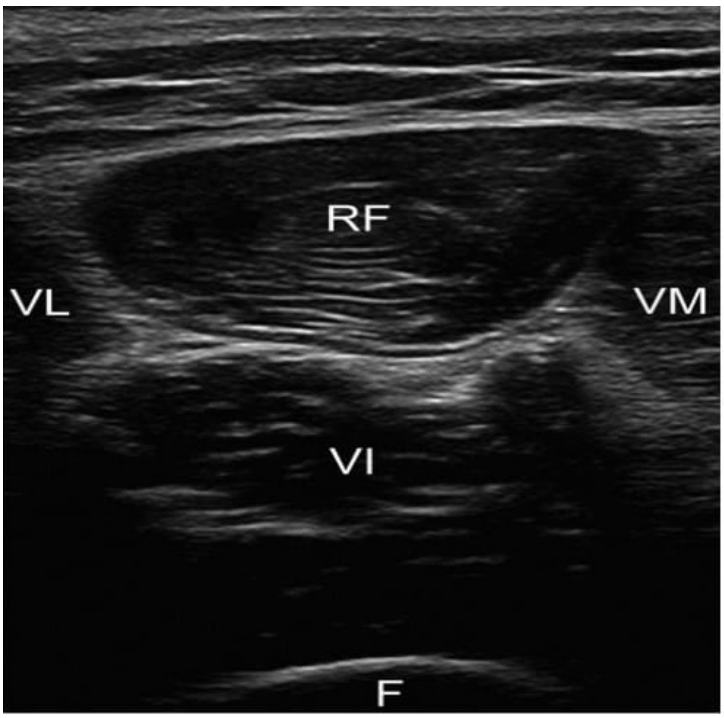
## MATERIALS AND METHOD

Our study included patients aged ≥ 65 years who underwent elective surgery at our university hospital between November 2021 and May 2022. Ethics Committee approval was obtained on (21 October 2021; No:156). Written informed consent was obtained from all the patients. The exclusion criteria were patients younger than 65 years, patients where local anesthesia was administered, and patients who underwent emergency surgery. The same anesthesia resident performed all the preoperative assessments of the patients included in this study at the preoperative care unit. Preoperative patient data were obtained from the hospital database. The demographic data (sex, age, weight, height, body mass index [BMI]) of all patients were recorded. The type of operation, diagnosis, concomitant diseases, previous operations, surgical risk class, and American Society of Anesthesiology Physical Risk Classification (ASA) were recorded in the preoperative care unit. Marital status, income level, education level, cognitive impairment, and household status such as living alone were recorded. All patients were evaluated using the Fried Frailty Index to diagnose frailty (5). If the Frailty index score was 1 or 2, it was defined as prefrail, and if it was 3 or above, it was defined as frail.

All patients underwent USG assessment (Esaote MyLabtmSix) in B mode for sarcopenia using a linear high-frequency probe, and rectus femoris muscle

measurements were made in the preoperative care unit. Rectus femoris muscle height and surface area were measured in all patients in the preoperative care unit. All measurements were performed by the same anesthesia resident to prevent inter-rater variation. Each measurement was performed three times and the average measurement was recorded. USG assessments and measurements were performed with the patient in a supine position, with both hips and knees in full extension, and at rest. The midpoint of the distance between the lateral epicondyle and trochanter major of the femur was determined as the reference point for measurements in all patients. A linear USG probe was placed in the transverse plane along the upper part of the thigh. A large amount of gel was applied to minimize muscle compression and avoid pressure on the muscle. Cross-sectional images of the rectus femoris muscle were obtained. After the images were obtained, rectus femoris thickness and cross-sectional area measurements were performed (Figure 1).

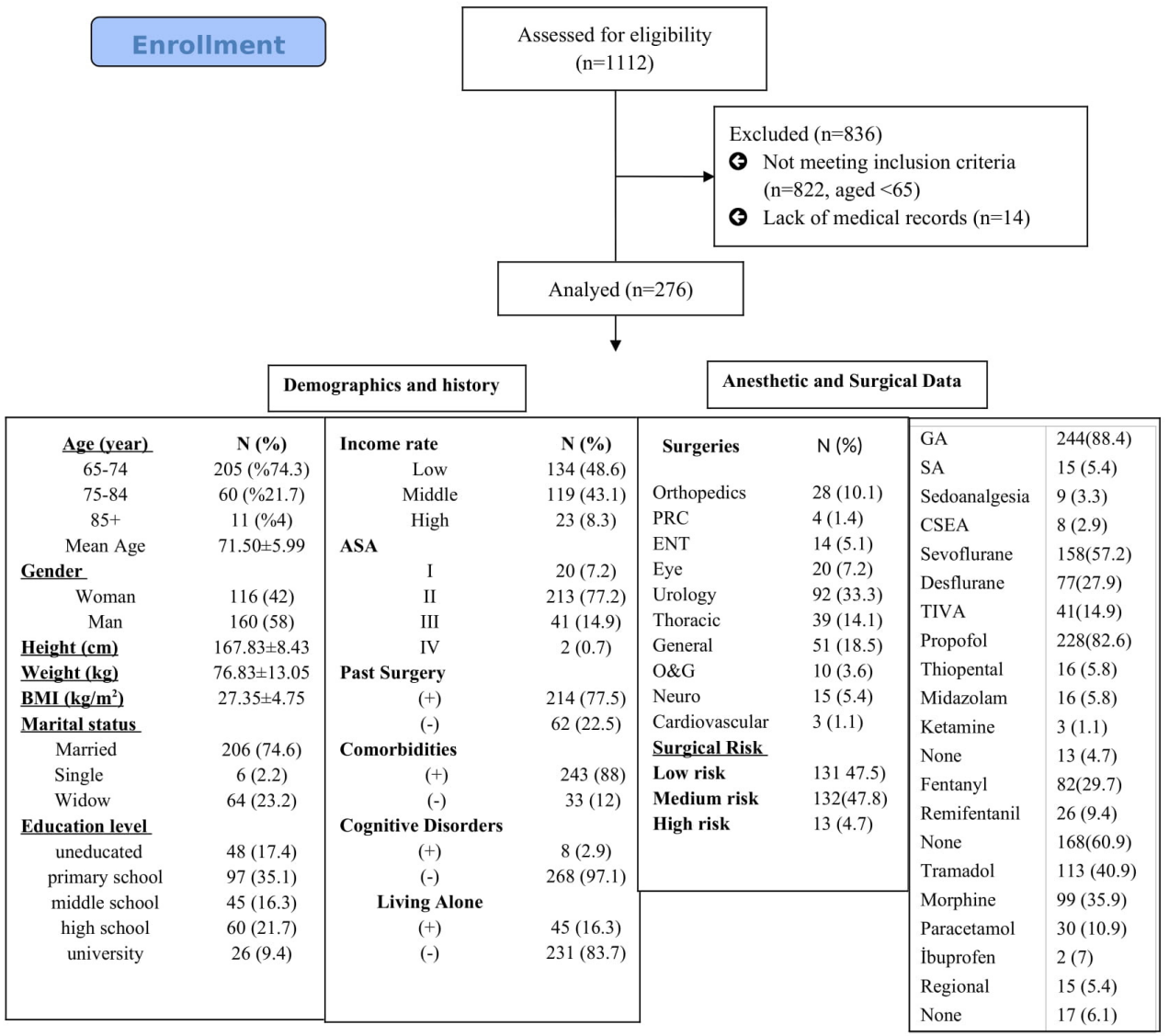
To ensure that the preanesthetic assessment time was as short as possible, we did not assess muscle strength, and sarcopenia was defined based on low muscle mass, as determined using USG. To determine the cut-off value for the diagnosis of sarcopenia, rectus femoris muscle measurements with USG were obtained from 50 ASA I–II patients aged 20–40 years who were not recruited to the study population. Based on these measurements, we determined the cut-off values for defining sarcopenia. Which values below 3.36 $cm^2$ and 4.56 $cm^2$ for the rectus femoris cross-sectional area and, 11.11 mm and 11.9 mm for rectus femoris thickness in females and males, respectively, assumed as sarcopenia. This method was previously described by Kara et al (13).




**RF:** Rectus femoris
**VL:** Vastus lateralis
**VI:** Vastus intermedius
**VM:** Vastus medialis
**F:** Femur

**Figure 1.** Ultrasound Image of Rectus Femoris

## Flow Diagram




| Age (year) | N (%) |
|---|---|
| 65-74 | 205 (%74.3) |
| 75-84 | 60 (%21.7) |
| 85+ | 11 (%4) |
| Mean Age | 71.50±5.99 |
| **Gender** | |
| Woman | 116 (42) |
| Man | 160 (58) |
| **Height (cm)** | 167.83±8.43 |
| **Weight (kg)** | 76.83±13.05 |
| **BMI (kg/m²)** | 27.35±4.75 |
| **Marital status** | |
| Married | 206 (74.6) |
| Single | 6 (2.2) |
| Widow | 64 (23.2) |
| **Education level** | |
| uneducated | 48 (17.4) |
| primary school | 97 (35.1) |
| middle school | 45 (16.3) |
| high school | 60 (21.7) |
| university | 26 (9.4) |

| Income rate | N (%) |
|---|---|
| Low | 134 (48.6) |
| Middle | 119 (43.1) |
| High | 23 (8.3) |
| **ASA** | |
| I | 20 (7.2) |
| II | 213 (77.2) |
| III | 41 (14.9) |
| IV | 2 (0.7) |
| **Past Surgery** | |
| (+) | 214 (77.5) |
| (-) | 62 (22.5) |
| **Comorbidities** | |
| (+) | 243 (88) |
| (-) | 33 (12) |
| **Cognitive Disorders** | |
| (+) | 8 (2.9) |
| (-) | 268 (97.1) |
| **Living Alone** | |
| (+) | 45 (16.3) |
| (-) | 231 (83.7) |

| Surgeries | N (%) |
|---|---|
| Orthopedics | 28 (10.1) |
| PRC | 4 (1.4) |
| ENT | 14 (5.1) |
| Eye | 20 (7.2) |
| Urology | 92 (33.3) |
| Thoracic | 39 (14.1) |
| General | 51 (18.5) |
| O&G | 10 (3.6) |
| Neuro | 15 (5.4) |
| Cardiovascular | 3 (1.1) |
| **Surgical Risk** | |
| **Low risk** | 131 47.5) |
| **Medium risk** | 132(47.8) |
| **High risk** | 13 (4.7) |

| | |
|---|---|
| GA | 244(88.4) |
| SA | 15 (5.4) |
| Sedoanalgesia | 9 (3.3) |
| CSEA | 8 (2.9) |
| Sevoflurane | 158(57.2) |
| Desflurane | 77(27.9) |
| TIVA | 41(14.9) |
| Propofol | 228(82.6) |
| Thiopental | 16 (5.8) |
| Midazolam | 16 (5.8) |
| Ketamine | 3 (1.1) |
| None | 13 (4.7) |
| Fentanyl | 82(29.7) |
| Remifentanil | 26 (9.4) |
| None | 168(60.9) |
| Tramadol | 113 (40.9) |
| Morphine | 99 (35.9) |
| Paracetamol | 30 (10.9) |
| İbuprofen | 2 (7) |
| Regional | 15 (5.4) |
| None | 17 (6.1) |

**Figure 2.** Flow diagram

Regarding the perioperative period, data on the type of anesthesia, duration of anesthesia, complications, and drugs were obtained from the anesthesia charts and the hospital's information record system. Patients' medical records during the postoperative period (postoperative care unit and/or 30$^{th}$ day of surgery) were searched, and complications (hypoxemia, hypotension,

hypertension, bradycardia, tachycardia, arrhythmias, reintubation, bleeding, etc.), discharge time, and intensive care unit admission were recorded.

### Statistical Analysis

The Statistical Package for the Social Sciences (SPSS 23.0) program was used in the statistical analysis of the data. Categorical measurements are presented as numbers and percentages, and continuous measurements as mean and SD (median and minimum-maximum where appropriate). Chi-square and Fisher's exact tests were used to compare categorical data. The independent Student's t-test was used for normally distributed parameters and Mann-Whitney U test was used for non-normally distributed parameters. Logistic regression analysis was conducted to determine relationships between the variables.

## RESULTS

A total of fourteen (1112) patients underwent surgery between November 2021 and May 2022 in our hospital, and 290 patients were aged ≥ 65 years. A total of 290 patients were recruited for the study during the designated time period, but 14 patients were excluded because of a lack of medical records. A total of 276 patients aged ≥ 65 years who underwent elective surgery were included in the study. The patient demographics, medical history, anesthetic and surgical data are shown in Flow diagram (Figure 2). A total of 176 patients (63.8%) experienced intraoperative complications, 115 patients (41.7%) experienced postoperative complications. Hypotension was the most common intraoperative complication (N=100, 38 %). Sarcopenia was detected in 98 (35.5%), 89 (32.2%), and 70 (25.4 %) patients according to the cross-sectional area, RF thickness, and both (cross-sectional area and RF thickness), respectively. Frailty was detected in 151 patients (54.7%) [112 patients (74.2%) pre-frail and 39 patients (25.8%) frail. (Table 1). Relation between sarcopenia, frailty and complications are shown in Table 2. The hypotension (67.1 %), tachycardia (21.4%), arrhythmia (25.7%), hypoxia (22.9%), bleeding (31.4%) and ST changes (10%) risks are increased at intraoperative period and hypotension (22.9%), tachycardia (34.3%), arrhythmia (18.6%), hypoxia (40%), ST changes (18.6%) and exitus (10%) risks are increased during postoperative period in sarcopenic patients. Hypotension (74.4%) and arrhythmia (35.9%) risks increased during the intraoperative period and hypotension (38.9%), bradycardia (2.9%), arrhythmia (25.6%), hypoxia (53.8%), and ST changes (20.5%) increased during the postoperative period in frail patients. Intraoperative complications

**Table 1.** Sarcopenia and Frailty

| | N (%) |
|---|---|
| **Sarcopenia** | |
| By cross-sectional area | 98 (35.5) |
| By RF thickness | 89 (32.2) |
| By both cross-sectional area and RF thickness | 70 (25.4) |
| **Frailty** | 151 (54.7) |
| Pre-frail | 112 (74.2) |
| Frail | 39 (25.8) |

Data presented as number and percentage. (N/%)

**Table 2.** Sarcopenia, Frailty and Complications

| | Sarcopenia | | P | Frailty | | P |
|---|---|---|---|---|---|---|
| | (-) (n=206) | (+) (n=70) | | Pre-Frail (n=112) | Frail (n=39) | |
| **Intraoperative Complications** | 112 (54.4) | 64 (91.4) | **<0.001** | 87 (77.7) | 39 (100) | **0.001** |
| **Intraoperative Complications** | | | | | | |
| Hypotension | 58 (28.2) | 47 (67.1) | **<0.001** | 53 (47.3) | 29 (74.4) | **<0.001** |
| Hypertension | 37 (18) | 14 (20) | **0.704** | 32 (28.6) | 6 (15.4) | 0.102 |
| Bradycardia | 17 (8.3) | 7 (10) | **0.654** | 10 (8.9) | 6 (15.4) | 0.259 |
| Tachycardia | 14 (6.8) | 15 (21.4) | **0.001** | 14 (12.5) | 8 (20.5) | 0.222 |
| Arrhythmia | 15 (7.3) | 18 (25.7) | **<0.001** | 11 (9.8) | 14 (35.9) | **<0.001** |
| Hypoxia | 24 (11.7) | 16 (22.9) | **0.021** | 23 (20.5) | 13 (33.3) | 0.106 |
| Bleeding | 25 (12.1) | 22 (31.4) | **<0.001** | 24 (21.4) | 14 (35.9) | 0.073 |
| ST change | 1 (0.5) | 7 (10) | **<0.001** | 4 (3.6) | 4 (10.3) | 0.108 |
| **Postoperative Complications** | 58 (28.2) | 57 (81.4) | **<0.001** | 64 (57.1) | 34 (87.2) | 0.001 |
| **Postoperative Complications** | | | | | | |
| Hypotension | 9 (4.4) | 16 (22.9) | **<0.001** | 9 (8.0) | 15 (38.9) | **<0.001** |
| Hypertension | 29 (14.1) | 14 (20.0) | 0.238 | 25 (22.3) | 8 (20.5) | 0.814 |
| Bradycardia | - | 2 (2.9) | 0.064 | - | 2 (2.9) | **0.016** |
| Tachycardia | 19 (9.2) | 24 (34.3) | **<0.001** | 26 (23.2) | 13 (33.3) | 0.214 |
| Arrhythmia | 3 (1.5) | 13 (18.6) | **<0.001** | 6 (5.4) | 10 (25.6) | **<0.001** |
| Hypoxia | 27 (13.1) | 28 (40) | **<0.001** | 29 (25.9) | 21 (53.8) | **0.001** |
| Bleeding | 2 (1.0) | - | 0,408 | 1 (0.9) | 1 (2.6) | 0.432 |
| ST change | 1 (0.5) | 13 (18.6) | **<0.001** | 6 (5.4) | 8 (20.5) | **0.005** |
| Atelectasis | 15 (7.3) | 10 (14.3) | 0.078 | 15 (13.4) | 7 (17.9) | 0.487 |
| Exitus | 3 (1.5) | 7 (10.0) | **0.003** | 5 (4.5) | 5 (12.8) | **0.071** |
| **Length of stay in hospital [Med (25-75)]** | 4 (2-6) | 6,5 (3-14) | **<0.001** | 3 (2-4) | 5 (3-8) | **<0.001** |
| **Intensive Care Unit Admission** | 13 (6.3) | 21 (30) | **<0.001** | 15 (13.4) | 19 (48.7) | **<0.001** |
| | **Others (n=239)** | **Both Sarcopenic and Frail (n=37)** | | **p** | | |
| **Intraoperative Complications** | 139 (58.2) | 37 (100) | | **<0.001** | | |
| **Postoperative Complications** | 82 (34.3) | 33 (89.2) | | **<0.001** | | |

Chi-square test and Fisher exact test were used

**Table 3.** Relation between Sarcopenia, Frailty, Age and Surgical Risk with Intraoperative and Postoperative Complications

| | Intraoperative Complications | | | | | Postoperative Complications | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | β | Sig | Exp (β) | 95% CI EXP (β) | | β | Sig | Exp (β) | 95% CI EXP(β) | |
| | | | | Upper | Lower | | | | Upper | Lower |
| **Sarcopenia** | 1.552 | 0.001 | 4.719 | 1.958 | 11.375 | 1.312 | 0.000 | 3.712 | 1.814 | 7.596 |
| **Frailty** | 1.418 | 0.000 | 4.130 | 2.197 | 7.761 | 1.858 | 0.000 | 6.408 | 3.252 | 12.627 |
| **Age** | -0.004 | 0.908 | 0.996 | 0.936 | 1.061 | 0.011 | 0.707 | 1.011 | 0.953 | 1.073 |
| **Surgical risk** | 1.389 | 0.000 | 4.012 | 2.189 | 7.354 | 1.366 | 0.000 | 3.919 | 2.093 | 7.338 |

were observed in all of both sarcopenic and frail patients (N=37), while postoperative complications were observed in 33 patients (89.2%) ($p<0.001$ and $p<0.001$, respectively) (Table 2), and there was a statistically significant relationship between sarcopenia, frailty, and surgical risk with intraoperative and postoperative complications in logistic regression analysis. In patients with sarcopenia, the risk of intraoperative complications is increased by 4.79 times, the risk of postoperative complications is increased by 3.71 times, in patients with frailty, the risk of intraoperative complications is increased by 4.13 times, the risk of postoperative complications is increased by 6.40 times, in patients with medium-high surgical risk, the risk of intraoperative complications is increased by 4.01 times, and the risk of postoperative complications is increased by 3.91 times (Table 3). The age did not affect to the intraoperative and postoperative complications in patients aged ≥ 65 years.

## DISCUSSION

In our study, we assessed patients aged ≥ 65 years in the preoperative period in terms of sarcopenia and fragility and associated intra and postoperative complications. The results revealed that both frailty and sarcopenia were related to intraoperative and postoperative complications.

When we assessed both rectus femoris muscle thickness and cross-sectional area, we found that 70 patients (25.4%) had sarcopenia. In a recent article on 160 cases, Yi et al. concluded that the measurement of rectus femoris thickness and echogenicity on USG was useful in demonstrating sarcopenia (14). In a study published in 2020, Kan et al. reported that the prevalence of sarcopenia among geriatric patients in Turkey was 26% (15). We found higher rates of sarcopenia in our study and detected sarcopenia in. All patients aged > 85 years were sarcopenic.

We determined that a low level of education, low-income level, presence of cognitive impairment, and living alone were significant risk factors for the development of sarcopenia. These risk factors are likely linked to poor nutritional status, resulting in sarcopenia. In our study, the rate of sarcopenia development was 21% and 26% in women and men, respectively. This result was consistent with the literature (16).

In a prospective study of 255 patients who underwent gastrointestinal surgery, Wang et al. assessed sarcopenia preoperatively based on various factors, such as lumbar skeletal muscle index, hand grip strength, and walking speed, and detected sarcopenia in 32 (12%) patients (17). They found a significant correlation between sarcopenia and low BMI, preoperative serum

albumin, and hemoglobin levels in these patients. In their study, the postoperative complication rates, length of hospital stay, and hospital costs were higher in the patients with sarcopenia. In our study, the incidence of postoperative complications (hypotension, tachycardia, arrhythmia, and hypoxia) was significantly higher in patients with sarcopenia.

Previous research has been shown that sarcopenia is associated with a prolonged postoperative recovery period and hospital stay time, in addition to increased morbidity and mortality (18). Similarly, in our study, the postoperative mortality rate in patients with sarcopenia was significantly higher. In the present study, sarcopenia was detected more frequently in medium- or high-risk patients, according to the surgical risk classification.

Using Fried's frailty index, we detected frailty in 151 (54.7%) patients, with 112 (74.2%) patients classified as prefrail and 39 (25.8%) patients classified as frail. Hoover et al. reported frailty in 11–25% of individuals older than 65 years and in 50% of individuals older than 85 years (19). Bandeen et al. conducted a comprehensive population survey of frailty in the U.S. population in 2011 that included over 7,000 individuals aged 65–90 years (20). In their study, 15.3% of the participants were frail, 45.5% were prefrail, and 39.2% were healthy. These results were consistent with the incidence of frailty observed in the present study.

Khandelwal et al. examined the relationship between frailty, mortality risk, and length of stay in hospitalized patients (N= 250) (21). They determined that 83 patients (33.2%) were frail and that the risk of mortality and prolonged hospitalization were higher among frail than nonfrail patients (21). In a meta-analysis consisting of 23 studies examining the relationship between frailty and postoperative outcomes, frailty was associated with increased mortality, postoperative complications, and prolonged hospitalization (13). In our study, the rate of intensive care hospitalization was higher in frail patients than prefrail patients. In addition, the frail group had a significantly higher mortality rate in the postoperative period than the prefrail and nonfrail groups did.

In a study by Polidoro et al., atrial fibrillation was associated with frailty, independent of age, sex, and some common systemic diseases (22). In our study, arrhythmia in the postoperative period was higher in the frail group than in the prefrail and nonfrail groups. Thirty-three (89.2%) of 37 patients who were both sarcopenic and frail developed postoperative complications. Furthermore, sarcopenia, frailty, and higher surgical risk classifications increased intraoperative and postoperative complications.

## LIMITATIONS

Our study has some limitations. First, this was a cross-sectional study, and data were obtained only from patients undergoing elective surgeries. Therefore, the patient population was heterogeneous. A subsequent study could perhaps include patients undergoing emergency surgeries or specific surgical interventions. In addition, with the aim of shortening the preanesthetic evaluation time, we used only USG to evaluate sarcopenia. Clearly, a diagnosis of sarcopenia requires an assessment of muscle strength. To confirm the diagnosis of sarcopenia, other methods, such as dual-energy X-ray absorptiometry or magnetic resonance imaging, would have been needed. The diagnosis of sarcopenia based on muscle mass only using USG is a limitation of our study. However, USG is a practical, noninvasive method for the rapid prediction of sarcopenia in daily practice.

## CONCLUSION

The assessment of sarcopenia with bedside USG is a very easy and useful method for daily practice. In this study, we assessed frailty and sarcopenia preoperatively in older patients and found that both sarcopenic and frail individuals were at risk for postoperative complications. We assumed that the detection of sarcopenia and frailty in

the preoperative period could provide better perioperative conditions and prevent complications in elderly patients undergoing surgical procedures.

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ORIGINAL ARTICLE

# A NEW PROGNOSTIC SCALE IN ISCHEMIC STROKE: THE SELCUK SCORE

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## Abstract

**Introduction:** The incidence of stroke is increasing worldwide; thus, prognostic scales with higher predictive values are becoming more important. We aimed to develop a new, simple and useful prognostic scale with high predictive power to predict stroke prognosis.

**Materials and Method:** The blood samples, imaging data, and clinical parameters of 1697 stroke patients were analyzed retrospectively to evaluate hospital mortality. Binary logistic regression analysis was applied, and appropriate parameters were determined. The Hosmer-Lemeshow test was used for the calibration, and internal validation was applied to the model. Comparisons were performed using the Totaled Health Risks in Vascular Events score and Ling et al. scores (2019), which were evaluated.

**Results:** Level of consciousness, length of hospital stay, albumin level, National Institutes of Health Stroke Scale score, lesion volume, periventricular hypodensity, and age were the most significant preevaluation parameters. The sensitivity and specificity of the model in predicting mortality were 83.6% (78.4–88%) and 81.2% (79.1–83.2%), respectively. The area under the curve for our developed model was 0.884 (0.868–0.899) ($p<0.001$). This value was higher than the Totaled Health Risks in Vascular Events score of 0.822 (0.803–0.840) and Ling et al. score (2019) of 0.864 (0.847–0.880) in the literature.

**Conclusions:** The novel Selcuk scoring system, has a better predictive power than other well-known scales used to evaluate mortality. Although the system was proven to be accurate by internal validation, it should be tested in different environments. After further clinical validation studies, our model is anticipated to be useful and promising in clinical daily practice.

***Keywords:*** Mortality; Prognosis; Stroke; Risk Factor; Geriatrics.

## INTRODUCTION

A significant portion of the patient burden in neurology and intensive care units (ICUs) mainly consists of stroke patients, most of whom are from the geriatric population. It is the clinician's responsibility to evaluate the severity of the clinical condition, approach the challenge in terms of acute treatment, investigate the risk factors, provide an appropriate medication to minimize the risk of recurrent stroke, and discharge the patient as soon as possible.During the acute and post-acute treatment process, especially patients and their relatives expect to acquire prompt information from health-care providers. The physician's past experience is used to evaluate the condition, but it may not always be easy to predict the current state, severity, and future state of the clinical syndrome. At the same time, personal assessments may not always be objective in making decisions. In the Clinician Judgment vs Risk Score to Predict Stroke Outcomes (JURaSSiC) study, where clinicians evaluated patients to estimate the incidence rates of death and disability, and only 16.9% of the estimations matched the facts (1). In an environment where patients and their relatives expect accurate and easily accessible information from physicians and plan the next treatment modalities, the importance of scales that can reevaluate patients and predict their prognosis becomes more evident.

In the present study, our aim was developing a unique prognostic scale that can be used to predict stroke prognosis, especially in elderly patients. We achieved this by retrospectively evaluating patients treated for stroke in our clinic, where the study was conducted. Thus, we chose to call the scale "the Selcuk score."

## METHODS

The present study, which had a retrospective and cross-sectional design, was conducted in the Department of Neurology, Faculty of Medicine, Selcuk University. Approval was obtained from the Local Ethics Committee for Clinical Researches of Selcuk University before the study (approval number: 2020-473). Patients older than 18 years who were admitted to the hospital with the diagnosis of acute stroke between 2016 and 2020 were included and evaluated in the study. Patients with a diagnosis of head trauma, subarachnoid hemorrhage, subdural or epidural hematoma, and sinus vein thrombosis were excluded from the study. Of the 2030 patients enrolled, 188 had transient ischemic attacks and 145 had parenchymal hemorrhages. The study was conducted with 1697 ischemic stroke patients.

The date of admission, age and gender, dates of discharge or exitus, and the length of hospital stay were recorded. Comorbid conditions such as diabetes mellitus (DM), hypertension (HT), history of coronary artery disease (CAD) and/or exposure to any coronary intervention, malignancy, chronic renal failure (CRF) and/or undergoing dialysis treatment, dementia, smoking status, atrial fibrillation (AF), and previous stroke history were determined through the patients' hospital records and the etiological examination performed during hospitalization.

In the first examination, the state of consciousness, Vulpian sign, muscle strength in the upper and lower extremities, presence of cranial nerve involvement, speech status, Glasgow coma scale (GCS) scores, National Institutes of Health Stroke Scale (NIHSS) score, and the modified Rankin score (mRS) were evaluated. Cranial computed tomography (CT) and diffusion magnetic resonance imaging (MRI) tests were performed to determine the localization and size of the lesions. The formula (largest diameter × number of slices × slice thickness/2) was used to calculate the volume of the lesion, which reveals the diffusion restriction in the cerebrum and cerebellum. Stroke lesions with an average volume of $<5$ cm$^3$ were considered small, those between 5 and 15 cm$^3$ were considered medium-sized, and those $>15$ cm$^3$ were regarded as large stroke lesions. In the brain stem, however,

while stroke lesions < 1 $cm^3$ were classified as small, those between 1 to 1.5 $cm^3$ and >1.5 $cm^3$ were accepted to be medium- and large-volume stroke lesions. The presence of periventricular hypodensity and carotid artery stenosis were evaluated using CT angiography, carotid and vertebral artery Doppler ultrasonography, MRI angiography, and digital subtraction angiography. The patients' blood samples drawn at the time of hospitalization were also analyzed. The reference values for blood glucose level (mg/dL), leukocyte count (K/μL), and levels of hemoglobin (g/dL), creatinine (mg/dL), urea (K/μL), C-reactive protein (CRP; mg/L), and albumin (g/dL) were recorded. The type of recanalization treatment administered to the patients due to the indications and the time the treatment was started were also recorded. Whether the complications were systemic or related to the central nervous system (CNS), the subtype of CNS complications, the need for intensive care and ventilation support, and the requirement for a decompressive craniectomy operation were determined. The Trial of Org 10172 in Acute Stroke Treatment (TOAST) (2), which was etiologically evaluated during hospitalization, was specified, and the mRS, GCS score, Glasgow outcome scale (GOS) score, and NIHSS score were recorded at discharge.

### Statistical Analysis

All statistical analyses were performed using R-3.6.0 for Statistical Computing for Windows (https://www.r-project.org) program. Before the analyses, the normality of the data was checked with the Shapiro-Wilk normality test and Q-Q graphs, and the homogeneity of the variances was checked using the Levene test. The parameters with an extremely skewed distribution to the right were analyzed by applying a logarithmic transformation. Numerical data were expressed as mean ± standard deviation (SD) for the variables with normal distribution, as a geometric mean (95% confidence interval [CI]) for the parameters with logarithmic transformation, and as median (interquartile range [IQR]) for those without logarithmic transformation. Categorical data were presented as frequency (n) and percentile (%). The independent-sample *t* test, Welch *t* test, Mann-Whitney *U* test, or Yuen (robust) independent-sample test were used to compare the numerical parameters related to mortality status. The Pearson chi-square, Yates continuity corrected chi-square, or Fisher exact chi-square test was used to compare the categorical variables. For the primary purpose of the study, binary logistic regression was performed using univariate and multivariate analyses to develop a new scoring system based on the risk model for mortality. Possible independent risk factors were determined by investigating the effects of blood parameters, demographic characteristics, and clinical findings related to mortality in the univariate binary logistic regressions. In the univariate binary logistic regression analysis, significant candidate independent risk factors of mortality were modeled together, and using the stepwise variable selection method, the insignificant variables were removed from the model. Therefore, a novel risk model that predicts mortality during hospitalization was created for patients with ischemic stroke. The coefficients in the multivariate binary logistic regression model were used to calculate the new risk score. The scores were obtained by rounding the regression coefficients to the nearest value.

In addition, to show that the variables in this new risk model are indeed significant parameters for classifying mortality, the patients were classified as either exitus or survivors under the algorithm of the gradient boosting classification. Twenty percent of the data were used for testing, whereas 80% were utilized for training; however, 20% of the 80% for training were used for validation in the gradient boosting algorithm. The results of the gradient boosting classification algorithm were presented as the values of precision, recall, F1 measurement, and area under curve (AUC). The variables used in the risk model were also shown to be significant.

The calibration of the newly created risk model was checked with the Hosmer-Lemeshow test, and the discrimination was checked by evaluating the area under the ROC curve.

On the other hand, the diagnostic performance of the newly developed risk scoring system in predicting mortality was calculated in terms of sensitivity, specificity, and positive (PPV) and negative predictive values (NPV)and compared with those in the literature that were determined using the DeLong method (3). The sensitivity and specificity values of the risk scores were compared using the McNemar test, and PPVs and NPVs were compared with the weighted generalized statistical test scores (4). Missing data were excluded from the analysis, and in evaluating the statistical tests, a significance level of 5% was considered.

## RESULTS

A total of 1697 patients, including 913 men (53.8%) and 784 women (46.2%), were enrolled in the present study, with a mean age of 66.92 ± 14.16 years (range, 19–98 years). Whereas 1447 (85.26%) of the patients were discharged, 250 (14.73%) died in the hospital. The baseline information of all patients is shown in Table 1. The results of the binary logistic regression analysis of the risk factors of poor prognosis in patients with acute ischemic stroke (AIS) are shown in Table 2.

As a result of the multiple logistic regression analysis, nine candidate markers were identified for the proposed model in the estimation of the mortality risk and calculated as in Table 3.

In terms of statistical significance, 0.5 point was assigned for each of urea level (>44 mg/dL), age (≥70 years), and periventricular hypodensity. However, 1 point was assigned for each of consciousness (somnolence, lethargy, and coma), speech (dysphasia and aphasia), hospital stay (≥14 days), and albumin level (<3.5 g/dL). One and 2 points were assigned for NIHSSs between 10–19 and ≥20. For medium and large volume stroke lesions, 0.5 and 1 point were assigned. Therefore, a new prediction model with a total score of 8.5 points was achieved. The ROC curve analysis was performed to compare the diagnostic performance of the Selcuk score, which we developed in our study, with those of the THRIVE (5) and Ling et al. scores (6), and the findings from the comparisons are indicated in Figure 1. The findings from the ROC curve analysis, sensitivity, specificity, cutoff value, PPV, and NPV of the Selcuk, THRIVE (5), and Ling et al. (6) scores are summarized in Table 4. The AUC value of the Selcuk score was significantly higher than those of the other models investigated in the study.

## DISCUSSION

AIS is a common disease that can lead to serious consequences. Stroke is one of the most important causes of morbidity and mortality, especially in the geriatric age group, as age is the most important factor that increases the prevalence of stroke. Researchers have been trying to define prognostic factors related to AIS for years, which include stroke severity (7), localization of the lesion and volume (8), stroke etiology (9), acute treatment method, certain blood parameters (10), need for intensive care during hospitalization, and the development of complications (11). Although these factors may individually affect patient prognosis, the estimation accuracy of the scales created by combining several of these factors is likely to increase.

Although researchers have developed numerous scaling systems for assessing stroke prognosis, many healthcare professionals still do not widely use them. Several reasons explain why scales are not applied in daily practice, including the complex scoring system of the scale, the physician's inability to remember the scoring easily, the need for complex imaging and examinations, and the requirement for an expert's opinion or a specialist's examination. Owing to our country's current health

**Table 1.** Evaluation of demographic and clinical features, clinical imaging and laboratory findings of patients with acute ischemic stroke

| Parameters | | All patients n=1697 | Survivors n=1447 | Exitus n=250 | p-value |
|---|---|---|---|---|---|
| Age (years) | ≥70 | 825 (48.62%) | 653 (45.13%) | 172 (68.80%) | <0.001 [a] |
| Gender | Male | 913 (53.80%) | 808 (55.84%) | 105 (42.00%) | <0.001 [a] |
| Number of hospitalization days | ≥14 | 425 (25.04%) | 325 (22.46%) | 100 (40%) | <0.001 [a] |
| Recurrent stroke | Yes | 456 (26.87%) | 382 (26.40%) | 74 (29.60%) | 0.292 [a] |
| DM | Yes | 641 (37.77%) | 540 (37.32%) | 101 (40.40%) | 0.353 [a] |
| Hypertension | Yes | 1029 (60.64%) | 873 (60.33%) | 156 (62.40%) | 0.537 [a] |
| History of cardiac disease | Yes | 483 (28.46%) | 385 (26.61%) | 98 (39.20%) | <0.001 [a] |
| Malignancy | Yes | 110 (6.48%) | 91 (6.29%) | 19 (7.60%) | 0.437a |
| CKD/dialysis | Yes | 78 (4.60%) | 56 (3.87%) | 22 (8.80%) | <0.001 [a] |
| Dementia | Yes | 66 (3.89%) | 45 (3.11%) | 21 (8.40%) | <0.001 [a] |
| AF | Yes | 361 (21.27 %) | 300 (20.73%) | 61 (24.40%) | 0.191 [a] |
| Stroke volume | Small | 1030 (60.73%) | 980 (67.73%) | 50 (20.00%) | <0.001 [a] |
| | Medium | 347 (20.45%) | 289 (19.97%) | 58 (23.20%) | |
| | Large | 320 (18.86%) | 178 (12.30%) | 142 (56.80%) | |
| Periventricular hypodensity | Yes | 646 (38.07%) | 529 (36.56%) | 117 (46.80%) | 0.002 [a] |
| Rate of carotid stenosis | ≥50 | 284 (19.67%) | 254 (19.00%) | 30 (28.04%) | 0.024 [a] |
| Level of consciousness | Somnolence, lethargy, coma | 221 (13.02%) | 81 (5.60%) | 140 (56.00%) | <0.001 [a] |
| Vulpian sign | Yes | 178 (10.49%) | 93 (6.43%) | 85 (34.00%) | <0.001 [a] |
| Speech | Dysphasia-aphasia | 1018 (59.99%) | 783 (54.11%) | 235 (94.00%) | <0.001 [a] |
| NIHSS | <10 | 1210 (71.34%) | 1162 (80.36%) | 48 (19.20%) | <0.001 [a] |
| | ≥10-19 | 368 (21.70%) | 250 (17.29%) | 118 (47.20%) | |
| | ≥20 | 118 (15.50%) | 34 (2.35%) | 84 (33.60%) | |
| ICU | Yes | 734 (43.25%) | 484 (33.45%) | 250 (100.00%) | <0.001 [a] |
| Recanalization procedure | None | 1351 (79.61%) | 1194 (82.52%) | 157 (62.80%) | <0.001 [a] |
| | IV tPA | 147 (8.66%) | 115 (7.95%) | 32 (12.80%) | 0.012 [a] |
| | IA tPA | 36 (2.12%) | 28 (1.94%) | 8 (3.20%) | 0.200 [a] |
| | Thrombectomy | 94 (5.54%) | 70 (4.84%) | 24 (9.60%) | <0.002 [a] |
| | IV tPA+thrombectomy | 69 (4.07%) | 40 (2.76%) | 29 (11.60%) | <0.001 [a] |
| CNS complications | Yes | 154 (9.07%) | 55 (3.80%) | 99 (39.60%) | <0.001 [a] |
| Systemic complications | Yes | 260 (15.3%) | 117 (8.1%) | 143 (57.2%) | <0.001 [a] |
| Decompressive craniectomy | Yes | 52 (3.06%) | 9 (0.62%) | 43 (17.20%) | <0.001 [a] |
| Blood glucose | | | 126 (104-175) | 142 (110-215) | <0.001[b] |
| Log- creatinine | | | 0.86 (0.86-0.87) | 0.97 (0.94-0.99) | <0.001 [c] |
| Albumin | | | 3.42±0.51 | 2.95±0.64 | <0.001[e] |
| Log-CRP | | | 17.83 (4.59-69.31) | 48.55 (13.02-181.05) | <0.001[d] |
| Log-urea | | | 39.55 (26.14-39.22) | 51.10 (32.26-80.95) | <0.001[d] |
| CRP/albumin | | | 6.64 (2.35-21.39) | 24.13 (6.24-57.57) | <0.001[b] |
| Hg | | | 13.47±1.96 | 12.78±2.21 | <0.001 [d] |
| Log-WBC | | | 8.77 (8.70-8.85) | 10.03 (9.80-10.26) | <0.001[c] |

[a]: Data were presented as numbers (n) and percentages (%). A p-value was calculated by Pearson chi-square test.[b]: Mann Whitney U test, [c]: Yuen test, [d]: student t-test, [e]: Welch t-test was applied. AF: Atrial fibrillation, CKD: Chronic Kidney Disease, CNS: Central nervous system, CRP: C-Reactive protein, DM: Diabetes mellitus, Hg: Hemoglobin, ICU: Intensive care unit, NIHSS: National Institutes of Health Stroke Scale, WBC: White blood count, IV: Intravenous, IA: Intraarterial, tPA: tissue plasminogen activator

**Table 2.** Mortality risk ratios of risk factors in acute ischemic stroke

| Parameters | | OR (%95 CI) | p-value |
|---|---|---|---|
| **Age (years)** | ≥70 | 2.681 (2.013 - 3.572) | <0.001 |
| **Gender** | Female | 1.746 (1.331 - 2.291) | <0.001 |
| **Number of hospitalization days** | ≥14 | 2.302 (1.737 - 3.050) | <0.001 |
| **Recurrent stroke** | Yes | 1.172 (0.872 - 1.575) | 0.292 |
| **DM** | Yes | 1.139 (0.866 - 1.498) | 0.354 |
| **Hypertension** | Yes | 1.091 (0.827 - 1.439) | 0.537 |
| **History of cardiac disease** | Yes | 1.778 (1.345 - 2.352) | <0.001 |
| **Malignancy** | Yes | 1.226 (0.733 - 2.049) | 0.438 |
| **CKD/dialysis** | Yes | 2.397 (1.435 - 4.002) | <0.001 |
| **Dementia** | Yes | 2.857 (1.671 - 4.885) | <0.001 |
| **AF** | Yes | 1.234 (0.900 - 1.691) | 0.191 |
| **Stroke volume** | Small | Reference | |
| | Medium | 3.934 (2.636 - 5.870) | <0.001 |
| | Large | 15.636 (10.912 - 22.404) | <0.001 |
| **Periventricular hypodensity** | Yes | 1.527(1.165 - 2.001) | 0.002 |
| **Rate of carotid stenosis** | ≥50 | 1.661 (1.066 - 2.588) | 0.025 |
| **Level of consciousness** | Somnolence, lethargy, coma | 21.464 (15.345 - 30.021) | <0.001 |
| **Vulpian sign** | Yes | 7.500 (5.362 - 10.491) | <0.001 |
| **Speech** | Dysphasia-aphasia | 13.286 (7.804 - 22.619) | <0.001 |
| **NIHSS (categorized)** | <10 | Reference | |
| | ≥10-19 | 11.426 (7.954 - 16.415) | <0.001 |
| | ≥20 | 59.809 (36.568 - 97.821) | <0.001 |
| **Recanalization procedure** | None | Reference | |
| | IV tPa | 2.116(1.383 - 3.239) | <0.001 |
| | IA tPA | 2.173 (1.383 - 3.239) | 0.058 |
| | Thrombectomy | 2.607(1.593 - 4.267) | <0.001 |
| | IV tPA+thrombectomy | 5.514(3.324 - 9.147) | <0.001 |
| **CNS complications** | Yes | 16.593(11.463 - 24.021) | <0.001 |
| **Decompressive craniectomy** | Yes | 33.191 (15.946 - 69.085) | <0.001 |

Data were presented at 95% confidence intervals (CI). A p-value was calculated by logistic regression analysis. AF: Atrial fibrillation, CKD: Chronic Kidney Disease, CNS: Central nervous system, DM: Diabetes mellitus, NIHSS: National Institutes of Health Stroke Scale; OR: Odds ratio, IV: Intravenous, IA: Intraarterial, tPA: tissue plasminogen activator

**Table 3.** Results of multivariate logistic regression analysis for the mortality prediction model

| Parameters | Estimates | SE | *p*-value | OR (%95 CI) | Wald | VIF | Tolerance | Score |
|---|---|---|---|---|---|---|---|---|
| **Level of consciousness** | | | | | | 1.318 | 0.758 | |
| Conscious or confused | [Reference] | | | | | | | |
| Somnolence, Lethargy or Coma | 1.10000 | 0.249 | <.001 | 3.004 (1.845–4.891) | 19.564 | | | 1 |
| **Speech** | | | | | | 1.090 | 0.917 | |
| Normal | [Reference] | | | | | | | |
| Dysphasia – Aphasia | 1.13381 | 0.309 | <.001 | 3.107 (1.697–5.689) | 13.503 | | | 1 |
| **Number of hospitalization days** | | | | | | 1.121 | 0.892 | |
| <14 days | [Reference] | | | | | | | |
| ≥ 14 days | 0.77589 | 0.205 | <.001 | 2.172 (1.453–3.248) | 14.295 | | | 1 |
| **Albumin (g/dL)** | | | | | | 1.061 | 0.943 | |
| ≥ 3.5 | [Reference] | | | | | | | |
| < 3.5 | 1.00292 | 0.195 | <.001 | 2.726 (1.861–3.993) | 26.515 | | | 1 |
| **Urea (mg/dL)** | | | | | | 1.037 | 0.964 | |
| ≤ 44 | [Reference] | | | | | | | |
| >44 | 0.52895 | 0.184 | .004 | 1.697 (1.181–2.438) | 8.191 | | | 0.5 |
| **NIHSS** | | | | | | 1.227 | 0.815 | |
| < 10 | [Reference] | | | | | | | |
| 10 – 19 | 1.24730 | 0.246 | <.001 | 3.481 (2.147–5.643) | 25.596 | | | 1 |
| ≥ 20 | 1.93459 | 0.372 | <.001 | 6.921 (3.337–14.355) | 27.016 | | | 2 |
| **Stroke volume** | | | | | | 1.115 | 0.897 | |
| Small | [Reference] | | | | | | | |
| Middle | 0.52213 | 0.253 | .040 | 1.685 (1.025–2.771) | 4.234 | | | 0.5 |
| Large | 1.14366 | 0.258 | <.001 | 3.138 (1.889–5.211) | 19.533 | | | 1 |
| **Periventricular hypodensity** | | | | | | 1.125 | 0.889 | |
| No | [Reference] | | | | | | | |
| Yes | 0.42297 | 0.205 | .036 | 1.526 (1.027–2.268) | 4.379 | | | 0.5 |
| **Age (years)** | | | | | | 1.121 | 0.892 | |
| < 70 | [Reference] | | | | | | | |
| ≥ 70 | 0.52372 | 0.206 | .011 | 1.688 (1.127–2.528) | 6.455 | | | 0.5 |

| **Model Fit Measures** | **Pseudo $R^2$ (Coefficient of determination)** |
|---|---|
| AIC (Akaike Information Criteria) = 878.81 | McFadden's $R^2$ = 0.397 |
| BIC (Bayesian Information Criteria) = 944.05 | Cox & Snell's $R^2$ = 0.283 |
| $\chi^2$=563.66, $p$<.001 | Nagelkerke's $R^2$ = 0.500 |
| Deviance = 854.81 | Tjur $R^2$ = 0.412 |

AIC: Akaike information criteria, BIC: Bayesian information criteria, CI: Confidence interval, NIHSS: National Institutes of Health Stroke Scale, OR: Odds ratio, R2: Coefficient of determination, SE: Standard Error, VIF: Variance inflation factor,

**Table 4.** Comparisons of The Selcuk Score recommended to predict hospital mortality in patients with acute ischemic stroke with predicting performances of THRIVE and Ling et al. (2019) scores

| | Selcuk Score | THRIVE | Ling et al. (2019) |
|---|---|---|---|
| **ROC Analysis Results** | | | |
| AUC (%95 CI ) | 0.884 (0.868–0.899)≠ | 0.822 (0.803–0.840) | 0.864 (0.847–0.880) |
| *p*-value | <.001 | <.001 | <.001 |
| Cut-off value | >3 | >3 | >3 |
| AUC Comparison | | *p*<.001 | *p*=.035 |
| **Statistical Diagnostic Measures** | | | |
| Sensitivity (%) | 83.6 (78.4–88) | 75.2 (69.4–80.4) | 74.8 (68.9–80.1) |
| Specificity (%) | 81.2 (79.1–83.2) | 79.1 (76.9–81.2) | 84.8 (82.8–86.6) |
| PPV | 43.5 (40.5–46.4) | 38.4 (35.5–41.3) | 45.9 (42.5–49.5) |
| NPV | 96.6 (95.6–97.4) | 94.9 (93.7–95.8) | 95.1 (94–96) |

≠Demonstrates the significant difference between Selcuk score and THRIVE score (p<.001). AUC: Area under curve, CI: Confidence interval, NPV: Negative predictive value, PPV: Positive predictive value

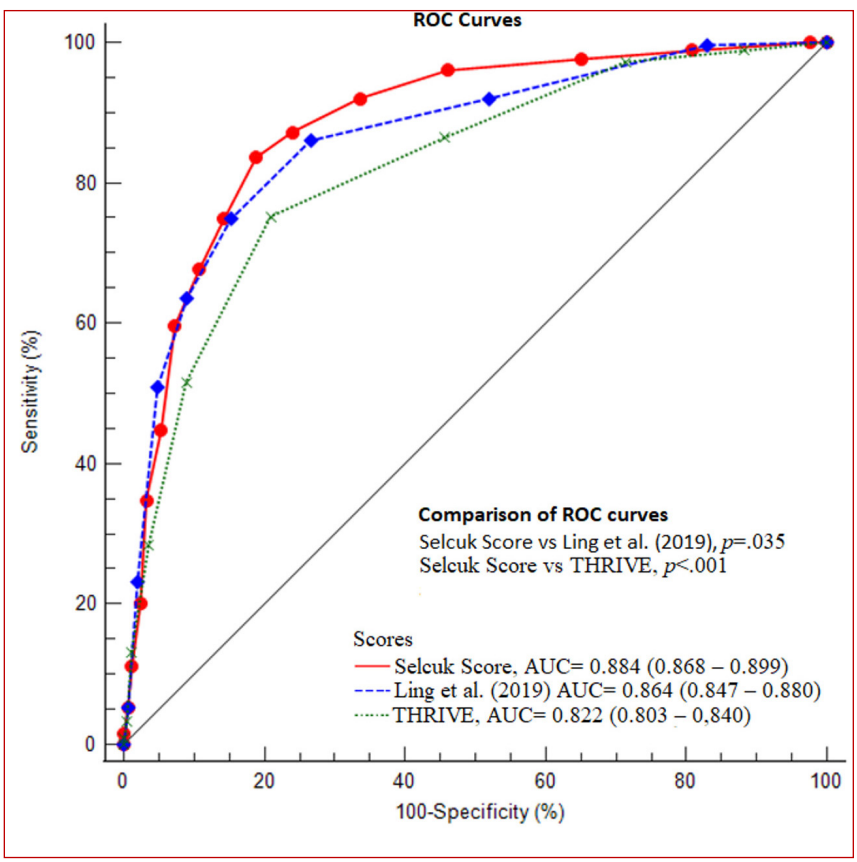


**Figure 1.** Comparison of the prediction performances of the scoring systems.

and automation infrastructures, advanced referral system, easy access to treatment by specialist physicians, and advanced imaging opportunities, we consider that the Selcuk scoring system we developed will become easier to use.

On the basis of the comparisons between our study findings and those reported in the literature, our study shows similar incidence rates of stroke according to sex. Moreover, our patients experienced stroke at an earlier age, as different from the outcomes of the studies. According to the literature, the most common comorbidity was hypertension (6, 10, 12-14).

The literature has reported the development of several prognostic scales specific to conditions such as intravenous tissue plasminogen activator (tPA), thrombectomy, and intraarterial tPA. Such procedures may provide dramatic improvements in patients' clinical condition and lead to the development of complications and unexpected deteriorations, making it difficult to predict prognosis. Scoring modalities such as the Acute Stroke Registry and Analysis of Lausanne (ASTRAL) score, the PLAN score (preadmission comorbidities, level of consciousness, age, and neurological deficit), and the Bologna Outcome Algorithm for Stroke (BOAS) were not compared with our scoring system in terms of prediction performance because acute treatment approaches were excluded in these scoring systems (13, 15, 16). We consider our study to be intriguing and outstanding because we included all patients with ischemic stroke, including those receiving acute treatment.

The parameters such as age (6, 10, 12-16), state of consciousness (6, 13, 16), NIHSS (6, 16), stroke lesion size (15), and dysphasia (13) included in the Selcuk score have also been evaluated in other scores. However, to our knowledge, no study has included and investigated length of hospital stay, presence of periventricular hypodensity, and albumin and urea levels as significant components together. Our study has the potential to contribute to the field of prognostic prediction in terms of revealing that different parameters can also be involved in the prediction of prognosis.

The present study has several limitations. First, it was planned as a retrospective and cross-sectional study. Second, we couldn't evaluate national and geographical characteristics because we used data from a single center. Therefore, our study findings cannot be applied to populations from other regions. The evaluation of serum markers in the study might have been affected by many clinical and structural conditions, and we were unable to assess the long-term prognostic factors (in the third and sixth months, or first year) and causes of mortality. As data obtained on hospital admission were examined, no dynamic variabilities in neurological deficits that might have developed in the patient and affected the prognosis could be evaluated in the study. Owing to this dynamic process, stroke prognosis is not easy to predict, and unpredictable results may occur not only in the Selcuk score but also in all prognostic scales owing to patients displaying such a clinical course. Therefore, prognostic scales should not be replaced with clinical observation and evaluation. Although prognostic scores for both ischemic and hemorrhagic stroke have been reported in the literature, the Selcuk scoring system includes only patients with AIS. We have shown using internal validation methods that the scale we developed is valid. However, the validity of the Selcuk score should also be tested in different populations using prospective validation clinical studies.

## CONCLUSION

The Selcuk score was developed to standardize the clinical prediction of prognosis in stroke patients. It is the first prognostic score to be developed for ischemic stroke in our country. We consider that the Selcuk score can significantly support clinicians in the prognostic evaluation of patients with AIS and in managing the disease process.

### Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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ORIGINAL ARTICLE

# EXPLORING THE RELATIONSHIP BETWEEN HOPELESSNESS AND DISABILITY IN ELDERLY INDIVIDUALS WITH DIABETES

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## Abstract

**Introduction:** This study aimed to investigate the association between hopelessness and disability in elderly individuals with diabetes.

**Materials and Method:** The study involved 500 elderly patients diagnosed with diabetes who were registered with family health centers. Data were collected via the Socio-demographic Information Questionnaire, the Beck Hopelessness Scale, and the Brief Disability Questionnaire. Analysis methods included calculating numbers, percentages, means, standard deviations, and conducting correlation and regression analyses. The statistical significance level was accepted as $p < 0.05$.

**Results:** The mean age of the participants was 70.98 ± 6.63 years. On the Beck Hopelessness Scale, participants scored an average of 9.93 ± 1.48 total points, while on the Brief Disability Questionnaire, they scored 12.27 ± 5.43 total points. It was found that 90.4% of the participants had a disability, with 50.8% classified as having a severe disability. There was a statistically significant difference between disability and various factors including gender, cohabitation status, educational attainment, employment status, income level, duration of diabetes, and the presence of other chronic diseases ($p < 0.05$).

**Conclusion:** The study findings revealed that participants had a moderate level of hopelessness, with only a small proportion having no disability, while approximately half of the participants experienced severe disability. Additionally, a very weak positive relationship was observed between participants' disability levels and their scores on the Beck Hopelessness Scale ($p = 0.005$). Based on these results, suggestions were formulated to address the implications of the findings in the study.

***Keywords:*** Cognitive Dysfunction; Diabetes Mellitus; Aged.

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## INTRODUCTION

Diabetes is a chronic illness resulting from either insufficient insulin production by the pancreas or ineffective utilization of the insulin produced by the body. Insulin, a hormone responsible for regulating blood sugar levels, plays a crucial role in this process. Prolonged periods of uncontrolled diabetes often lead to hyperglycemia, characterized by elevated blood sugar levels, which can inflict significant harm on various bodily systems, particularly the nerves and blood vessels (1). The population growth rate around the world has also caused an increase in urbanization, unbalanced nutrition, obesity, and aging; Consequently, the incidence of diabetes is on the rise as well (2). According to the International Diabetes Federation, 463 million people (adults aged 20–79 years) worldwide had type 2 diabetes in 2019, and this number is expected to rise to 700 million by 2045 (3). After being diagnosed with diabetes, patients may experience difficulties in maintaining metabolic control because of the adaptation problems they experience with diabetes, and they may also experience social and psychological problems (4, 5). The prevalence of depressive and anxiety symptoms in adults with type 2 diabetes in China was 56.1% and 43.6%, respectively (5). Enhancing hope levels in individuals with diabetes leads to better coping mechanisms for both physical and psychological complications. Moreover, it fosters improved adaptation to the treatment process, acceptance of their disease status, and overall increased happiness in life (6). Beck (1985) defines hopelessness as the basis of depression in his cognitive theory. Since feelings such as helplessness, worthlessness, indecision, the inability to take action, guilt and suicidal ideation can be observed alongside hopelessness, the susceptibility to depression increases (7). As a result, it can be concluded that as depression increases in individuals with diabetes, the level of hopelessness may also increase in direct proportion. According to the results of several studies, depression is one of the most common mental problems in individuals with diabetes (5). Some studies have indicated that individuals with chronic conditions such as diabetes, as well as those experiencing disabilities, tend to exhibit higher levels of hopelessness (8). Regarding the consequences of disability among the elderly, it adversely impacts public health, diminishes the quality of daily life activities, and elevates healthcare expenditures (9). Moreover, disability leads to the loss of independence, decreased quality of life and increased use of health services (10), which can precipitate mental problems in individuals. The prevalence of disability is expected to rise within the population and is projected to persist until the 2060s (11).

The primary objective of this study was to assess the levels of hopelessness among individuals with diabetes and associated conditions, as well as to examine the disability factors influencing their mental well-being. Based on the findings, healthcare professionals can offer targeted counseling and guidance to individuals with diabetes, focusing on addressing mental health concerns. Recommendations pertaining to the psychological effects of diabetes can be formulated, and educational programs can be designed to provide support and resources. Furthermore, it is envisaged that this research will serve as a groundwork for future experimental studies in this area.

### Research Questions

- What are the participants' levels of hopelessness and disability?
- Do the socio-demographic data and hopelessness levels of the patients have an effect on disability?
- Is there a relationship between the participants' levels of hopelessness and levels of disability?

## MATERIALS AND METHODS

**Population and Sample:** The population of the study consisted of elderly individuals with diabetes aged 65 years and over who were registered with family health centers affiliated with the Kars Central Community Health Center. A total of 500 participants were included in the study, and no specific sampling calculation was conducted.

**Data Collection Tools:** The study questionnaire consisted of three parts: the Socio-demographic Information Questionnaire, the Beck Hopelessness Scale and the Brief Disability Questionnaire.

**Socio-demographic Information**

**Questionnaire:** This questionnaire was developed by the researcher by reviewing the literature. The questionnaire included participant information such as gender, age, marital status, the presence of children, cohabitation, education level, employment status, perception of income level, years living with diabetes and the presence of chronic diseases other than diabetes (12, 13).

Beck Hopelessness Scale (BHS): The BHS was developed by Beck et al. (1974), and the Turkish validity and reliability was conducted by Seber et al. (1993). The scale consists of 20 articles, which are scored between 0 and 1. The score interval varies between 0 and 20. An increase in the scores is interpreted as a high level of hopelessness in the participant. The Cronbach alpha coefficient of the BHS was 0.86 (14,15). In this study, Cronbach's alpha value was calculated as 0.91.

**Brief Disability Questionnaire (BDQ):** The BDQ was developed by Stewart in 1988 to assess physical and social disability. The validity and reliability study of the BDQ in Turkey is conducted by Kaplan (1995) and it consists of 11 questions. Scores obtained from the scale vary between 0 and 22. Scores ranging from zero to four points indicated "no disability", 5-7 points indicated "mild disability", 8-12 points were considered as "moderate disability" and 13 and above points indicated "severe disability" (16,17). In this study, Cronbach's alpha value was calculated as 0.884.

**Data Collection Process:** After receiving approval from the ethics committee and obtaining the necessary permissions from the family health centers, the data were collected via the face-to-face interview method and the online (online, via Google forms) questionnaire method at the family health centers.

**Data Evaluation:** The data were evaluated using the SPSS 26.0 software program. Descriptive statistical methods (number, percentage, mean, and standard deviation), parametric tests, and correlation and linear regression analyses were used in the evaluation of the data.

**Limitations:** The research encountered challenges in accessing individuals with diabetes, primarily due to the constraints imposed by the Covid-19 pandemic. Special efforts were made to contact participants via telephone, particularly considering that elderly individuals often lack access to android phones or may not be active internet users. However, these efforts resulted in data loss and prolonged the data collection process. The research was constrained by the dimensions measured by the instruments used and the outcomes of the participants in the study. Therefore, the results cannot be generalized to all individuals.

**Strengths of the Study:** No studies could be found that addressed hopelessness and disability in elderly diabetes patients during the Covid-19 pandemic. One of the strengths of the study is the establishment of a data network representing the country during the pandemic, contributing to the literature.

**Ethical Principles:** In the study, ethics committee permission was obtained from the chairmanship of the non-invasive studies ethics committee of a state university with the date

02.11.2021 and decision number 81829502-903/254. Permission was obtained to use the measurement tools in the study. Only participants who agreed to participate in the study were included.

**Expected Benefit from the Research:** The anticipated benefits of the research include the acquisition of comprehensive socio-demographic data, along with insights into the levels of hopelessness and disability among participants with diabetes. Additional benefits include supporting the counseling of individuals in line with the results and planning effective training, and thus, improving the quality of life of individuals. Lastly, another benefit of the research will be to create a basis for future studies on individuals with diabetes.

**Research Implementation Time:** The research was conducted between November 2021 and May 2022.

## RESULTS

In total, 500 elderly individuals with diabetes participated in this study. As shown in Table 1, among the participants, a total of 51.6% were male, 89.4% were married, 84.4% had children, 69% lived with their spouses and children, 43.4% were primary/secondary school graduates, 66% were unemployed, 81.4% had a middle-level income, 42% had diabetes for six to 10 years and 54.8% had chronic diseases other than diabetes. The mean age of the participants was 70.98±6.63 years. In the last month, the participants were absent from work for an average of 8.00±8.48 days due to disability and spent an average of 8.66±7.94 days in bed due to illness or injury.

As shown in Table 2, the participants obtained 9.93±1.48 points on the Beck Ho pelessness Scale (BHS) and 12.27±5.43 points on the Behavioral Dysfunction Questionnaire (BDQ).

Most of the participants had a disability (90.4%), and a total of 50.8% of the participants had a severe disability (Table 3).

Table 4 demonstrates the results of the multiple regression analysis between the participants' level of disability and their socio-demographic data. In the regression analysis of the level of disability of the participants, the main variables were age, the number of days of disruption of daily tasks in the last month, the number of days spent in bed in the last month due to illness or injury, gender, cohabitants, income level, diabetes duration and the presence of chronic diseases other than diabetes mellitus ($p<0.001$). The analysis results revealed that the model was significant (F: 23.896; $p<0.001$). The adjusted R2 value was 0.408, and the explanatory power of the model was 40.8%. The level of disability of the participants was affected by increasing age ($\beta=0.006$), the increasing number of days of missed work in a month ($\beta=0.005$) and the increasing number of days in bed in a month ($\beta=0.020$). In addition, being female ($\beta=0.091$), living with relatives ($\beta=0.005$) or others ($\beta=0.005$), living with a spouse or children ($\beta=0.005$), having a medium income level ($\beta=0.122$), having diabetes for more than 11 years ($\beta=-0.289$) and having chronic diseases other than diabetes ($\beta=0.170$) were found to be 40.8% effective factors for disability ($p<0.001$). There was no statistically significant difference between the disability questionnaire and the level of hopelessness, marital status and having children in the model ($p>0.05$).

It revealed a weak positive correlation between the level of disability and the BHS ($r=0.125$; $p=0.005$). The analysis also revealed a weak positive correlation between disability and age ($r=0.307$), as well as the number of days in the last month that participants did not perform their daily tasks ($r=0.415$). Additionally, a moderate positive correlation was observed between disability and the number of days spent in bed in the last month due to illness or injury ($r=0.524$; $p<0.001$).

**Table 1.** Distribution of Socio-Demographic Data of the Participants (N=500)

| Variables | | n | % |
|---|---|---|---|
| **Gender** | Male | 242 | 48.4 |
| | Female | 258 | 51.6 |
| **Marial Status** | Married | 447 | 89.4 |
| | Single | 53 | 10.6 |
| **Child Status** | No | 78 | 15.6 |
| | Yes | 422 | 84.4 |
| **Cohabitant** | Alone | 44 | 8.8 |
| | With my spouse/children | 345 | 69.0 |
| | With relatives | 96 | 19.2 |
| | Other | 15 | 3.0 |
| **Educational Background** | Literate | 171 | 34.2 |
| | Primary/secondary school | 217 | 43.4 |
| | High school | 83 | 16.6 |
| | College/Bachelor's Degree | 8 | 1.6 |
| **Working Condition** | Employed | 170 | 34.0 |
| | Unemployed | 330 | 66.0 |
| **Level of Income** | Satisfactory | 93 | 18.6 |
| | Moderate | 407 | 81.4 |
| **For how many years they have had diabetes** | 1-2 years | 62 | 12.4 |
| | 3-5 years | 143 | 28.6 |
| | 6-10 years | 210 | 42.0 |
| | 11 years and above | 85 | 17.0 |
| **Presence of chronic disease other than diabetes** | Yes | 274 | 54.8 |
| | No | 226 | 45.2 |
| | | **Min-Max** | **Mean ± SD.** |
| **Age (in years)** | | 65-97 | 70.98±6.63 |
| **In the last month, how many days in total did you skip your daily work?** | | 0-59 | 8.00±8.48 |
| **How many days in total did you spend in bed in the last month due to illness or injury?** | | 0-56 | 8.66±7.94 |

**Table 2.** Distribution of the BHS and the BDQ Total Scores of the Participants (N=500)

| | N | Min. ± Max. | Mean ± SD. |
|---|---|---|---|
| **Beck Hopelessness Scale Total Score** | 500 | 3.00±15.00 | 9.93±1.48 |
| **Brief Disability Questionnaire Total Score** | 500 | 0.00±22.00 | 12.27±5.43 |

**Table 3.** Distribution of the BDQ Findings of the Participants (N=500)

| | n | % |
|---|---|---|
| **No disability** | 48 | 9.6 |
| **Mild disability** | 60 | 12.0 |
| **Moderate disability** | 138 | 27.6 |
| **Severe disability** | 254 | 50.8 |

**Table 4.** Multiple Regression Analysis Results between the Disability Score and the Socio-demographic Characteristics of the Participants

| | | β | SE | t | *p* | Adj. $R^2$ | F |
|---|---|---|---|---|---|---|---|
| **Constant** | | 0.046 | 0.283 | 0.164 | **<0.001** | 0.408 | 23.896 |
| **Age** | | 0.006 | 0.003 | 1.915 | **0.050** | | |
| **Number of days in the last month that they did not perform daily tasks** | | 0.005 | 0.003 | 2.049 | **0.041** | | |
| **Number of days spent in bed in the last month due to illness or injury** | | 0.020 | 0.003 | 6.974 | **<0.001** | | |
| **Beck Hopelessness Scale** | | 0.019 | 0.012 | 1.568 | 0.118 | | |
| **Gender** | Male[a] | 0.0 | - | - | - | | |
| | Female | 0.091 | 0.035 | 2.599 | 0.010 | | |
| **Marial status** | Married | 0.088 | 0.087 | 1.017 | 0.310 | | |
| | Single[a] | 0.0 | - | - | - | | |
| **Child status** | Yes | -0.007 | 0.075 | -0.096 | 0.924 | | |
| | No[a] | 0.0 | - | - | - | | |
| **Cohabitants** | Alone | 0.039 | 0.070 | 0.560 | 0.576 | | |
| | With relatives | 0.115 | 0.052 | 2.210 | **0.028** | | |
| | Other | 0.277 | 0.103 | 2.700 | **0.007** | | |
| | With spouse/children[a] | 0.0 | - | - | - | | |
| **Income level** | Satisfactory[a] | 0.0 | - | - | - | | |
| | Moderate | 0.122 | 0.045 | 2.714 | **0.007** | | |
| **For how many years they have diabetes?** | 1-2 years | -0.289 | 0.070 | -4.113 | **<0.001** | | |
| | 3-5 years | -0.112 | 0.059 | -1.911 | 0.057 | | |
| | 6-10 years | -0.078 | 0.052 | -1.507 | 0.133 | | |
| | 11 years and above[a] | 0.0 | - | - | - | | |
| **Presence of chronic disease other than diabetes** | Yes | 0.170 | 0.036 | 4.687 | **<0.001** | | |
| | No[a] | 0.0 | - | - | - | | |

[a]: reference value, β: regression coefficient, SE: standard error. $p$ <0.05.

**Table 5.** The relationship between some variables of the participants and disability

| | | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|
| **1.** Age | **r** | 1 | | | | |
| | **p** | | | | | |
| **2.** Number of days in the last month that they did not perform daily tasks | **r** | 0.411** | 1 | | | |
| | **p** | 0.000 | | | | |
| **3.** Number of days spent in bed in the last month due to illness or injury | **r** | 0.330** | 0.606** | 1 | | |
| | **p** | 0.000 | 0.000 | | | |
| **4.** Beck Hopelessness Scale | **r** | 0.095* | 0.122** | 0.036 | 1 | |
| | **p** | 0.034 | 0.006 | 0.427 | | |
| **5.** Brief Disability Questionnaire | **r** | 0.307** | 0.415** | 0.524** | 0.125** | 1 |
| | **p** | 0.000 | 0.000 | 0.000 | 0.005 | |

* Correlation is significant at the 0.05 level (2-tailed). ** Correlation is significant at the 0.01 level (2-tailed)

## DISCUSSION

The purpose of this study was to investigate the levels of hopelessness and disability among elderly individuals with diabetes, as well as to identify potential factors associated with these conditions. From a review of related literature, it is apparent that research on the levels of hopelessness in elderly diabetic patients is limited. In this sense, this study gains importance and is discussed in light of the available studies. In this study, the participants had moderate levels of hopelessness. According to a study conducted by Morewitz et al. (2010) on patients with diabetes, it was observed that the levels of hopelessness were higher among female patients aged over 61 compared to other patient groups (18). Ghazavi et al. (2015) found that patients with diabetes were moderately hopeful (6). In a study conducted on dialysis patients, 16% of the participants were found to experience moderate levels of hopelessness, and 32% were found to experience severe levels of hopelessness. The hopelessness levels of the participants support the findings of the study. In the study conducted by Durmuş et al. (2022) on individuals with diabetes, it was observed that hopelessness levels were below the moderate level (19). In another study, the hopelessness levels of adults diagnosed with diabetes was found to be 17.2% (12). The disparity between the findings of the current research and those of previous studies may be attributed to several factors such as the difference in the age ranges (with younger age groups in the related studies), the effective differences in the chronic disease group and the notion that advanced age and diabetes may cause hopelessness in individuals.

It was observed that a total of 90.4% of the participants with diabetes had a disability and that 50.8% had a severe disability. In addition to such high levels, according to the results of the regression analysis of this study, it was revealed that disability is especially affected by increasing age, by the increasing number of days of disrupted work in a month and by the number of days in bed in a month. With this, being female, living with relatives or others, having a middle-level income, having had diabetes for more than 11 years and having a chronic disease other than diabetes were found to be 40.8% effective factors of disability. From these results, it can be concluded that most individuals with chronic

diseases such as diabetes face disability and that this situation is related to many factors. The literature review indicated a scarcity of studies on disability among individuals with diabetes, with no recent research available on this topic. Therefore, the most recent research was discussed in this study. Rizzuto et al. (2017) found that a total of 69% of individuals with chronic diseases were severely disabled (20). It is thought that if diabetes is not under control, it will increase the risk of disability and premature death caused by diabetes (21). According to the results of a study that examined the level of disability in individuals with diabetes, disability increased as the duration of diabetes increased. According to the data of the same study, the rate of disability in individuals with diabetes for more than 10 years was determined to be 76.9% (22). In the same direction, a study conducted by Gülseren et al. (2001) revealed that individuals that had diabetes for more than 10 years had more disability than individuals that had diabetes for 10 years or less (23). The results of this study are consistent with the literature: as the duration of diabetes increased, the physical and psychological difficulties attributed to the disease may have increased the level of disability in these individuals.

In line with the literature (13,22), it was revealed that the level of disability increased as the age of the participants increased and that this increase could be associated with the increase in the duration of diabetes and the emergence of other chronic diseases with age.

In this study, having a middle-level income was found to be an effective factor of disability. In Dönmez's (2019) study on dialysis patients, it was found that people with high income levels had low disability scores. The literature review indicated that having a low-level income affects disability (24, 25).

In this study, the presence of a chronic disease other than diabetes was found to affect the level of disability of the participants. The findings of a study by Mollaoğlu and Yanmış (2018) revealed high disability levels for individuals with chronic diseases (20). In a study that examined the levels of disability in the elderly, it was observed that disability increased 2.97 times for individuals with chronic diseases (13). The findings of this study are consistent with those of the reviewed studies. Conversely, in a study conducted by Gülseren et al. (2001), the presence of chronic disease did not show a significant difference in disability (23). It can be concluded that this difference may be attributed to the average age of the participants: in this study, the average age was 70.98 years, while the average age in the other study was 58.4 years. It was observed that disability increased with advancing age.

A review of a study by Gülseren et al. (2001), which examined the effect of gender on disability levels, found that females suffered moderate to severe levels of disability compared to males (23). Consistent with the findings of the literature review, the female participants in this study were found to be an effective factor of disability.

In this study, participants with diabetes who lived with relatives or others exhibited higher levels of disability compared to participants living with their spouses or children. It is believed that this difference may be attributed to the findings that individuals who live with their first-degree family feel safer and that social support in the family had a positive effect on the level of disability. It was found that the disability levels of individuals with chronic diseases and living alone are significantly higher (20). In a study of the elderly, staying with children/relatives/caregivers was found to be an effective variable of disability (13). This study's results support the findings of the literature review.

A significant, although weak, positive relationship was observed between disability, which is one of the main research areas of this study, and hopelessness. It was found that as the disability of the participants increased, their hopelessness levels also significantly increased. Although the disability levels of the participants were high, their hopelessness levels

were found to be moderate and to affect the levels of hopelessness of individuals with diabetes, possibly because 70% of the participants lived with their families and a sense of trust and social support were provided.

## CONCLUSION

The findings of this study indicated that participants exhibited a moderate level of hopelessness. Additionally, a small proportion of participants did not have a disability, while approximately half of the participants experienced a severe level of disability. The factors found to significantly affect disability in this study included gender, cohabitants, educational status, employment status, income level, duration of diabetes, and the presence of chronic diseases other than diabetes. It is recommended that interventions based on physical and psychological health include practices that specifically consider women, those who live with individuals other than their spouses and children, those who do not work, those with a middle-level income, those that have had diabetes for more than 11 years and individuals with chronic diseases other than diabetes. It is also recommended that further interventions be provided to reduce the disability level of individuals and that counseling be provided by health professionals. In recent years, there have been no studies on disabilities in individuals with diabetes in Turkey, and studies on hopelessness levels are limited worldwide. Hence, it is recommended to conduct further research focusing on prevalent chronic conditions like diabetes, particularly those allowing for psychological assessments. Experimental studies investigating aspects such as disabilities in individuals with diabetes should be emphasized, as these factors can significantly influence their well-being. The aim would be to mitigate feelings of hopelessness and enhance overall quality of life for affected individuals.

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ORIGINAL ARTICLE

# VACCINATION FREQUENCY AND ASSOCIATED FACTORS IN OLDER ADULTS: A PRIMARY CARE-BASED CROSS-SECTIONAL STUDY

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## Abstract

**Introduction:** There is currently a lack of primary care or community-based regional and national data concerning vaccination rates among older individuals in Turkey. Thus, the present study aimed to determine the pneumococcal, influenza, and herpes zoster vaccination rates associated factors among individuals aged 65 and over in Efeler, the central district of Aydın Province, Turkey.

**Materials and Method:** An analytical, cross-sectional study was performed between September 2022 and November 2022 at 10 family health centers randomly selected from a total of 34 such centers in Efeler. The study's calculated sample size was 321 participants. During the study period, a researcher administered data collection forms that had been developed via a literature review to older patients on a face-to-face basis. The data were analyzed using IBM SPSS 20.0 statistical software, while descriptive statistics as well as chi-square and logistic regression tests were employed to identify the factors associated with vaccination rates among this population. The statistical significance level was set as $p < 0.05$.

**Results:** Among the 321 participants, 51.4% were male, 70.7% were in the 65–74 age range, 77.0% were married, and 88.2% had at least one chronic disease. Moreover, 90.0% were aware of the vaccines recommended for their age group, while 81.3% stated that vaccines had been recommended to them after the age of 60. In the past year, 39.3% of participants had received an influenza vaccine, 6.2% had received at least two doses of pneumococcal vaccine, and 0.3% had received a herpes zoster vaccine. The influenza vaccine coverage in the past year was 2.1 times higher in those aged 75 years and over than in younger participants ($p = 0.005$), while it was 3.9 times higher in those with chronic diseases compared to those without ($p = 0.004$). The participants with active employment had received at least two doses of pneumococcal vaccine, indicating a vaccine rate 13.1 times higher than among those without employment ($p < 0.001$), while participants with chronic obstructive pulmonary disease (COPD) and/or asthma had a vaccination rate 7.8 times higher than participants without either condition ($p < 0.001$).

**Conclusion:** The overall vaccination coverage among the participants was quite low. While the influenza vaccine was commonly received, the herpes zoster vaccine was only rarely administered. An older age and the presence of chronic diseases were associated with higher influenza vaccination rates, while being in active employment and having COPD and/or asthma were associated with higher pneumococcal vaccination rates. Further qualitative studies are required to elucidate the behaviors and attitudes of the younger members of the older adult age group who do not have chronic diseases when it comes to receiving vaccines included in the program.

***Keywords:*** Pneumococcal Vaccine; Influenzavirus Vaccine; Zoster Vaccine; Aged

## INTRODUCTION

Ensuring immunity via vaccination entails an ongoing, lifelong process. While there is global awareness and implementation of newborn and childhood vaccinations, adult vaccination programs have not yet been widely and routinely adopted in every country (1). Inadequate adult vaccination leaves individuals, especially those with chronic conditions, highly susceptible to infections. Thus, routine administration of influenza, pneumococcal, and herpes zoster vaccines has become common practice in older adults, with other vaccinations recommended on an as-needed basis (2).

Vaccination rates among the older population vary significantly worldwide, with only a few countries having achieved the World Health Organization (WHO) vaccination targets for older people (3,4). The lack of information, awareness, and health literacy, along with negative beliefs and attitudes, contribute to the failure to reach the desired levels of adult vaccination (5,6).

Studies conducted among older individuals who visited various outpatient clinics of university or research hospitals identified influenza vaccination rates ranging from 12–33% and pneumococcal vaccination rates ranging from 3–10% (7-10). Two studies conducted in hospital-based family practice clinics revealed influenza vaccination rates of 22%–34% and pneumococcal vaccination rates of 4%–10% (11,12).

These prior studies were primarily conducted in hospitals or highly limited primary care centers, and there is currently little research evidence regarding herpes zoster vaccination rates (12). Indeed, our literature review identified only two studies conducted at the primary care level in Turkey. Uzuner et al. performed their study in a district of Istanbul, revealing notably low vaccination rates among individuals aged 18 and over, although the specific rates for those aged 65 and over were not provided (13). Ünal et al. retrospectively reviewed the records of all the primary care centers in Denizli in 2011 to assess the influenza and pneumococcal vaccination rates among individuals aged 65 and over (14); however, this study only considered vaccinations administered in primary care centers and so lacked information about vaccinations administered elsewhere.

Our literature review identified no community-based, regional, or national primary care-based studies that assessed the influenza, pneumococcal, and herpes zoster vaccination rates among individuals aged 65 and over. To address this gap in the literature, the present study was designed to determine the pneumococcal, influenza, and herpes zoster vaccination rates among individuals aged 65 and over who visited family health centers in Efeler, the central district of Aydın Province. Additionally, this study also aimed to identify the factors associated with vaccination behaviors of older people.

## MATERIALS AND METHOD

A descriptive, cross-sectional study was performed between September 2022 and November 2022 in Efeler, the central district of Aydın Province, Turkey. The study population comprised individuals aged 65 and over who were registered at all the family health centers in Efeler. The study's sample size was calculated to be 321 individuals based on the population of older adults in Efeler (35,422), an expected influenza vaccination prevalence of 30%, a 0.05 alpha level, and a 0.05 sampling error (3). Older individuals who volunteered to participate in the research were included in the study. The exclusion criteria for the study were having a mental or cognitive condition that hindered reading, comprehending, and/or completing the survey, in addition to having recently participated in another study.

To determine the study sample, we compiled a list of the 34 family health centers in Efeler. From these,

a total of 10 family health centers were randomly selected, considering the geographical distribution of the population, including two centers in rural areas and eight in urban areas. The required number of participants was determined for each center based on the number of family medicine units and the total registered population. During the study period, a researcher (RSS) visited the centers as part of a program and administered a data collection form developed via a literature review to older adult patients who visited the centers on the days in question. The survey was conducted on a face-to-face basis. The survey administration continued at each center consecutively until the predetermined number of participants was reached. The survey gathered socio-demographic information, general health information, and information related to behaviors regarding pneumococcal, influenza, and herpes zoster vaccinations and the associated factors.

The older adults' behaviors in terms of receiving vaccinations for elderly specific diseases were considered to be the dependent variable in the study. The socio-demographic characteristics, certain habits, and clinical features of the older adults were considered independent variables that influence the dependent variable.

The gathered data were analyzed using IBM SPSS Statistics 20.0 software. In addition to descriptive statistics, binary (chi-square test) and multiple (regression) tests were performed to identify factors associated with vaccination status. A level of $p < 0.05$ was considered to be statistically significant.

Ethical approval to conduct this study was obtained from the Aydin Adnan Menderes University Faculty of Medicine Non-Interventional Research Ethics Committee (protocol number: 2022/119; date: 15/06/2022), while administrative permission was obtained from the Provincial Directorate of Health in Aydın (letter number: 44021967-605.01; date: 21/07/2022).

## RESULTS

Between September and November 2022, a total of 321 individuals aged 65 and over, who visited the 10 selected family health centers for any reason, were included in the study. Among the older adult participants, 51.4% were male and 70.7% were in the 65–74 age range. The participants' surveyed socio-demographic characteristics and habits are summarized in Table 1.

Among the participants, 88.2% had at least one chronic clinical condition, with cardiovascular disease (70.4%) and diabetes (33.6%) being the most commonly reported chronic conditions. Data concerning the participants' chronic clinical conditions are presented in Table 2.

Moreover, 289 (90.0%) participants reported knowing vaccines that are administered to people of their age, while 261 (81.3%) stated that vaccines had been recommended for them after the age of 60 years. The most common source of vaccine recommendations was family physicians (n=163, 50.8%).

Regarding vaccine awareness, 313 participants (97.5%) had heard about the influenza vaccine, with 291 (90.7%) about the pneumococcal vaccine, and 22 (6.9%) about the herpes zoster vaccine. Among the participants, 39.3% (n=126) had received the influenza vaccine in the past year, 47.0% (n=151) had received the pneumococcal vaccine once, 6.2% (n=20) had received the pneumococcal vaccine at least twice, and 0.3% (n=1) had received the herpes zoster vaccination.

The most common reasons for not getting vaccinated were the lack of perceived need concerning the influenza (n=66, 66.0%) and pneumococcal (n=95, 63.3%) vaccines, while a lack of awareness was the primary reason for not receiving the herpes zoster vaccine (n = 299, 93.4%).

### *Factors influencing influenza vaccination*

According to the results of this study, age, income

**Table 1.** Sociodemographic characteristics and habits of the participants (n = 321)

| Sociodemographic characteristic/habit | | Number | % |
|---|---|---|---|
| **Gender** | Male | 165 | 51.4 |
| | Female | 156 | 48.6 |
| **Education level** | Less than 9 years | 203 | 63.2 |
| | 9–12 years | 75 | 23.4 |
| | More than 12 years | 43 | 13.4 |
| **Income status*** | Low | 58 | 18.1 |
| | Medium | 213 | 66.4 |
| | High | 50 | 15.6 |
| **Income–expenditure perception** | Income is less than expenditure | 69 | 21.5 |
| | Income equals expenditure | 189 | 58.9 |
| | Income is more than expenditure | 63 | 19.6 |
| **Age** | 65–74 years | 227 | 70.7 |
| | 75+ years | 94 | 29.3 |
| **Marital status** | Single/widowed/divorced | 74 | 23.1 |
| | Married | 247 | 76.9 |
| **Employment status** | Not working | 305 | 95 |
| | Working | 16 | 5 |
| **Occupation** | Worker | 42 | 13.1 |
| | Civil servant | 82 | 25.5 |
| | Self-employed | 81 | 25.2 |
| | Housewife | 116 | 36.1 |
| **Smoking status** | No | 164 | 51.1 |
| | Quit (at least 1 year) | 117 | 36.4 |
| | Yes | 40 | 12.5 |
| **Alcohol consumption** | No | 248 | 77.3 |
| | Quit | 46 | 14.3 |
| | Yes | 27 | 8.4 |
| **Total** | | **321** | **100** |

* Below 4500 TL: Low income status; 4500–4000 TL: Medium income status; above 14000 TL: High income status.

**Table 2.** Participants' chronic clinical conditions (n = 321)

| Clinical Characteristic | | Number | % |
|---|---|---|---|
| Chronic condition | Absent | 38 | 11.8 |
| | Present | 283 | 88.2 |
| Cardiovascular disease | Absent | 95 | 29.6 |
| | Present | 226 | 70.4 |
| COPD*/asthma | Absent | 259 | 80.7 |
| | Present | 62 | 19.3 |
| Diabetes | Absent | 213 | 66.4 |
| | Present | 108 | 33.6 |
| Chronic kidney disease | Absent | 305 | 95 |
| | Present | 16 | 5 |
| Obesity | Absent | 285 | 88.8 |
| | Present | 36 | 11.2 |
| Cancer | Absent | 306 | 95.3 |
| | Present | 15 | 4.7 |

* COPD: Chronic obstructive pulmonary disease.

**Table 3.** Independent variables affecting receiving influenza vaccine in the last year in binary and multiple analyses

| Dependent Variable: Receiving Influenza Vaccine in the Last Year | | | | | | |
|---|---|---|---|---|---|---|
| Independent Variable | Binary Logistic Regression Analysis | | | Multiple Logistic Regression Analysis[Þ] | | |
| | OR* | 95% CI* | p | OR* | 95% CI* | p |
| **75 years and older** (Ref: Under 75 years) | 2.126 | 1.300–3.476 | 0.003 | 2.058 | 1.249–3.390 | 0.005 |
| **High-income individuals** (Ref: Low-income individuals) | 2.900 | 1.313–6.405 | 0.008 | --- | --- | NS± |
| **High-income individuals** (Ref: Middle-income individuals) | 2.472 | 1.311–4.664 | 0.005 | --- | --- | NS± |
| **Individuals with chronic diseases** (Ref: Those without chronic diseases) | 4.025 | 1.631–9.936 | 0.003 | 3.857 | 1.551–9.589 | 0.004 |
| **Individuals with CVD*** (Ref: Those without CVD) | 1.936 | 1.151–3.255 | 0.013 | --- | --- | NS± |
| **Individuals with diabetes** (Ref: Those without diabetes) | 1.830 | 1.137–2.944 | 0.013 | --- | --- | NS± |

* OR: Odds ratio; CI: Confidence interval; CVD: Cardiovascular disease.

Þ Forward LR: Multiple logistic regression analysis; ±NS: Not significant.

**Table 4.** Independent variables affecting receiving pneumococcal vaccination at least twice in binary and multiple analyses (reference: never received)

| Dependent Variable: Receiving Pneumococcal Vaccination at Least Twice (Ref: Not Fully Vaccinated) | | | | | | |
|---|---|---|---|---|---|---|
| **Independent Variable** | **Binary Logistic Regression Analysis** | | | **Multiple Logistic Regression Analysis[þ]** | | |
| | **OR*** | **95% CI*** | **p** | **OR*** | **95% CI*** | **p** |
| **75 years and older** (Ref: Under 75 years) | 2.966 | 1.131–7.777 | 0.027 | 4.230 | 1.366–13.105 | 0.012 |
| **Active workers** (Ref: Non-active workers) | 3.861 | 1.067–13.977 | 0.040 | 13.522 | 2.874–63.626 | 0.001 |
| **Those with COPD*/asthma** (Ref: Those without COPD*/asthma) | 6.048 | 2.246–16.287 | <0.001 | 10.175 | 3.167–32.689 | <0.001 |
| **Those with diabetes** (Ref: Those without diabetes) | --- | --- | NS± | --- | --- | NS± |

OR: Odds ratio; CI: Confidence interval; COPD: Chronic obstructive pulmonary disease.
þ Forward LR: Multiple logistic regression analysis; ±NS: Not significant.

**Table 5.** Independent variables affecting receiving at least two pneumococcal vaccinations (being fully vaccinated) in binary and multiple analyses (reference: not fully vaccinated)

| Dependent Variable: Receiving at Least Two Pneumococcal Vaccinations (Reference: Not Fully Vaccinated) | | | | | | |
|---|---|---|---|---|---|---|
| **Independent Variable** | **Binary Logistic Regression Analysis** | | | **Multiple Logistic Regression Analysis[þ]** | | |
| | **OR*** | **95% CI*** | **p** | **OR*** | **95% CI*** | **p** |
| **Men** (Reference: Women) | 3.020 | 1.070–8.521 | 0.037 | --- | --- | NS± |
| **Active workers** (Ref: Non-active workers) | 5.979 | 1.733–20.631 | 0.005 | 13.111 | 3.260–52.732 | <0.001 |
| **Alcohol users** (Reference: Non-alcohol users) | 4.197 | 1.395–12.625 | 0.011 | --- | --- | NS± |
| **Individuals with COPD*/asthma** (Reference: Those without COPD/asthma) | 4.863 | 1.925–12.286 | 0.001 | 7.762 | 2.682–22.181 | <0.001 |

OR: Odds ratio; CI: Confidence interval; COPD: Chronic obstructive pulmonary disease.
þ Forward LR: Multiple logistic regression analysis; ±NS: Not significant.

level, presence of a chronic disease, presence of cardiovascular disease (CVD), and presence of diabetes all had a significant influence on the influenza vaccination rate ($p < 0.05$). Those participants who had received the influenza vaccine during the past year were older than 75 years, had higher income levels, and had a chronic disease, CVD, and/or diabetes. The other assessed demographic and clinical characteristics did not significantly affect the influenza vaccination rate ($p > 0.05$).

Binary and multiple logistic regression analyses were also performed to determine the extent of the influence of the related independent variables on the participants' decision to receive the influenza vaccine during the past year. In the multiple logistic regression analysis involving six variables, two variables were included in the model. Here, the frequency of receiving the influenza vaccine during the past year was 2.1 times higher in the older adult participants aged 75 and over when compared with those aged below 75, while it was 3.9 times higher among those with a chronic disease when compared with those without a chronic disease. The independent variables that influenced the frequency of receiving the influenza vaccine during the past year in the binary and multiple logistic regression analyses are listed in Table 3.

*Factors influencing pneumococcal vaccination*

In this study, receiving pneumococcal vaccination at least twice was interpreted as complete vaccination. Moreover, age, employment status, presence of chronic obstructive pulmonary disease (COPD) and/or asthma, and presence of diabetes were all found to significantly influence the pneumococcal vaccination rate ($p < 0.05$). When compared with not receiving any pneumococcal vaccine, the complete vaccination rates were higher in participants aged 75 and over, in those engaged in active employment, and in participants with COPD and/or asthma and diabetes. In addition, when compared with not receiving any pneumococcal vaccine or receiving it only once, the complete vaccination rates were higher in male participants, in those engaged in active employment, in those who consumed alcohol, and in those with COPD and/or asthma. The other demographic and clinical characteristics did not significantly affect the pneumococcal vaccination rate ($p > 0.05$).

Binary and multiple logistic regression analyses were also performed to determine the extent of the influence of the relevant independent variables on complete pneumococcal vaccination. In the multiple logistic regression analysis for the dependent variable of complete vaccination (with not receiving any pneumococcal vaccine as the reference), three variables were included in the model. Having received pneumococcal vaccination at least twice was 4.2 times more likely in participants aged 75 and over ($p = 0.012$), 13.5 times more likely in those engaged in active employment ($p = 0.001$), and 10.2 times more likely in participants with COPD and/or asthma ($p < 0.001$).

In the multiple logistic regression analysis for the dependent variable of complete vaccination (with not receiving any pneumococcal vaccine or receiving it only once as the reference), two variables were entered into the model. The situation of having received at least two pneumococcal vaccinations was 13.1 times more likely in those participants engaged in active employment ($p < 0.001$) and 7.8 times more likely in those participants with COPD and/or asthma ($p < 0.001$). The independent variables that were effective in terms of receiving at least two pneumococcal vaccinations in both the binary and multiple analyses are shown in Tables 4 and 5, respectively.

## DISCUSSION

According to the results of our study, nine out of ten older adults are aware of the vaccines recommended for individuals of their age group, while four out of five older adults were recommended to receive vaccines after the age of 60 years. However, the vaccination rates for the recommended vaccines remain quite low. Two-thirds of those who choose not to get vaccinated believe that the vaccines are unnecessary. A higher percentage of those who are older and those with any chronic illness have received the influenza vaccine during the past year. Older individuals, those not engaged in active employment, and those with chronic respiratory diseases have a higher likelihood of having received complete vaccination.

The rate of receiving the influenza vaccine is higher than that of receiving the pneumococcal vaccine. While the majority of participants stated that they have been informed about the vaccines recommended for those over the age of 60 years, the crucial point to emphasize is that a significant portion of those who choose not to get vaccinated do so due to the belief that they do not require vaccination. The situation is different for the herpes zoster vaccine. The low awareness of the herpes zoster vaccine among older adults might be explained by the recent inclusion of the vaccine in the older adult vaccination program. In some prior studies conducted in Turkey, the rates of citing lack of knowledge or not being recommended as reasons for not getting vaccinated have been found to be much higher than those in our study (11,12).

In addition, in Turkey, two studies conducted in primary care centers have reported lower influenza vaccination rates than those identified in our findings. The influenza vaccination rate was found to be 24% among adults aged 18 and over in Istanbul district family health centers in the study by Uzuner et al. (13), In a retrospective study based on records from all the primary care centers in Denizli, Unal et al. found a rate of 14% (14). While this study only considered vaccinations conducted and recorded in primary care centers, our study also included vaccinations conducted outside primary care centers based on participant reports. Although Uzuner et al. conducted their study in primary care centers, they did not provide a separate vaccination rate for those aged 65 and over (13). Studies conducted in hospital-based family medicine clinics also reported lower rates than in our study (11,12). Moreover, studies conducted in various clinics of secondary and tertiary hospitals reported influenza vaccination rates between 10% and 71% (7-9,15-17).

According to the results of our study, only two independent variables appear to affect the frequency of receiving the influenza vaccination within the past year. Older adults aged 75 and over were 2.1 times more likely to have received the influenza vaccination than younger members of the older adult age group. Similar findings were reported in two previous studies conducted in Turkey (11,17). The increase in influenza vaccination rates with advancing age may be attributed to the higher prevalence of chronic diseases among older adults, leading to more healthcare visits, and consequently, more awareness of vaccination. By contrast, some prior studies have shown that vaccination rates decrease with age (8,18).

Moreover, having any chronic illness increases the likelihood of having received the influenza vaccine within the past year by 3.9 times. Interestingly, the specific chronic illness does not seem to be significant in this regard. In other studies, conducted in Turkey, unlike the present results, higher influenza vaccination rates were found among individuals with chronic heart diseases (11) and individuals with COPD, diabetes, and chronic heart diseases (7).

According to our results, the rate of being fully vaccinated against pneumococcal disease is quite low (6%). A study based on records from all the primary care centers in Denizli has found a rate of 12% (15). Similar rates have also been reported in studies conducted in hospital-based family medicine clinics (4–10%) (11,12), while studies conducted in various clinics of secondary and tertiary hospitals reported pneumococcal vaccination rates ranging from 3% to 27% (7-9,15-17).

Two telephone-based survey studies conducted in Canada among individuals aged 65 and over reported influenza vaccination rates of 65% and 70% as well as pneumococcal vaccination rates of 42% and 58%, respectively (17,19). In Germany, community-based studies among individuals aged 60 and over reported influenza vaccination rates of 50–66% and pneumococcal vaccination rates of 12–31% (18,20). In the United States, two studies conducted among individuals aged 65 and over determined influenza vaccination rates of 66–75% and pneumococcal vaccination rates of 62–72% (21,22). As these findings indicate, the vaccination rates reported in studies performed in Western

countries are higher than those found in Turkey. However, the criteria for being vaccinated varied in these studies. Both in Turkey and in other countries, influenza vaccination rates appear to be higher than pneumococcal vaccination rates. Similar patterns have been observed in studies conducted in both community settings and hospital-based clinics (20,23).

The results of this study also revealed that older adults aged 75 years and over, those engaged in active employed, and those with chronic respiratory diseases are more likely to have received at least two doses of the pneumococcal vaccine. According to the pneumococcal vaccination schedule in Turkey, adults aged 65 and over need to receive at least two pneumococcal vaccines. Evaluating those who are fully vaccinated when compared with those who have not received any vaccine indicated that individuals aged 75 and over are 4.2 times more likely to be vaccinated. Similar to the situation with influenza, the increasing prevalence of chronic diseases and healthcare visits with increasing age might have led to better awareness, and subsequently, to higher vaccination rates among the older adults. By contrast, the fact that many unvaccinated participants believed vaccination to be unnecessary might suggest that the increasing health issues with increasing age might change older adults' attitudes concerning the necessity of vaccination. Employment status also appears to have an impact on full vaccination status. The likelihood of receiving at least two doses of the vaccine was found to be 13 times higher in participants engaged in active employment. The presence of actively employed older adults in the community might expose them more to infectious diseases, which might influence their behavior regarding pneumococcal vaccination.

In individuals aged 65 and over with COPD and/or asthma, the likelihood of being fully vaccinated was 10.2 times higher when compared with those who had never received any vaccination, while it was 7.8 times higher when compared with those who were partially vaccinated. In the study by Mutlu et al., it was determined that individuals with chronic lung disease, chronic heart disease, and/or chronic kidney disease were more likely to receive pneumococcal vaccination, while no significant differences were observed for those with diabetes, hypertension, and/or chronic liver disease (11).

In our study, only one participant had received the herpes zoster vaccine (0.3%). This finding is consistent with the low awareness of the herpes zoster vaccine among older adults. Similar results have been obtained in two other primary care-based studies in Turkey (12,13), while in a study conducted in an internal medicine outpatient clinic among individuals aged 65 and over, the rate was slightly higher (7%) (3).

*Strengths and limitations of the study*

One of the strengths of the present study is the fact that it was conducted in primary care centers that reflect the older adult population in Efeler. The inclusion of vaccinations received not only in family health centers but also in other healthcare facilities enhances the representativeness of our results for the community.

However, the vaccination status of older adults was evaluated based on their declarations. The lack of vaccination cards and difficulties in recalling some vaccinations represent limitations of our study. Additionally, only older adults who received services from family health centers were included in the present study, which is another limitation, considering that those who received home care services during the study period were not included.

## CONCLUSION AND RECOMMENDATIONS

The full vaccination rates among the participants in this study were quite low. While the influenza vaccine was relatively more commonly received, the herpes zoster vaccine was only rarely administered. Older adults and those with any chronic condition were more likely to have received the influenza vaccine

during the past year. Considering full vaccination status, older participants, those who actively continue to work, and participants with COPD and/or asthma were more likely to have received the pneumococcal vaccine.

Similar to the influenza and pneumococcal vaccines, family physicians can play a crucial role in educating older adults about the herpes zoster vaccination. Despite having information and receiving recommendations, a significant portion of older adults in this study did not perceive the necessity of receiving the influenza and pneumococcal vaccines. Family physicians should be more sensitive when it comes to changing their patients' misconceptions about vaccines. In particular, during the process of educating patients, family physicians should emphasize the linkage between vaccination and chronic disease. Besides, it needs public health policies and health interventions increasing for older people being in need of influenza, pneumococcal and herpes zoster vaccinations.

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ORIGINAL ARTICLE

# THE EFFECT OF LOW-FLOW VERSUS HIGH-FLOW ANESTHESIA ON POSTOPERATIVE COGNITIVE FUNCTIONS IN GERIATRIC PATIENTS UNDERGOING TUR-P SURGERY

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## Abstract

**Introduction:** This paper investigates the effect of low-flow anesthesia applications on postoperative cognitive function in geriatric age group (≥65 years old) patients who underwent elective transurethral resection of the prostate surgery.

**Materials and Method:** A total of 98 patients aged 65 and over who underwent elective transurethral resection of the prostate surgery under general anesthesia between December 2021 and November 2022 in Hatay Mustafa Kemal University Research Hospital's Department of Anesthesiology and Reanimation were included in the study. The patients were subjected to a mini mental test the day before the operation and postoperatively at six hours, one day, three days, and seven days. Visual analogue scale scores were evaluated at 3, 6, 12, 24, 48, and 72 hours. The data obtained were compared between the patient groups who underwent low-flow (1 L/min, n: 49) and high flow (4 L/min, n: 49) anesthesia. P< 0.05 was considered statistically significant.

**Results:** A comparison between the postoperative 6thhour, 1st day, 2nd day, 3rd day, and 7th day mini mental testing scores of the low-flow anesthesia and high flow anesthesia groups did not exhibit any notable variations (p: 0.668, 0.785, 0.745, 0.705, respectively). The visual analogue scale scores of the cases at 3, 6, 12, 24, 48, and 72 hours did not differ statistically according to the type of flow applied (p: 0.316, 0.925, 0.651, 0.548, 0.624, 0.466, respectively).

**Conclusion:** It is thought that low-flow anesthesia can be applied safely, but it does not have a significant effect on cognitive functions compared to high flow anesthesia.

***Keywords:*** Anesthesia, General; Sevoflurane; Cognitive Dysfunction; Geriatrics.

## INTRODUCTION

The purpose of general anesthesia (GA) in surgery is to provide appropriate surgical conditions by ensuring early recovery without side effects. With advancing age, brain volume decreases, especially in gray matter, current neurotransmitter levels, receptor numbers, afferent transmission pathways, and speed decrease; moreover, blood-brain barrier permeability increases and cerebral blood flow decreases (1). Therefore, cognitive functions such as orientation, attention, memory, concentration, as well as motor, sensory, and autonomic functions are affected (2). Cognitive dysfunction in patients undergoing general anesthesia may delay healing and prolong hospital stay.

The volatile anesthetics, which are rapidly eliminated with minimal metabolic extinction, may reduce cognitive dysfunction and provide faster recovery in patients in the postoperative period. There are various potential advantages of low flow anesthesia (LFA). It improves the flow dynamics of inspired air, raises mucociliary clearance, keeps body temperature, decreases fluid loss, preserves up to 75%, and diminishes greenhouse gas emissions and costs (3, 4). Some studies have examined the degradation products of low-flow (LF) sevoflurane anesthesia and its effect on organ toxicity (5). It is uncertain how postoperative cognitive dysfunction (POCD) and recovery are affected by low flow sevoflurane anesthesia, and – to our knowledge – very few studies have been undertaken on this topic. In this study, we investigated whether the fresh gas flow (FGF) level affects cognitive functions after LFA with sevoflurane. Although LFA is widely used in clinical practice, our study is one of the few that compare the effects of LF and high-flow (HF) sevoflurane anesthesia on cognitive function in elderly patients. The primary objective, therefore, of this randomized, prospective study was to compare the effect of LF sevoflurane anesthesia and HF sevoflurane anesthesia on cognitive function in elderly patients who underwent elective transurethral resection of the prostate (TUR-P) surgery under general anesthesia. The secondary objective was to identify the factors associated with POCD.

## MATERIALS AND METHOD

The study was approved by a decision of the Hatay Mustafa Kemal University Clinical Research Ethics Committee, dated 21.12.2021, with the number 2021/180. The purpose of the study was explained to patients who were taking part in the study and the method to be used, and their written consent was obtained. The prospective, randomized, double-blind study was conducted between December 2021 and November 2022 at Hatay Mustafa Kemal University Health Research and Application Hospital in accordance with the Universal Code of Ethics contained in the Declaration of Helsinki.

American Society of Anesthesiologists (ASA) I–III patients aged 65 and over who were scheduled for elective TUR-P surgery under GA were included in the study. Conditions that cause major bleeding during the operation and increase tissue oxygen consumption (septicemia, thyrotoxicosis, hyperthermic cases, etc.), uncontrolled diabetes, alcoholism, active substance use or withdrawal symptoms, allergy to anesthetic agents to be used, cognitive dysfunction (such as Alzheimer's disease, dementia, delirium, etc.), illiterate patients, and those who did not accept the study were excluded from the study.

In a similar study, the effect size value calculated according to the statistical findings of the study comparing high and low flow by obtaining the difference between the postoperative sixth-hour mini mental test (MMT) values and the preoperative MMT values was 0.407. According to this result, the minimum number of patients to be recruited with 80% power was 96 (6). Using the closed-envelope method, patients who met the inclusion criteria were randomized, and 98 patients completed the

study. In the preoperative period, patients' age, body mass index (BMI) and ASA classification were recorded and MMT was applied. The next day, electrocardiography, peripheral oxygen saturation ($SpO_2$), noninvasive blood pressure (NIBP), and end-tidal carbon dioxide ($EtCO_2$) monitoring were performed on all patients admitted to the operating room. Following the opening of the intravenous (IV) route, 0.9% NaCl infusion was administered in all patients. GA was subsequently induced with 0.03 mg/kg midazolam, 1 mcg/kg fentanyl, 2–2.5 mg/kg propofol, and 0.6–1 mg/kg rocuronium, and the patients received orotracheal intubation. After intubation, 40% $O_2$ + 60% air + 2.5% sevoflurane mixed FGF was adjusted to 6 L/min, and mechanical ventilation was started. When the minimum alveolar concentration (MAC) of sevoflurane reached a value between 0.8 and 1.2, anesthesia was maintained by adjusting the flow to 1 L/min in patients with LF and 4 L/min in patients with HF. Remifentanil infusion for intraoperative analgesia was administered by titration to 0.05–0.2 µcg/kg/min so that the heart rate (HR) was ± 20% of the preoperative value. During the operation, inspiratory $O_2$ concentrations ($FiO_2$) were monitored and were not allowed to fall below 35%. In the case of a decrease, the applied $O_2$ concentration was increased by 10%. During the operation, NIKB, $SpO_2$, HR, $FiO_2$, MAC and $EtCO_2$ values were checked and recorded every 10 minutes. In the intraoperative period, body temperature was measured and recorded with the help of an esophageal temperature probe at 30-minute intervals following the induction. Eye-opening time was defined as the time to eye opening after discontinuation of the volatile agent. In the LFA group, the sevoflurane was turned off 15–20 minutes before the end of the surgery. At the end of the surgery, the FGF was raised to 6 L/min and the $FiO_2$ was 100%. In the HFA group, after the sevoflurane was turned off, the FGF was raised to 6 L/min and the $FiO_2$ to 100%. Rocuronium was antagonized with 2 mg/kg sugammadex. When the extubation criteria were met, the patients were extubated and eye-opening times were recorded. The cognitive functions of the patients were re-evaluated and recorded by the anesthesiologist at the sixth hour, and on the first, third, and seventh day postoperatively via MMT. In addition, postoperative visual analogue scale (VAS) scores were recorded after 3, 6, 12, 24, 48, and 72 hours. Diclofenac sodium 2x1 IM was administered to the patients for two days in the treatment of postoperative pain. Moreover, 15 mg/kg paracetamol IV was administered to patients with VAS ≥4. The data obtained for the LFA and HFA groups were compared.

Statistical analysis was performed via the SPSS 22 (Statistical Package for the Social Sciences, IBM, USA) program. Pearson chi-square test was applied to compare the percentages of qualitative data. The suitability of quantitative data for normal distribution was confirmed with the Kolmogorov-Smirnov test. The Mann-Whitney U test was applied in the comparison between two groups of quantitative variables that did not exhibit normal distribution. The Student's t test was used to compare two groups with normally distributed quantitative variables, and the one-way ANOVA test was used to compare more than two groups. The least significant difference test was used to make a pairwise comparison after ANOVA. The correlations of quantitative variables were evaluated using Spearman's correlation analysis. Statistical significance was accepted as $p<0.05$.

## RESULTS

The study was conducted with 98 patients who underwent elective TURP surgery under GA, 50% (n=49) of whom received HFA and 50% (n=49) LFA.

When comparing the age, BMI, ASA classification, and operation time of the patients according to the type of flow, no statistically remarkable results were found between the LFA and HFA groups ($p>0.05$; Table 1).

When comparing mean arterial pressure (MAP), mean pulse, and eye-opening times according to

flow type, no statistically remarkable results were found between the LFA and HFA groups (p>0.05; Table 1).

In the comparison of MMT scores according to flow type, the preoperative and postoperative sixth-hour, first-, third-, and seventh-day MMT scores of the various cases did not reveal any statistically remarkable result (p>0.05; Table 2).

No statistically remarkable result was found in the comparison of the difference between MMT scores according to flow type in all time periods (p>0.05; Table 3).

When the VAS scores of the cases after 3, 6, 12, 24, 48, and 72 hours were compared according to the flow type, no statistically remarkable result was identified (p>0.05).

Although the initial temperature values were higher than the 30-, 60-, and 90-minute temperature values in both flow types, there was no statistical difference according to the flow type (p>0.05). However, in all other time periods (30, 60, and 90 minutes), a statistically remarkable result was found in the temperature values according to the flow type (p<0.001). Although the temperature values in both groups decreased compared to the baseline, this decrease was greater in the HFA group.

**In analyses involving all cases**, a strong positive correlation (at the level of 0.781) between age and

**Table 1.** Age, ASA Scores, BMI, Mean Arterial Pressures (MAP), Mean Heart Rates (MHR), Eye Opening Time and Operation Time (min) Distribution of the Cases by Flow Type

| | | Total | Flow Type | | p |
|---|---|---|---|---|---|
| | | | LFA (n=49) | HFA (n=49) | |
| **Age (year)** | Min-Max (Median)<br>Mean±SD | 65-92 (74)<br>74,58±6,97 | 65-92 (74)<br>75,00±7,76 | 65-87 (74)<br>74,16±6,13 | Z= -0,203<br>p=0,839* |
| **ASA n (%)** | ASA I<br>ASA II<br>ASA III | 15 (15,3)<br>57 (58,2)<br>26 (26,5) | 7 (14,3)<br>30 (61,2)<br>12 (24,5) | 8 (16,3)<br>27 (55,1)<br>14 (28,6) | $\chi^2$: 0,378<br>p=0,828** |
| **BMI** | Min-Max (Median)<br>Mean±SD | 20,5-29,7(25,25)<br>25,20±2,53 | 20,5-29,7(25,3)<br>25,23±2,52 | 20,5-29,7(25,2)<br>25,17±2,56 | T=0,109<br>p=0,913*** |
| **Operation Time (min)** | Min-Max (Median)<br>Mean±SD | 68-98(90)<br>87,75±7,46 | 68-98(90)<br>87,71±7,78 | 68-98(88)<br>87,79±7,22 | Z= -0,071<br>p=0,943* |
| **MAP (mmHg)** | Min-Max (Median)<br>Mean±SD | 71-93(78)<br>79,05±5,04 | 71-93(78)<br>79,46±5,16 | 71-90(78)<br>78,63±4,93 | Z=-0,898<br>p=0,369* |
| **MHR** | Min-Max (Median)<br>Mean±SD | 58,90-72,10 (66,70)<br>66,77±2,27 | 62,30-72,10 (66,60)<br>66,62±2,19 | 58,90-71,40 (67,00)<br>66,92±2,36 | T=-0,646<br>p=0,520** |
| **Eye Opening Time (min)** | Min-Max (Median)<br>Mean±SD | 7-13(10)<br>9,85±1,54 | 7-13(10)<br>9,69±1,45 | 7-13(10)<br>10,02±1,63 | Z=-0,954<br>p=0,340* |

*Mann Whitney U Test ** Pearson Chi-Square Test ($\chi^2$) ***Student T Test (T) Z: Z score P< 0.05 was considered statistically significant.

**Table 2.** Comparison of MMT scores by flow type

| | | Flow Type | | p |
|---|---|---|---|---|
| | | LFA (n=49) | HFA (n=49) | |
| Preop. MMT | Min-Max (Median) | 21,00-29,00(25,00) | 19,00-29,00(25,00) | F=-0,488 |
| | Mean±SD | 24,85±2,09 | 25,06±2,04 | *0,626 |
| 6th hr MMT | Min-Max (Median) | 18,00-29,00(23,00) | 16,00-27,00(24,00) | F=-0,430 |
| | Mean±SD | 23,22±2,71 | 23,44±2,44 | *0,668 |
| 1st day MMT | Min-Max (Median) | 20,00-29,00(24,00) | 19,00-28,00(24,00) | F=-0,273 |
| | Mean±SD | 24,10±2,33 | 24,22±2,09 | *0,785 |
| 3rd day MMT | Min-Max (Median) | 21,00-29,00(25,00) | 19,00-29,00(25,00) | F=-0,326 |
| | Mean±SD | 24,73±2,21 | 24,87±2,11 | *0,745 |
| 7th day MMT | Min-Max (Median) | 21,00-29,00(25,00) | 19,00-29,00(25,00) | F=-0,380 |
| | Mean±SD | 24,81±2,15 | 24,97±2,09 | *0,705 |

*Student T Test, F: F test, P< 0.05 was considered statistically significant.

**Table 3.** Comparison of the difference between MMT scores according to flow type

| MMT score difference | LFA | HFA | P* | Z value |
|---|---|---|---|---|
| | Mean±SD | Mean±SD | | |
| Preop- 6th hr difference in MMT score | 1,63±0,97 | 1,61±0,95 | 1,0 | 0,00 |
| Preop- 1st day difference in MMT score | 0,75±0,63 | 0,83±0,58 | 0,474 | -0,716 |
| Preop- 3rd day difference in MMT score | 0,12±0,33 | 0,18±0,39 | 0,402 | -0,837 |
| Preop- 7th day difference in MMT score | 0,04±0,19 | 0,08±0,27 | 0,402 | -0,838 |

*Mann-Whitney U Test, Z: Z score, P< 0.05 was considered statistically significant.

**Tablo 4.** Correlation between age and MMT scores

| Difference | | Age | | |
|---|---|---|---|---|
| | | Total | LFA (n=49) | HFA (n=49) |
| Preop-6th hr | R | 0,781 | 0,848 | 0,707 |
| | p* | <0,001 | <0,001 | <0,001 |
| Preop-24th hr | R | 0,375 | 0,435 | 0,293 |
| | p* | <0,001 | 0,002 | 0,041 |
| Preop-3rd day | R | 0,185 | 0,282 | 0,084 |
| | p* | 0,068 | 0,049 | 0,566 |
| Preop-7th day | R | 0,084 | 0,234 | -0,042 |
| | p* | 0,413 | 0,106 | 0,773 |

*Sperman Korelasyon, R: korelasyon, P< 0.05 was considered statistically significant.

**Tablo 5.** Comparison of MMT scores according to ASA PS Classification

| | | ASA PS Classification | | | Test value | Making the difference |
|---|---|---|---|---|---|---|
| | | ASA I (n=15) | ASA II (n=57) | ASA III (n=26) | p | |
| **Preop. MMT** | Min-Max (Median) | 22-29(27) | 22-29(25) | 19-27(23,5) | F=11,400 | ASA III |
| | Mean±SD | 26,13±1,95 | 25,29±1,83 | 23,53±1,90 | **<0,001 | |
| **6th hr MMT** | Min-Max (Median) | 21-28(26) | 20-29(24) | 16-25(21) | F=29,357 | ASA III |
| | Mean±SD | 25,4±1,80 | 23,92±2,05 | 20,84±2,14 | **<0,001 | |
| **1st day MMT** | Min-Max (Median) | 21-28(26) | 21-29(24) | 19-26(22,5) | $\chi^2$: 0,378 | ASA III |
| | Mean±SD | 25,46±1,72 | 24,63±1,96 | 22,38±1,96 | * <0,001 | |
| **3rd day MMT** | Min-Max (Median) | 21-29(27) | 22-29(25) | 19-26(23) | F=12,985 | ASA III |
| | Mean±SD | 26,06±2,12 | 25,19±1,86 | 23,23±1,96 | **<0,001 | |
| **7th day MMT** | Min-Max (Median) | 21-29(27) | 22-29(25) | 19-27(23,5) | F=10,873 | ASA III |
| | Mean±SD | 26,06±2,12 | 25,24±1,85 | 23,46±1,98 | **<0,001 | |

*Kruskal-Wallis **Anova test, F: F test, $\chi^2$: Chi-Square Test

changes in sixth-hour MMT scores according to preoperative scores was found to be statistically remarkable (p<0.001). There was a weak positive correlation (at the level of 0.375) between age and the changes in the first-day MMT scores according to the preoperative scores, and it was found to be statistically remarkable (p<0.001). Although a very weak positive correlation was identified between age and the changes in the third- and seventh-day MMT scores according to the preoperative scores, it was not found to be statistically remarkable (p>0.05; Table 4).

**In the LFA group,** a strong positive correlation (at the level of 0.848) was identified between age and the changes in the sixth-hour MMT scores according to the preoperative scores, which was statistically remarkable (p<0.001). A weak positive correlation (at the level of 0.435) was identified between age and the changes in the first-day MMT scores according to the preoperative scores, which was statistically remarkable (p=0.002). A weak positive correlation (at the level of 0.282) was identified between age and the changes in the third-day MMT scores according to the preoperative scores, which was statistically remarkable (p=0.049). Although a very weak positive correlation was found between age and the changes in the seventh-day MMT scores according to the preoperative scores, it was not statistically remarkable (p>0.05; Table 4).

**In the HFA group**, a strong positive correlation (at the level of 0.707) was found between age and the changes in the sixth-hour MMT scores according to the preoperative scores, which was statistically remarkable (p<0.001). A weak positive correlation (at the level of 0.293) was found between age and the changes in the first-day MMT scores according to the preoperative scores, which was statistically remarkable (p=0.041). Although there were very weak positive correlations between age and the changes in the third-day and seventh-day MMT scores according to the preoperative scores, they were not found to be statistically remarkable (p>0.05; Table 4).

When MMT scores were compared according to the ASA classification, it was seen that the

difference in MMT scores preoperatively, 24th hour, 3rd day and 7th day time periods was between ASA II and III and ASA I and III, while there was a difference in all groups in the case of the sixth-hour scores. When the change in MMT scores according to the ASA classification (MMT score of two or more changes) was compared, the most notable change was identified in the ASA III classification (Table 5).

## DISCUSSION

There are several studies examining the effects of GA and spinal anesthesia on postoperative cognitive functions in urological surgeries (7). However, there are a limited number of studies investigating the effects of LFA and HFA on cognitive functions, and these studies indicate different results regarding cognitive functions. The objective of this study was to identify the effects of LFA and HFA on cognitive functions in elderly patients by standardizing the factors that may cause POCD. In our study, it was observed that LFA was not superior to HFA in the case of postoperative cognitive functions in patients aged 65 years and older who underwent elective TUR-P surgery under GA. According to the type of flow, the preoperative and postoperative sixth-hour, and first-, third-, and seventh-day MMT scores of the various cases did not exhibit any statistically significant differences. When the change (decrease) in the postoperative sixth-hour and first-, third-, and seventh-day MMT scores according to the preoperative scores in the HFA group was compared with the change in the LFA group, it was not found to be statistically significant. However, preoperative MMT scores and seventh-day MMT scores were found to be similar in the LFA group. When the temperature changes were compared, it was seen that there were temperature drops in both groups, yet fewer in the LFA group than in the HFA group. The temperature was maintained better in the LFA group than in the HFA group.

As mentioned above, there are a limited number of studies on cognitive function change in relation to LFA and HFA. In a study by Sandeep et al, which included 60 patients, no notable difference was found between LF and HF sevoflurane anesthesia in terms of cognitive dysfunction (8). In our study, the decrease and change in the sixth-hour, twenty-fourth-hour, and third-, and seventh-day MMT scores according to the preoperative MMT scores were similar in both groups. However, MMT scores in the LFA group were similar in the preoperative period and on the seventh day.

Age-related decline in organ function can affect the metabolism and excretion of anesthetic drugs, change the clinical effects of anesthesia, and prolong recovery after anesthesia. The International Study of Postoperative Cognitive Dysfunction (ISPOCD-1) is the first major study on postoperative cognitive impairment. The ISPOCD-1 applied neurocognitive testing at regular intervals postoperatively to patients older than 60 who had major non-cardiac surgery and had an operation lasting >2 hours. Cognitive dysfunction was found in 25.8% of the patients one week after the operation and 9.9% of the patients three months later. Moreover, in follow-ups that lasted between one and two years it was determined that 10% of these patients continued to experience cognitive disorders (9). This study revealed the importance of postoperative cognitive functions in the geriatric population. The incidence of POCD in different age groups has been shown to vary. In the study by Monk TG et al., which included 117 young, 112 middle-aged and 138 elderly patients, the incidence of POCD was found to be 36.6% for those aged 18–39, 30.4% for those aged 40–59, and 41.4% for those over the age of 60. All of these patients had undergone major non-cardiac surgery, and after three months, the rate was 5.7% in the young group, 5.6% in the middle-aged group, and 12.7% in the group aged over 60 (10).

In a study conducted by Tuman et al., it was stated that the incidence of POCD in patients undergoing coronary artery surgery with cardiopulmonary bypass was 0.9% in people <65 years of age, 3.6% in patients

aged 65–74, and 8.9% in people aged >75 years (11). According to the review by Luo et al., advanced age is considered an independent risk factor for POCD. Increasing evidence has demonstrated that neuroinflammation plays a serious role in POCD. The findings of the abovementioned review indicate that the neuroinflammatory pathogenesis of POCD is age dependent (12). All the cases in the present study revealed a strong positive correlation between age and changes in sixth-hour MMT scores according to preoperative scores; moreover, a weak positive correlation was found between age and the changes in the first-day MMT scores according to the preoperative scores, which was statistically significant. Although a very weak positive correlation was found between age and the changes in the third- and seventh-day MMT scores according to the preoperative scores, it was not statistically significant. These findings are similar to those found in the literature and emphasize that there is a linear relationship between advancing age and POCD.

Elderly population are vulnerable to hypothermia due to impared thermoregulation ability (13). Postoperative hypothermia may cause masking of hypovolemia, delayed recovery, cardiac ischemia, arrhythmia, coagulopathy, wound infection, increased blood loss, decreased drug metabolism, negative nitrogen balance, and prolonged hospitalization. As a result of shivering following hypothermia, oxygen consumption may increase by 400% to 500%, which may result in hypoxia. It has been demonstrated that cardiac morbidity can be reduced by 55% due to normothermia. Prevention of hypothermia is therefore of vital importance in elderly patients (14). In the study by Gua-Liang Gong et al., using the logistic regression of 70 patients, hypothermia was considered a risk factor for POCD (15). In the study by Yu Cui et al., which included 249 neonatal patients, hypothermia was observed less frequently in the group using fresh low gas flow than in the control group (16). In our study, although there was a decrease in other time periods compared to preoperative temperature scores in both types of flow, the decrease was greater in the HFA group. Temperature is better preserved in the LFA group.

Findings in the literature demonstrate that ASA risk classification is also effective in relation to cognitive functions. In a study conducted with 118 patients over the age of 75 who underwent major abdominal surgery, postoperative delirium and cognitive dysfunction were observed in 28 patients (24%). In this study, ASA III–IV group was stated as one of the risk factors (17). In the review by S Bala Bhaskar et al., it was observed that increased comorbidity increased the incidence of POCD (18). In our study, there was no notable change between the two groups in terms of quantity, since the ASA classification was homogeneously distributed. When MMT scores were compared according to the ASA classification, it was seen that the difference in the preoperative, twenty-fourth hour, third-day, and seventh-day MMT scores was between ASA II and III and ASA I and III, while there was a difference in all groups at the sixth hour. When the change in MMT scores (MMT score of 2 and/or more changes) according to the ASA classification was compared, the greatest change was observed in the ASA III group.

Prolonged anesthesia and hypotension/hypertension during surgery have been implicated as risk factors for POCD (19). In a study by Lukasz et al. involving 7,000 patients, hypotension and hypertension were considered as risk factors for POCD (20). Yocum GT et al. included 21 normotensive and 24 hypertensive elderly patients who underwent lumbar laminectomy or microdiscectomy in a study on cognitive function. Preoperative and postoperative first-day and first-month neurocognitive tests were applied to the patient groups. It was found that the low mean arterial pressure values observed in the hypertensive patient group were associated with poor cognitive

functions observed on the postoperative first day and first month (21). In our study, there was no notable change in mean arterial pressure changes between the two groups. Prolonged anesthesia duration (>2 hours) may lead to POCD by increasing anesthetic uptake and accumulation and creating a tendency to hypothermia in non-cardiac surgeries. POCD may be more common and severe after serious and long operations (22). In our study, the duration of anesthesia did not exceed two hours and there was no notable change between the two groups.

Although postoperative pain levels vary, the pain can be extremely severe in certain patients. Postoperative pain can be severe at levels of extensive surgical trauma, which can cause mental stress and sleep disturbances and increase the risk of POCD (23). In a study involving 225 elderly patients, J jiang et al. found that postoperative pain and analgesia were associated with the occurrence and development of POCD (24). In the present study, no notable change was detected between the two groups in terms of VAS scores.

Observing and comparing the change in cognitive functions during a single type of surgical intervention can be regarded as one of the positive aspects of the present study. It is therefore predicted that the relative anesthesia duration, estimated VAS scores, and surgical stress levels are more easily standardized. The fact that ASA scores, age, BMI, mean HR, mean arterial blood pressure, and VAS scores were not notably different between the two groups is thought to support our comparison of the effect of LF and HF sevoflurane anesthesia on cognitive functions, which was the primary objective of the study.

The limitations of this study include the use of only one test to evaluate cognitive functions and the fact that the groups were not compared according to education levels.

## CONCLUSION

In the presence of the necessary equipment – and with its advantages in relation to reducing costs, preventing environmental pollution, minimizing heat loss, and respiratory physiology – LFA can be safely applied in geriatric patients. However, LFA is not thought to have a significant effect on cognitive functions compared to HFA. Nevertheless, investigating its effect in long-term follow-ups may contribute to the literature.

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ORIGINAL ARTICLE

# IS BEING IN THE GERIATRIC AGE GROUP AN ADDITIONAL RISK FACTOR OR CONTRAINDICATION FOR LIVING DONOR LIVER TRANSPLANTATION?

## Abstract

**Introduction:** While advanced age was once a contraindication for liver transplantation, it is now routinely performed for individuals over (≥) 65. This study aimed to analyze preoperative findings, preoperative findings, perioperative graft-related and surgical factors, and postoperative complications in geriatric recipients (≥65 years) to assess the feasibility and outcomes of living-donor liver transplantation in this age group.

**Materials and Method:** Data regarding sex, model for end-stage liver disease score, Child score, body mass index, blood type, graft type (right or left lobe), ascites, esophageal variceal hemorrhage, hepatic encephalopathy, spontaneous bacterial peritonitis, preoperative INR, platelet, sodium, albumin, total bilirubin and creatinine, diabetes, hypertension, coronary artery disease, anhepatic phase, cold ischemia time, operation time, blood products transfusion rates, graft-to-recipient weight ratio, intensive care unit and hospital stay, biliary complications, hepatic vein thrombosis, portal vein thrombosis, postoperative hemorrhage, sepsis, and primary graft dysfunction were analyzed statistically in geriatric patients.

**Results:** The use of the right lobe was significantly higher in the ≥65 age group (p=0.036). Additionally, body mass index (p=0.039) and creatinine (p=0.018) were statistically higher in the group.

**Conclusion:** Living-donor liver transplantation can be safely performed in patients aged ≥65 years.

***Keywords:*** Liver; Survival; Transplantation.

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## INTRODUCTION

Living-donor liver transplantation (LDLT), a procedure effectively practiced worldwide, offers a life-saving option for patients suffering from end-stage liver failure across all age groups. Once considered an obstacle, advanced age alone is no longer a barrier to successful LDLT, thanks to advancements in transplant techniques and patient care. This applies to individuals over (≥) 65 years old, provided that their respiratory and cardiovascular functions are adequately maintained (1).

In LDLT recipients, age has been extensively studied as a factor influencing surgical success. However, the presence and severity of pre-operative decompensation findings, such as ascites, esophageal variceal hemorrhage (EVH), hepatic encephalopathy (HE), and spontaneous bacterial peritonitis (SBP), play a crucial role alongside co-existing chronic diseases, perioperative graft-related and surgical factors, and post-operative complications. These factors impact hospital stays and recovery times in geriatric patients (those aged ≥65) compared to younger recipients (2,3).

This study aims to analyze demographic data, pre-operative decompensation findings, chronic disease presence, liver failure markers like the model for end-stage liver disease (MELD) and Child scores, perioperative graft-related and surgical factors, post-operative complications, and infection rates in geriatric patients undergoing LDLT, comparing them to data from younger recipients.

## MATERIALS AND METHOD

Our study retrospectively examined the hospital computerized record system, patient follow-up files, files containing surgical findings, and operation notes, including the liver transplant database, and identified 276 patients who underwent LDLT for end-stage liver cirrhosis between July 2021 and October 2023. We analyzed the data by comparing two age groups: (≥65 years) and younger adult patients (18-64 years). Pediatric liver recipients under the age of 18 and cadaveric adult recipients have been excluded from the study. All LDLT patients included study were consecutive. The analysis compared these groups across various factors, including demographics, (sex, MELD score, Child score, weight, body mass index [BMI], and graft type [right or left]), decompensation findings (ascites, EVH, HE, and SBP), pre-operative laboratory values (blood INR, platelet count, sodium [Na], albumin total bilirubin, and creatinine), prevalence of chronic diseases (diabetes mellitus [DM], hypertension [HTN], and coronary artery disease [CAD]), perioperative findings (anhepatic phase, cold ischemia time, operation time, blood products transfused, and graft-to-recipient weight ratio [G.R.W.R.]), and post-operative outcomes (intensive care unit [ICU] stay, hospital stay, biliary complications, hepatic vein thrombosis [HVT], portal vein thrombosis [PVT], postoperative hemorrhage, sepsis, and primary graft dysfunction [PGD].

As the study was retrospective, written informed consent was not obtained from patients. All procedures were conducted in accordance with the ethical standards of the committees concerned with human experimentation (institutional and national) and the 1964 Declaration of Helsinki and its later editions. This study was approved by the İstanbul Aydın University Human Experiments Ethics Committee (approval numbered 2023/127, dated 10/18/2023).

### Statistical analysis

Nominal and ordinal parameters were described using frequency analysis, while scale parameters were summarized with means and standard deviations. Differences between categorical parameters were assessed using Chi-Square or Chi-Square Likelihood tests, as appropriate. The Kolmogorov-Smirnov test was employed to assess the normality of scale parameters. Since the distributions were found to be non-normal, the Mann-Whitney U test was used for the analysis of

differences. All statistical analyses were conducted SPSS 17.0 (SPSS Inc., Chicago, 3., USA) for Windows with a 95% confidence interval.

## RESULTS

### Findings on Age

In this study, the age range spanned from 65 to 78 years for the group aged ≥65 years, while patients aged <65 fell within the range of 18 to 64 years. Of the total participants, 20% (n:55) belonged to the ≥65 group, while the remaining 80% (n:221) were in the <65 group.

### Preoperative Demographic Findings (Table 1)

Among recipients aged ≥65 years, males represented 18.5%, while females constituted 23.1%. The mean MELD score was 14.7. Child scoring revealed 29.3% as Child A, 16.7% as Child B, and 18.1% as Child C. The average BMI was 28.4. Regarding etiologies, hepatocellular carcinoma (HCC) led with 33%, followed by hepatitis C virus (HCV) (28.6%), hepatitis B virus (HBV) (24.3%), nonalcoholic steatohepatitis (23.5%), and cryptogenic cirrhosis (23.2%). Additionally, the prevalence of chronic diseases in the ≥65 group was 19.7% for DM, 25.8% for HTN, and 10% for CAD. When it comes to decompensation findings, 20.5% had ascites, 20% exhibited HE, and 12.5% experienced EVH. Notably, SBP was not observed in this group. Preoperative laboratory values showed an average INR of 1.42, platelet count of 126 T/mm$^3$, Na level of 136 mm/L, creatinine level of 0.95 mg/dl, total bilirubin level of 4.1 mg/dL, and albumin level of 3.2 g/dL.

There were no statistically significant differences between recipients aged ≥65 years and younger recipients in terms of sex ($p$=0.404), blood type ($p$=0.226), MELD score ($p$=0. 276), Child score ($p$=142), etiology ($p$=0.681), comorbid conditions like DM ($p$=0.887), HTN ($p$=0.417), and CAD ($p$=406), decompensation findings like ascites ($p$=0.992), EVH ($p$=0.092), HE ($p$=926), and SBP ($p$=0.209), or laboratory parameters like INR ($p$=0.076), platelet ($p$=0.260), Na ($p$=0.965), albumin ($p$=0,473), and total bilirubin ($p$=0.501). BMI ($p$=0.039) and creatinine ($p$=0.018) were significantly higher in the ≥65 age group.

### Perioperative Findings (Table 2)

In patients aged ≥65 years, the perioperative blood transfusion rate was 25.7%. The mean duration of the anhepatic phase was 83.5 minutes, and the mean cold ischemia time was 64.4 minutes. The mean operation time was 478.2 minutes. The G.R.W.R. was 1.06. The right lobe was used in 21% of cases, while the left lobe was not utilized in any patients. The average length of ICU stay was 2.8 days, and the average total hospital stay was 13.8 days.

There was no statistical difference between the age groups regarding perioperative parameters like blood transfusion ($p$=0.432), anhepatic phase duration ($p$=0.180), cold ischemia time ($p$=0.964), mean operation time ($p$=0.653), G.R.W.R. ($p$=0.373), length of ICU stay ($p$=0.650), and total hospital stay ($p$=0.662). However, the use of the right lobe was significantly higher in patients aged ≥65 years ($p$=0.036).

### Postoperative complications (Table 3)

Among patients aged ≥65 years, the rate of PVT, HVT, and biliary complications were 20%, 25%, and 19.9%, respectively. Additionally, 16.7% experienced sepsis and 9.1% had intra-abdominal bleeding. Notably, PGD was not observed in this group. Hepatic artery thrombosis was not observed in any of the patients, regardless of age.

There were no statistically significant differences between the age groups in terms of the occurrence of PVT ($p$=0.680), HVT ($p$=0.754), biliary complications ($p$=0.103), sepsis ($p$=0.660), or intraabdominal bleeding ($p$=0.341). PGD also showed no statistically significant difference between the groups ($p$=0.470).

**Table 1.** Preoperative Demographic Findings, Comorbidities, Decompensation Findings, Laboratory Parameters and Statistical Results

| | >65 years (n:55) | <65 years (n:221) | p value |
|---|---|---|---|
| **Gender** | | | |
| Male | 18.5% | 81.5% | 0.404 |
| Female | 23.1% | 76.9% | |
| **MELD score** | 14.7 (+5.8)/(12.9-16.4) | 15.9 (+6.6)/(14.9-16.9) | 0.276 |
| **Child** | | | |
| A | 29.3% | 70.7% | |
| B | 16.7% | 83.3% | 0.142 |
| C | 18.1% | 81.9% | |
| **BMI** | 28.4 (+4.3)/(27.1-29.7) | 26.9 (+5.3)/(26.1-27.7) | **0.039** |
| **Etiology** | | | |
| HBV | 24.3% | 75.7% | 0.681 |
| NASH | 23.5% | 76.5% | |
| Cryptogenic | 23.2% | 76.8% | |
| HCC | 32.4% | 68.6% | |
| Ethanol | 0% | 100% | |
| Autoimmune | 6.7% | 93.3% | |
| HBV+HDV | 0% | 100% | |
| Budd Chiari Syndrome | 0% | 100% | |
| HCV | 28.6% | 71.4% | |
| Biliary Cirrhosis | 16.7% | 83.3% | |
| Primary Sclerosing Cholangitis | 25% | 75% | |
| Wilson Disease | 0% | 100% | |
| Hemochromatosis | 0% | 100% | |
| Hyperoxaluria | 0% | 100% | |
| Alagille Syndrome | 0% | 100% | |
| Caroli Disease | 0% | 100% | |
| Sjogren's syndrome | 0% | 100% | |
| Sarcoidosis | 0% | 100% | |
| **Comorbidities** | | | |
| DM | 19.7% | 80.3% | 0.887 |
| HTN | 25.8% | 74.2% | 0.417 |
| CAD | 10% | 90% | 0.406 |
| **Decompensation findings** | | | |
| Ascites | 20.5% | 79.5% | 0.922 |
| EVB | 12.5% | 87.5% | 0.092 |
| HE | 20% | 80% | 0.926 |
| SBP | 0% | 100% | 0.209 |
| **Laboratory parameters** | | | |
| Platelet (T/mm$^3$) | 126 (+87.5)/(100-152) | 113 (+87.5)/(100-126) | 0.260 |
| INR | 1.42 (+0.3)/(1.3-1.5) | 1.52 (+0.5)/(1.4-1.6) | 0.076 |
| Sodium (mmol/L) | 136.2 (+4.1)/(134-137) | 136.1 (+4.6)/(135-136) | 0.965 |
| Creatinine (mg/dl) | 0.95 (+0.54)/(0.7-1.1) | 0.86 (+0.7)/(0.7-0.9) | **0.018** |
| Total Bilirubin (mg/dl) | 4.1 (+7.2)/(2-6.3) | 4.5 (+6.3)/(3.6-5.5) | 0.501 |
| Albumin (g/dl) | 3.2 (+0.7)/(3-3.4) | 3.1 (+0.7)/(3-3.2) | 0.473 |

BMİ: Body Mass Index, CAD: Coronary Artery Disease, DM: Diabetes Mellitus, HBV: Hepatitis B virus, HCV: Hepatitis C virus, HDV: Hepatitis D virus, HE: hepatic encephalopathy, HTN: Hypertension, INR: International Normalized Ratio, NASH: Nonalcoholic steatohepatitis, OVB: Esophageal Variceal Bleeding, SBP: Spontaneous Bacterial Peritonitis

**Table 2.** Perioperative Blood Transfusion, Graft And Operation Time Findings And İCU/Hospital Stay

| | >65 years (n:55) | <65 years (n:221) | P value |
|---|---|---|---|
| **Blood Transfusion** | | | |
| Yes | 25.7% | 74.3% | 0.432 |
| No | 19.8% | 80.2% | |
| **Anhepatic phase (min)** | 83.5 (+28.5)/(73.2-93.8) | 93.1 (+36.2)/(87.2-99) | 0.180 |
| **Cold ischemia time (min)** | 64.4 (+31.2)/(53.3-75.5) | 65.7 (+35.2)/(59.9-71.5) | 0.964 |
| **Operation time (min)** | 478.2 (+84.9)/(445-511) | 462.3 (+78.8)/(446-477) | 0.653 |
| **G.R.W.R.** | 1.06 (+0.18)/(1-1.12) | 1.04 (+0.24)/(1-1.08) | 0.373 |
| **Graft Side** | | | |
| Right Lobe | 21% | 78.1% | **0.036** |
| Left Lobe | 0% | 100% | |
| **ICU stay (day)** | 2.88 (+2.7)/(2-3.7) | 2.46 (+1.9)/(2.1-2.7) | 0.650 |
| **Hospital Stay (day)** | 13.8 (+4.6)/(12.4-15.3) | 14.8 (+7.5)/(13.7-15.9) | 0.662 |

G.R.W.R.: Graft-To-Recipient Weight Ratio, ICU: Intensive Care Unit, Min: minute

**Table 3.** Postoperative Complications and Statistical Results

| | >65 years (n:55) | <65 years (n:221) | P value |
|---|---|---|---|
| **PVT** | | | |
| Yes | 20% | 80% | 0.680 |
| No | 23.8% | 76.2% | |
| **HVT** | | | |
| Yes | 25% | 75% | 0.754 |
| No | 20.5% | 79.5% | |
| **Bile complication (leakage and stricture)** | | | |
| Yes | 19.9% | 80.1% | 0.103 |
| No | 50% | 50% | |
| **Sepsis** | | | |
| Yes | 16.7% | 83.3% | 0.660 |
| No | 20.1% | 79.9% | |
| **Intraabdominal Hemorrhage** | | | |
| Yes | 9.1% | 90.9% | 0.341 |
| No | 20.9% | 79.1% | |
| **PGD** | | | |
| Yes | 0% | 100% | 0.470 |
| No | 20.7% | 79.3% | |

HVT: Hepatic Vein Thrombosis, PGD: Primary Graft Dysfunction, PVT: Portal vein Thrombosis.

### Mortality and Survival

The mortality rate was 18% in patients aged ≥65 years and 20% in those aged <65 years. No statistically significant difference in mortality was observed between the age groups ($p$=0.540). Mean survival for patients aged ≥65 years was 19.8 months (range: 16.4-23.1 months), while for those aged <65 years, it was 20.8 months (range: 19.1-22.1 months). Analysis revealed no statistically significant difference in patient survival between the age groups ($p$=0.554).

## DISCUSSION

The destructive impact of liver cirrhosis and the outcomes of liver transplantation can vary between elderly and young populations. While the research landscape presents diverse findings, objectively evaluating and understanding these discrepancies is crucial. Although some studies suggest male sex is less frequent among recipients aged ≥65 years (2,4,5) and BMI remains stable (6,7) or low (8), our study found no difference between sexes and a statistically higher BMI in the ≥65 group. With respect to other preoperative variables, while etiological factors may vary with age, MELD and Child scores tend to increase, leading to a shortened survival (7,9). However, other studies report lower MELD and Child scores in the elderly (4,5,8,10). While several studies show no significant difference in etiology between younger and older recipients (5,7,9), some suggested a higher prevalence of HBV or HCC in the elderly (4,8,10,11). Our study found no statistical differences in MELD and Child scores, or etiologic factors between the age groups.

The results pertaining to perioperative factors related to the graft suggest a potential worsening with advancing age (8). While some studies associate shorter anhepatic phase and cold ischemia time, increased blood transfusion needs, and unchanged operation times in patients aged over 65 years (4), it is essential to consider results that show no age-related differences in these parameters (5). In our study, no statistically significant differences were observed in terms of the anhepatic phase, cold ischemia time, operation time, or perioperative blood transfusion requirements.

In LDLT, the right lobe is generally preferred; however, evidence indicates no difference in complication rates between the right and left lobes in elderly recipients. In fact, some studies even suggest a preference for the left lobe in this age group. Furthermore, no disparity was noted across age groups with respect to G.R.W.R. (4,12). Interestingly, in our study, it was observed that the right lobe was statistically more utilized in patients aged ≥65 years; however, there was no difference in G.R.W.R.

Postoperative ICU and hospital stays might increase with additional comorbidities and treatment needs. While some studies suggest longer stays in elderly recipients, others report no age-related differences (4,5,11). Our findings align with the latter, showing no statistically significant differences in ICU or total hospital stay between the age groups.

While SBP, a decompensation finding, is often reported more frequently in elderly patients (2), studies have not consistently shown differences in the prevalence of EVH, HE, ascites, or SBP between older and younger recipients (5). Consistent with this, our study found no statistically significant differences in these decompensation findings between the age groups.

Meta-analyses have shown that comorbidities like DM, HTN, and CAD are more prevalent in recipients aged ≥65 years (2,5,6). However, it is important to acknowledge studies that report no age-related differences in these comorbidities (9). Additionally, higher mortality rates from cardiovascular diseases have been observed in the elderly (13,14). In our study, no statistically significant differences were found in DM, HTN, or CAD between the age groups.

Studies investigating complications have observed no statistically significant differences in biliary leakage or stenosis, portal vein, hepatic vein,

or hepatic artery thrombosis between recipients aged ≥65 and younger groups (4,5,7,15,16). Similarly, no significant difference was found in bleeding or PGD (4). While some studies report no difference in sepsis and infections between age groups (4-6), others suggest a lower prevalence in the ≥65 group (10). These literature findings are consistent with our study, demonstrating no statistically significant difference in vascular and biliary complications, PGD, or sepsis among age groups.

Mortality rates in the literature have been mixed, with some studies reporting higher rates in the elderly group (6,17,18) while others find no difference (7,12,15,19). Some studies even report shorter survival in older recipients (2,10,20). However, others find no age-related differences in mortality or survival (5,17). Our findings echo the latter, revealing no statistically significant differences in mortality or survival between recipients aged ≥65 and the younger group. Mortality rates and patient survival also remained similar between the two groups, in our study.

When analyzing preoperative laboratory parameters, we found no difference in platelet, albumin, INR, or total bilirubin between the groups. However, creatinine was statistically higher in patients aged ≥65 years (5,7). In our study, no statistically significant differences were observed in preoperative albumin, INR, total bilirubin, and platelet values; however, it was noted that only creatinine levels were elevated in the group aged ≥65 years. This finding underscores the importance of closely monitoring renal function after transplantation in elderly recipients, particularly for creatinine elevation.

The limitations of the study in terms of survival research may include the relatively low number of patients aged ≥65, lack of information about patients requiring preoperative hospitalization, and unspecified details about the administered treatment.

Given these findings on preoperative demographic, laboratory values, perioperative characteristics, and postoperative complication rates LDLT can be safely performed in patients aged ≥65 years. High creatinine and BMI-related issues also require careful attention in this population.

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ORIGINAL ARTICLE

# SINGLE-CENTRE ENDOSCOPIC GASTROSTOMY PLACEMENT RESULTS: EXPERIENCE AND MANAGEMENT OF COMPLICATIONS AND SIDE EFFECTS OF NUTRITIONAL PRODUCTS; REVIEW OF 426 CASE *PRESENTATIONS*

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## Abstract

**Introduction:** We aim to present the results, experience, and management of the complications and side effects of nutritional products in geriatric patients (age≥65 years) who underwent percutaneous endoscopic gastrostomy.

**Materials and Method:** Between January 01, 2018, and 31 December 2021 we examined 426 patients from the endoscopy and intensive care units. We assessed their primary diseases, insertion indications, procedural complications (endoscopy unit, patient bedside, surgery-household), consultations in the clinic, and procedural morbidity and mortality.

**Results:** Tubes were successfully placed in 426 patients but could not be inserted in 2 patients. The most common indication was cerebrovascular disease (45.3%) and the most common complication was catheter mobilization 16 (3.7%), primarily due to caregivers after discharge. In one patient, the tube passed through the transverse colon before reaching the stomach. This was noticed during colonoscopy and subsequently removed, after which the wound was closed primarily without any major complications. Wound infection resulting from leakage from the side of the tube, occurred in 12 patients (2.8%). Complications were more frequent in male patients aged > 70 years. The most common side effects of nutritional products in these patients were intolerance and diarrhoea.

**Conclusion:** Percutaneous endoscopic gastrostomy is safe and minimally invasive endoscopic procedure associated with low rate of morbidity. Clinicians can maximize outcomes and identify complications early by being aware of complications and utilizing preventive strategies. Furthermore, they need to be aware of the proper management of nutritional products' side effects.

***Keywords:*** Aged; Endoscopy; Critical Care; Gastrostomy.

## INTRODUCTION

The primary indication for enteral and parenteral feeding is to provide nutritional support to meet the metabolic requirements of the patients with inadequate oral intake. Enteral feeding is usually the preferred method over parenteral feeding in patients with a functional gastrointestinal (GI) system due to the associated risks of the intravenous route, higher costs, and the inability of parenteral nutrition to provide enteral stimulation, which could compromise the gut defence barrier. Moreover, it has been shown that enteric feeding can decrease the risk of bacterial translocation and corresponding bacteraemia (1). Tube feeding through the GI tract is primarily considered in patients with insufficient oral intake and a functional GI system, and tube insertion into the alimentary tract can be safely maintained (2). Percutaneous endoscopic gastrostomy (PEG) was first reported by Gauderer et al (3). in 1980 using endoscopy to insert a feeding tube into the stomach. Since its introduction by Gauderer et al. several different techniques have been developed for PEG tube insertion. Generally, all these methods share the common concept of inserting the gastrostomy tube through the abdominal wall at the point where the stomach and abdominal wall are in closest contact. In addition to the PEG endoscopy unit, this procedure can be easily performed at the bedside in ambulatory cases, with sufficient intravenous and local sedation, making it cheaper and less risky alternative to surgical gastrostomy, and with a shorter recovery time (4). PEG complications such as gastric wall necrosis, colon perforation, bleeding, and peritonitis are very rare, and catheter occlusion, port leakage, and port infection are the most common minor complications (5). This study aimed to assess the outcomes of hospital-based endoscopic gastrostomy placement and propose a novel method for comparing long-term major and minor complications, as well as managing nutritional side effects of PEG, in comparison to those reported in the literature.

## MATERIALS AND METHOD

In this study we examined the indications, complications, and long-term results of PEG tube placement at the patient bed in 428 patients in the endoscopy and intensive care units of the state hospital between January 01, 2018, and 31 December 2021. Two patients were found to have gastric ulcers and carcinoma during endoscopy and were therefore excluded from the study. All procedures followed the ethical rules and the principles of the Declaration of Helsinki. The study was initiated with the approval of the Medical Faculty Clinical Research Ethics Committee (Ethical no:2022-SBB-06919). Patient's demographic and clinical characteristics and PEG results were evaluated. Since the study was designed retrospectively, the need for written informed consent from the patients was waived. The decision to perform PEG was made by the neurologist and the anaesthesiologist for patients whose swallowing reflex in the feeding unit was not sufficient and for patients whose enteral nutrition was not sufficient due to prolonged intubation or comorbid disease in the intensive care unit. Patient's age, sex, primary diseases, reason for insertion, procedure-related complications, and associated morbidity and mortality were recorded. All patients in our study were aged ≥65 years. Routine laboratory examinations were conducted on all patients with PEG indications before the procedure. Prophylactic antibiotics were administered to all patients. All patients met the criteria for bleeding disorders [international normalized ratio (INR): <1.5, Platelet (Plt): >50,000], and gastroscopy was performed to rule out contraindications that could hinder the procedure, such as pathologies, diffuse acid in the abdomen, and gastrointestinal obstruction. All patients received peripheral oxygen during the procedure. Saturation, electrocardiography (ECG), and systolic and diastolic blood pressures were continuously monitored. Sedation was administered to all cases under the supervision of a physician. Prophylactic treatment and antibiotics were given

to each patient 2-4 hours before the procedure. The procedure was performed using the "pull" technique, paying attention to sterilization and the "Flowell Percutaneous Endoscopic Gastrostomy Tube" with a size of 16 fr was used. Enteral feeding was not initiated until 24 hours after the PEG procedure.

### Statistical Analysis

Statistical analysis was performed using the SPSS version 25.0 software (SPSS Inc., Chicago, IL, USA). Data are presented as the mean±standard deviation and frequency values for categorical variables. Data concerning surgical treatment results are presented as percentages.

## RESULTS

The number of patients who underwent PEG was 426; 238 (55.9%) were female, and 188 (44.1%) were male. Among them, 274 (64.3%) were patients who could not be fed due to a neurological pathology and were hospitalized in the intensive care unit (Table 1). Of these patients, 193 (45.3%) had cerebrovascular disease and 81 (19.8%) had chronic nervous system diseases, such as amyotrophic lateral sclerosis, multiple sclerosis, and dementia. In seven (1.64%) patients, PEG was applied due to trauma, malignancies such as head, neck, and oropharyngeal cancer in 16 (3.7%) patients, and prolonged intubation in 129 patients (30.2%) (Table 2). The mean follow-up period was 120.8(1-1090) days. A total of 194 patients (45.5%) were discharged from the hospital due to primary or comorbid diseases (118 patients, 60.8%). The most common early complication was catheter mobilization, which was observed in 16 (3.7%) patients, and was mainly accidentally done by their caregivers after discharge. Meanwhile, wound infection occurred in 12 patients (2.8%) (Table3). Most patients improved with medical treatment; however, catheter removal was required in five patients (1.2%) due to infection.

**Table 1.** Distribution by clinic

| Clinic | Number of patients | % |
|---|---|---|
| **İntensive care** | 274 | 64.3 |
| **Neurology service** | 80 | 18.7 |
| **Palliative service** | 72 | 16.9 |

**Table 2.** Distribution of cases according to their etiology

| Primary disease | Number of patients | % |
|---|---|---|
| **Cerebrovasculer disease** | 193 | 45.3 |
| **Chronic nervous diseases** | 81 | 19 |
| **Extended intubation** | 129 | 30.2 |
| **Malignancy** | 16 | 3.7 |
| **Trauma** | 7 | 1.64 |

**Table 3.** Complications of the PEG procedure

| Complication | Number of patients | % |
|---|---|---|
| **Catheter mobilization** | **12** | **2.8** |
| **Wound İnfection** | 5 | 1.1 |
| **Colon perforation** | 1 | 0.2 |

In one patient, the PEG had passed through the transverse colon's two layers before reaching the stomach, resulting in the transverse colon getting trapped between the stomach and the abdominal wall. Fortunately, there were no fatalities related to PEG insertion. The rate of complication development was higher in male patients aged 70-75 years.

## DISCUSSION

PEG for enteral nutrition has become widespread and offers distinct advantages in terms of cost and lower complication rates compared to parenteral nutrition (6).

Ekin et al. (7) found that 93% of PEG indications are primarily related to neurological discomfort. Takunaga et al (8). reported that 75% of patients had cerebrovascular disease. In our study, most PEG patients had neurological disease (64.3%), while others had undergone extended intubation, malignancy, and trauma.

There are controversial results in the literature on the use of prophylactic antibiotics before the procedure. In a published meta-analysis, a single dose of antibiotics was shown to reduce peristomal wound infection (8), but this was not observed in other study. In a study by Ekin et al (7). the effectiveness of prophylactic antibiotic use was not demonstrated. Meanwhile, Tokunaga et al (8). reported that prophylactic antibiotic use reduces procedural complications and the possibility of regional infection. Routine antibiotic prophylaxis (1000 mg cefazolin) was applied in our practice. Dormann et al (9). have shown that a single dose of ceftriaxone administered 30 minutes before percutaneouse endoscopic gastrostomy significantly reduces local and systemic infective complications. However, we preferred prophylactic antibiotic (1000 mg cefazolin) to reduce local and systemic infective complications. In this study the wound infection rate was as low as 1,1% when compared to 5-30% in the literature (10).

The literature lacks standardization regarding when and how to initiate feeding after a PEG procedure. Traditionally, limited feedings started 24 hours after the procedure, following gastrostomy data. Some studies have suggested starting feeding with in 1 hour, 24 hours, or the first 12 hours (11). In our routine practice, we commence the first feeding in the morning following the procedure.

Bankhead et al (12). found that the complication rate of the percutaneous endoscopic method was the lowest, followed by the open surgical method. Meanwhile, the laparoscopic method had the highest complication rate. PEG was the most frequently reported favourable option. Morbidity and mortality rates for the PEG procedure in surgical gastrostomy are higher than those for the endoscopic PEG procedure. Moreover, the endoscopic PEG procedure does not require general anaesthesia, can be performed at the bedside, and is cost-effective, making it a preferred choice (13).

The main complications are gastrocolic fistula and peritonitis. These complications are typically identified months after PEG placement, when the original PEG tube is removed or manipulated, or when the replacement tube is placed into the colon (14,15).

Preventing this complication involves using good transillumination and finger pressure to guide the puncture site placement. In our study, we observed a colonic injury while inserting a PEG tube. Four months later, a colonoscopy was performed, revealing that the tube had passed through the transverse colon's two layers without blocking the colonic passage. The tube was pulled out (Figure 1,2) and closed primarily without the need for an emergency procedure.

Zopf et al (16). identified four risk factors associated with complications and infections following PEG procedures: hospital stay, PEG tube size, the endoscopist' experience, and underlying malignant diseases. There were no reported cases of regional infection. Complications were observed in 1 case (7.6%), and PEG-related mortality was reported to be below 1%. In previous studies, the first 30-day mortality rates ranged from 8% to 26.8% in different series, with three-month mortality rates ranging from 15.7% to 42% due to external causes. In our study, no procedure-related mortality was observed. The previously reported

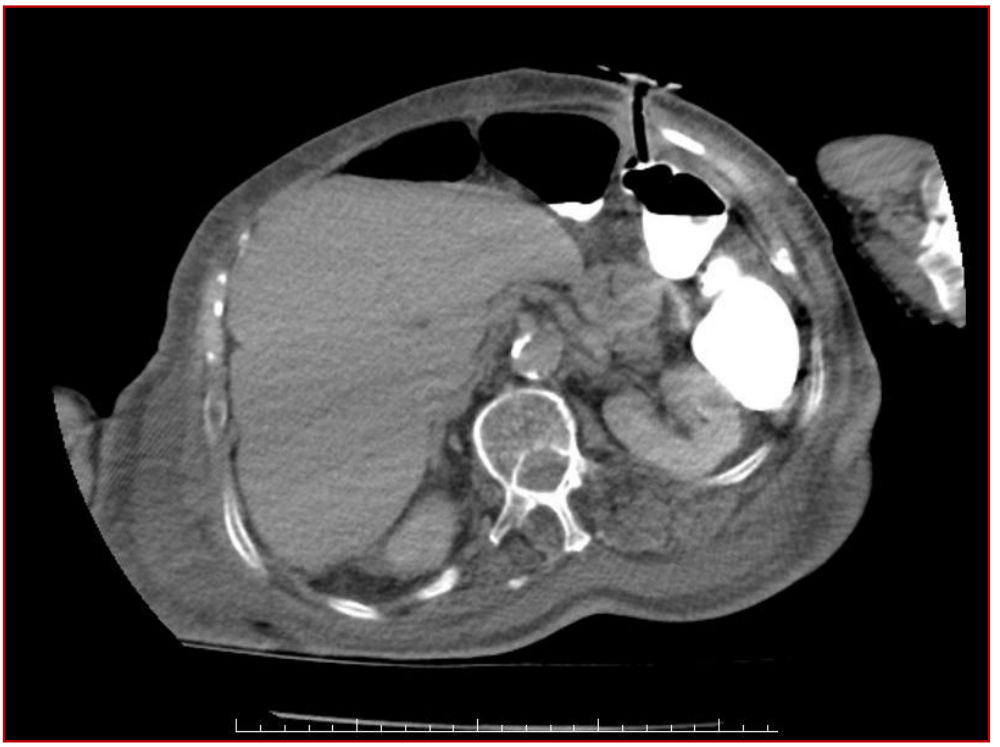

**Figure 1.** CT scanning of the Peg Tube

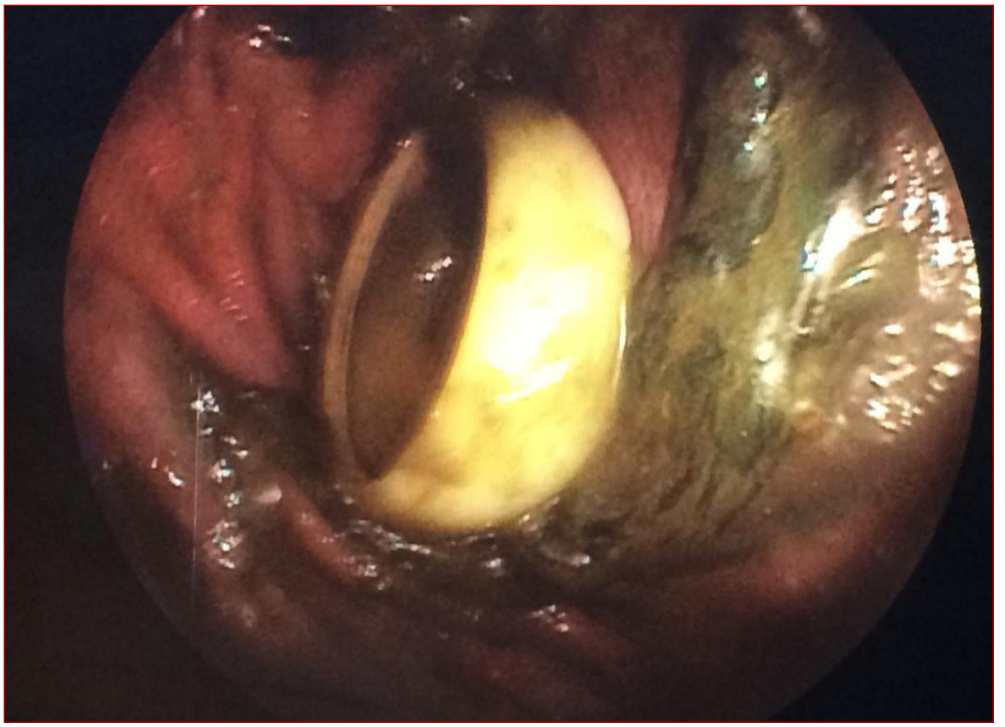

**Figure 2.** Peg tube in the transverse colon

risk factor for PEG tube insertion, increased age (16), was consistent with the findings in our study. Wound infection developed in 12 patients (2.8%). In cases of PEG catheter infection (whether early or late), wound cultures were obtained from the site and irrigated until culture results were available. Ciprofloxacin and topical fucidic acid were used, and systemic antibiotics were prescribed based on culture results. Enteral nutrition was discontinued if the infection worsened, and a switch to parenteral nutrition was made. If the issue persisted (as there was a foreign object), the PEG catheter was removed and we waited for the infected area to heal completely (2-3 weeks) before reinserting a new PEG. During this period, we halted NG and enteral/parenteral nutrition. For patients who presented to the emergency room, typically on the first or second day after the PEG catheter was removed by patients or their relatives at home to prevent closure of the catheter site due to epithelialization, we inserted a size 18 silicone Foley catheter. The balloon was inflated with 10 cc of sterile fluid, and the catheter was pulled back into the skin and secured. If it was not retracted and secured, it could move distally due to intestinal motility, potentially leading to closure, vomiting, and aspiration. During the COVID-19 epidemic, we encountered patients for whom we couldn't perform new PEG procedures for up to six months, and surprisingly, there were no problems. The non-closure of the lumen allowed us to reattach the PEG's with a lower risk of complications in patients who were enrolled in the PEG program using the same lumen. In cases where we suspected the PEG catheter was obstructed due to dressing beneath the stopper during mobilization (mainly stopper and tissue compression between the stomach and skin), we removed the catheter from the skin and gently pulled it upward, positioning it within the high-quartered superior area. If the catheter was 2 cm or less from the skin's surface and the bulb was palpable under the skin, we considered the catheter to be in place. We have seen this during repeat patient endoscopies. Consequently, if there was no infection, we initiated the PEG exchange program, performing endoscopy and PEG replacement during the same session. If there was an infection, we installed an NG tube, continued enteral feeding, detected the catheter, completed infection treatment, and then inserted a new PEG catheter. The rate of complication development was higher in male patients over the age of 70 years.

Management of side effects of nutritional products: In the past, the use of the enteral nutrition set (gravity) for meals, which relied on the patient's reflexes, often resulted in catheter blockages due to incorrect nutrition. However, we have observed no blockages when using the enteral feeding set with washing (pump feeding) during follow-up. With this set, enteral feeding is performed by washing with water. In patients starting nutrition, especially patients with diabetes mellitus(neuropathy), issues related to intolerance, stemming from reduced motility, are alleviated with the use of metoclopramide. However, for patients who develop intolerance and cannot be diagnosed with a condition obstructing luminal passage via endoscopy, continuous nutrition with pumps is considered. During this period, the enteral nutrition dose is reduced, and the remaining nutrition is administered intravenously. Enteral feeding is gradually increased to the full dosage as tolerance improves.

Regarding diarrhoea after enteral feeding, we conducted stool microscopy and stool culture when there were more than three episodes and a change in stool colour. We had previously obtained these samples from all patients, and many of the results were negative. We have observed that in most cases, diarrhoea is caused by the rapid enteral feeding in infants (17). That is why we initially administer feeding through a pump. If metoclopramide becomes necessary in a sequential approach, we pause enteral feeding, switch to a fibre-based enteral nutrition product, administer hyoscine-n-butyl bromide and prebiotic

products, reduce enteral nutrition, and complete the remaining nutrition parenterally in more resistant cases. Eventually, we discontinue enteral nutrition and provide parenteral nutrition. In our observations, we have seen the use of carbapenem, piperacillin/tazobactam, and teicoplanin in cases that are resistant to these treatments (18). Proper patient education is essential, particularly when there is a change in the patient's condition or care.

Removal of the PEG tube is recommended when it is no longer needed or when complications such as persistent leakage or buried bumper syndrome require its removal. Experts have suggested using a "cut and push" technique to remove PEGs in adults (19,20). However, reports of serious and sometimes fatal complications, such as small bowel perforation and obstruction, favour the use of endoscopic removal of PEG tubes. Generally, the PEG tract closes in the first few days after PEG removal; however, occasionally, a gastrocutaneous fistula persists, and several factors, such as prolonged duration of tube placement, local infection, and underlying poor tissue healing, contribute to delayed maturation of the PEG tract.

## CONCLUSION

Percutaneous gastrostomy is a safe and minimally invasive endoscopic procedure associated with a low morbidity rate. It is also easy to follow up and replace when a blockage occurs. Although it is generally considered safe, PEG tube placement can be associated with many potential complications. Awareness of these complications and the use of preventive strategies can allow endoscopists to maximize outcomes and identify complications early. Additionally, they must be knowledgeable about effectively managing the side effects of nutritional products.

**Ethics Committee Approval:** The study was carried out with the permission of the University Ethics Committee (Ethical no: 2022-SBB-06919).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

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ORIGINAL ARTICLE

# EVALUATING THE RISK OF DELIRIUM IN ELDERLY INPATIENTS IN COVID-19 INTENSIVE CARE: A PROSPECTIVE AND OBSERVATIONAL STUDY

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## Abstract

**Introduction:** Delirium is dangerous, often preventable, and associated with a high financial burden and increased morbidity and mortality. This study aimed to evaluate the risk of delirium in elderly inpatients in COVID-19 intensive care units.

**Materials and Method:** This study used a prospective and observational design. Between July and November 2022, 49 intensive care patients were admitted to a training and research hospital in northeast Turkey. The data were collected using the Patient Information Form, Critical-Care Pain Observation Tool, Ramsay Sedation Scale, and Nursing-Delirium Screening Scale.

**Results:** The patients' mean age was 76.90±8.29 years. The longer the length of stay in the intensive care unit, the incidence of delirium increased. The incidence of delirium increased in patients aged 70–95 years ($p$=0.007). Patients with delirium experienced insomnia and agitation and used more sedative drugs ($p$<0.05). The predictors of early delirium were sedation (β=0.869), agitation (β=-0.582), and diastolic blood pressure (β=0.258). The predictors of delirium were pain (β=-0.599) and sedation (β=0.267).

**Conclusion:** The study demonstrated that older age, agitation, sedation, pain, and diastolic blood pressure predicted delirium in elderly COVID-19 inpatients. It is necessary to identify and eliminate risk factors to reduce the risk of delirium in elderly patients. Nurses should play an active role in identifying and managing delirium in elderly COVID-19 patients.

***Keywords:*** COVID-19; Delirium; Aged; Intensive Care.

## INTRODUCTION

Delirium is a psychiatric disorder defined as acute brain failure that occurs due to reasons such as electrolyte imbalance, a chronic disease, trauma, and polypharmacy (1). It causes symptoms such as agitation, irritability, non-compliance with treatment and aggression, which lead to changes in consciousness such as confusion, lethargy, and stupor in patients. It also causes thought disorders such as delusions, perception disorders such as auditory and visual hallucinations and illusions, and intense emotional reactions such as anger in the patient (2). The diagnosis is often missed due to its subtle clinical manifestation, particularly in the hypoactive type. Delirium is dangerous, often preventable, and is associated with a high financial burden and increased morbidity and mortality.

Some precipitating and predisposing factors are important in the development of delirium. Evaluating and recording these factors before delirium develops and applying preventive interventions to patients at risk of delirium can contribute to the problem's solution (3). Predisposing factors for delirium are age, low mini-mental state assessment, being male, mood disorders, some chronic diseases, severity of the disease, nutritional disorders, visual and auditory diseases, and alcohol use. Precipitating factors are contaminations, drugs, dehydration, electrolytic disturbances, bladder catheters, surgical procedures, and hospitalization (4,5).

Delirium is an important indicator of mortality in adult COVID-19 patients and increases the risk of death in elderly patients. Delirium is also associated with prolonged hospital stays, intensive care unit admissions, and ventilator use (6). Delirium prolongs patient's stay in intensive care unit, and it causes death in elderly COVID-19 patients (7). For patients older than 65 years, the commonness, frequency, and death rates of delirium in COVID-19 patients were 28.2%, 25.2%, and 48.4%, respectively (8). Therefore, defining the risk of delirium in COVID-19 patients is important for the patient's survival and quality of life. The present study was conducted to evaluate the risk of delirium in elderly inpatients in COVID-19 intensive care units.

## MATERIALS AND METHOD

### Study design

This study was conducted as a prospective and observational study.

### Sample and setting

The study population included patients older than 65 years old who were hospitalized in the COVID-19 intensive care unit of a tertiary hospital between July and November 2022. As a result of the power analysis, with an effect size of 0.502, the power of the study was accepted as 80%, type 1 error was accepted as 5%, and the required sample size for the study was determined as 12 individuals (9). The sample included 49 intensive care patients who met the inclusion criteria. Inclusion criteria include (a) being 65 years old and older, (b) being conscious, and (c) obtaining verbal and written consent. Exclusion criteria include (a) taking propofol, (b) taking opioids, and (c) using neuromuscular blockers.

### Instruments

Data were collected using the Patient Information Form, Critical-Care Pain Observation Tool (CPOT), Ramsay Sedation Scale (RSS), and Nursing-Delirium Screening Scale (Nu-DESC). Assessments were performed on the first, third, fifth, and seventh days.

### Patient information form

Patient Information Form includes variables to determine the patient's social and demographic characteristics and vital signs which consisted of 20 questions, including age, gender, number of

days in the intensive care unit, the status of being connected to a mechanical ventilator, systolic blood pressure, diastolic blood pressure, respiratory rate, pulse rate, white blood cell (WBC), oxygen saturation ($SpO_2$), insomnia, agitation, sedation, neuromuscular blocker, propofol, opioid treatment, mortality, frailty index, length of intensive care unit stay, and length of hospitalization.

### Critical-care pain observation tool (CPOT)

The tool was developed by Gelinas et al. (10). The Turkish validity and reliability study was conducted by Gündoğan et al. (9), and the Cronbach's α value was found to be 0.87–0.99. The scale is divided into four subsections and each section is evaluated between 0 and 2 points, and the total score varies between 0 and 8. Intensive care patients who score above two on the scale are defined as painful. In this study, Cronbach's α values on the scale were 0.89, 0.87, 0.86, and 0.92 on the first, third, fifth, and seventh days, respectively.

### Ramsay sedation scale (RSS)

The RSS was a six-point Likert type scale and assessed the sedation level developed by Ramsay et al. (11). In the scale evaluation, score starts from 1: anxious, uneasy and restless and continues until score 6: no response. An increase in the score indicates an increase in the level of sedation.

### Nursing-delirium screening scale (Nu-DESC)

The scale was developed by Gaudreau et al. (12). The Turkish validity and reliability study was conducted by Karataş and Samancıoglu-Baglama (13), and Cronbach's α value was found to be 0.74. A score between 0 and 2 is given for each item, and 10 points can be obtained from the scale. According to reports, the threshold value for delirium is 2. In this study, Cronbach's α values of the scale were 0.87, 0.89, 0.88, and 0.90 on the first, third, fifth, and seventh days, respectively.

Delirium diagnosis was made by an anesthesiologist and two psychiatric nurses using Nu-DESC. According to the Nu-DESC, patients with a scale mean score of two or more (≥ 2) were considered to have delirium.

### The Clinical Frailty Scale (CFS)

The CFS is a straightforward and accessible tool that can be used to quickly and simply assess frailty (14). The CFS consisted of seven levels: One level = Very Fit = People who are vigorous, active, energetic, exercises regularly, is in the fittest group for her age. Two level = Fit = Previously known as well: People who have no intense disease symptoms but are less fit than level 1. Three level = Managing Well = People whose medical problems are well controlled. Four level = Living with Very Mild Frailty = A common complaint is being "slowed-up" and being tired during the day. Five level = Living with Mild Frailty = These people usually need help in higher-order instrumental activities of daily living. Six level = Living with Moderate Frailty = They need help with all outside activities and with keeping house. Seven level = Living with Severe Frailty = People who are characterized by progressive dependence in personal activities of daily living.

### Statistical analysis

The data obtained from the study were analyzed in SPSS 24 package program (IBM SPSS, New York, USA). Descriptive statistics, such as percentages, arithmetic mean, and standard deviation, were used to analyze social and demographic characteristics. The suitability of the sample for normal distribution was evaluated using the Kolmogorov–Smirnov test. Pearson Chi-Square and Fisher's Exact Test were used to compare demographic variables and physiological parameters of patients with and without delirium. The significance level ($p$) was considered 0.05.

The effect of independent variables (systolic blood pressure, diastolic blood pressure, respiratory rate, pulse rate, WBC, $SpO_2$, CPOT, and RSS) on the dependent variable (Nu-DESC) was studied using multiple linear regression analysis. This analysis was performed on Day 7 measurements. First, it was evaluated whether the six conditions for the analysis were met. The dependent variable is a continuous variable. All variables have a normal distribution. Skewness and kurtosis values range from −1 and +1. The correlation coefficient between independent variables is less than 0.80. It shows that there is no multicollinearity between independent variables. In the table of residual statistics, standard residual minimum and maximum values are between -3.29 and +3.29. The maximum value in the Cook's Distance row is less than 1.000. It shows that there are no outliers in the observed data. According to the histogram, the errors in the forecasts are normally distributed. The scatter plot shows that there is a linear relationship between the variables. As a result, it was determined that all six conditions for multiple linear regression analysis were met.

### Ethical considerations

Ethics committee approval was obtained from Aksaray University Clinical Research Ethics Committee (date: 23.06.2022, Decision No: 2022/12-04). The patients participating in the study and their relatives were informed about the study, and data were collected by explaining that personal information would be kept confidential. Written and verbal consent were obtained from the patients.

## RESULTS

### Delirium, mortality, frailty index, and hospitalization statistics

According to the Nu-DESC scoring, 36.7% of the patients showed delirium symptoms on the first day, 40.8% on the second day, and 49.0% on the fifth and seventh days (Table 1). The 90-day mortality rate of elderly patients with COVID-19 was 38.8%. The length of intensive care unit stay in patients was 20.55±22.36. The length of hospitalization was 23.36±22.87. The average frailty index was 5.70±1.60.

**Table 1.** Delirium, mortality, frailty index, and hospitalization statistics (n=49)

| | n | % |
|---|---|---|
| **Day 1 delirium (≥2)** | | |
| Yes | 18 | 36.7 |
| No | 31 | 63.3 |
| **Day 3 delirium (≥2)** | | |
| Yes | 20 | 40.8 |
| No | 29 | 59.2 |
| **Day 5 delirium (≥2)** | | |
| Yes | 24 | 49.0 |
| No | 25 | 51.0 |
| **Day 7 delirium (≥2)** | | |
| Yes | 24 | 49.0 |
| No | 25 | 51.0 |
| **90-day mortality** | | |
| Yes | 19 | 38.8 |
| No | 30 | 61.2 |
| | **Mean** | **SD*** |
| **Length of intensive care unit stay** | 20.55 | 22.36 |
| **Length of hospitalization** | 23.36 | 22.87 |
| **Frailty index** | 5.70 | 1.60 |

*SD=Standard Deviation

### Sample characteristics

The mean age of the elderly intensive care unit patients who participated in the study was 76.90 ± 8.29 (minimum of 65 and maximum of 95). Of the patients with delirium, 70.8% were between 76 and 95 years old, and 32.0% of the patients with no delirium were between 76 and 95 years old ($p$ = 0.007) (Table 2). Of the patients with delirium, 54.2% were male, and 60.0% of the patients with no delirium were male ($p > 0.05$).

**Table 2.** Descriptive characteristics of patients with and without delirium (n=49)

| Characteristics | Delirium (+) | | Delirium (-) | | test value* | p value |
|---|---|---|---|---|---|---|
| | n | % | n | % | | |
| **Age** | | | | | | |
| 65-75 years | 7 | 29.2 | 17 | 68.0 | 7.389 | 0.007 |
| 76-95 years | 17 | 70.8 | 8 | 32.0 | | |
| **Gender** | | | | | | |
| Female | 11 | 45.8 | 10 | 40.0 | 0.170 | 0.680 |
| Male | 13 | 54.2 | 15 | 60.0 | | |

*Pearson Chi-Square

**Table 3.** Physiological variables of patients with and without delirium (n=49)

| Variables | Delirium (+) | | Delirium (-) | | test value* | p value |
|---|---|---|---|---|---|---|
| | n | % | n | % | | |
| **Respiration** | | | | | | |
| Spontaneous | 18 | 75.0 | 23 | 92.0 | 2.590 | 0.138 |
| CPAP | 6 | 25.0 | 2 | 8.0 | | |
| **Insomnia** | | | | | | |
| Yes | 18 | 75.0 | 4 | 16.0 | 17.229 | p<0.01 |
| No | 6 | 25.0 | 21 | 84.0 | | |
| **Agitation** | | | | | | |
| Yes | 16 | 66.7 | 0 | 0.0 | 24.747 | p<0.01 |
| No | 8 | 33.3 | 25 | 100.0 | | |
| **Sedation** | | | | | | |
| No | 7 | 29.2 | 23 | 92.0 | 20.855 | p<0.01 |
| Seroquel | 10 | 41.7 | 2 | 8.0 | | |
| Dexmedetomidine+Seroquel | 2 | 8.3 | 0 | 0.0 | | |
| Dexmedetomidine | 5 | 20.8 | 0 | 0.0 | | |
| | Mean | SD | Mean | SD | test value** | p value |
| **Systolic blood pressure** | 121.79 | 20.45 | 121.12 | 19.30 | 0.118 | 0.906 |
| **Diastolic blood pressure** | 68.00 | 9.15 | 65.40 | 9.78 | 0.959 | 0.342 |
| **Respiratory rate** | 22.45 | 5.23 | 20.48 | 4.57 | 1.410 | 0.165 |
| **Pulse rate** | 93.83 | 18.51 | 84.00 | 10.79 | 1.949 | 0.057 |
| **WBC** | 11.89 | 6.79 | 10.67 | 4.55 | 0.741 | 0.462 |
| **$SpO_2$** | 95.16 | 4.28 | 95.24 | 2.20 | 0.076 | 0.940 |

*Fisher's Exact Test; ** Independent samples test, CPAP: Continuous Positive Airway Pressure, Seroquel: Quetiapine, WBC: White Blood Cell, $SpO_2$: Oxygen Saturation

**Table 4.** Predictors of the delirium in elderly patients with COVID-19

| | B (95% CI for B) | SE | β | t | *p* |
|---|---|---|---|---|---|
| **Day one** (R = 0.896, R2 = 0.803, F= 13.709, p < 0.01) | | | | | |
| SBP | -0.001 (-0.023-0.021) | 0.011 | -0.012 | -0.127 | 0.899 |
| DBP | 0.052 (0.013-0.091) | 0.019 | 0.258 | 2.704 | 0.010 |
| Respiratory rate | -0.077 (-0.160-0.005) | 0.041 | -0.176 | -1.904 | 0.065 |
| Pulse rate | 0.015 (-0.005-0.035) | 0.010 | 0.141 | 1.537 | 0.133 |
| WBC | 0.005 (-0.048-0.058) | 0.026 | 0.015 | 0.190 | 0.851 |
| SpO2 | 0.060 (-0.058-0.178) | 0.058 | 0.104 | 1.030 | 0.310 |
| Insomnia | -0.267 (-1.199-0.665) | 0.460 | -0.051 | -0.580 | 0.565 |
| Agitation | -4.342 (-6.205-2.479) | 0.919 | -0.582 | -4.722 | 0.000 |
| Sedation | 0.552 (-1.278-2.382) | 0.903 | 0.059 | 0.611 | 0.545 |
| CPOT | -0.634 (-1.760-0.492) | 0.556 | -0.121 | -1.141 | 0.261 |
| RSS | 2.433 (1.896-2.969) | 0.265 | 0.869 | 9.188 | 0.000 |
| **Day three** (R = 0.807, R2 = 0.651, F= 6.274, p < 0.01) | | | | | |
| SBP | -0.014 (-0.052-0.023) | 0.019 | -0.096 | -0.770 | 0.446 |
| DBP | 0.044 (-0.019-0.106) | 0.031 | 0.155 | 1.415 | 0.165 |
| Respiratory rate | 0.102 (-0.020-0.225) | 0.060 | 0.208 | 1.692 | 0.099 |
| Pulse rate | -0.017 (-0.050-0.015) | 0.016 | -0.131 | -1.077 | 0.289 |
| WBC | 0.008 (-0.112-0.128) | 0.059 | 0.016 | 0.139 | 0.890 |
| SpO2 | 0.090 (-0.136-0.315) | 0.111 | 0.097 | 0.805 | 0.426 |
| Insomnia | -0.247 (-1.590-1.095) | 0.663 | -0.044 | -0.373 | 0.711 |
| Agitation | -4.304 (-6.605-2.004) | 1.136 | -0.661 | -3.791 | 0.001 |
| Sedation | 0.492 (-0.532-1.515) | 0.505 | 0.166 | 0.974 | 0.337 |
| CPOT | -0.849 (-2.823-1.125) | 0.974 | -0.134 | -0.871 | 0.389 |
| RSS | 1.974 (1.094-2.853) | 0.434 | 0.612 | 4.546 | 0.000 |
| **Day five** (R = 0.757, R2 = 0.573, F= 4.508, p < 0.01) | | | | | |
| SBP | -0.011 (-0.047-0.024) | 0.018 | -0.096 | -0.648 | 0.521 |
| DBP | 0.010 (-0.068-0.088) | 0.038 | 0.033 | 0.262 | 0.795 |
| Respiratory rate | 0.094 (-0.028-0.215) | 0.060 | 0.189 | 1.561 | 0.127 |
| Pulse rate | -0.001 (-0.040-0.037) | 0.019 | -0.008 | -0.057 | 0.955 |
| WBC | 0.011 (-0.153-0.176) | 0.081 | 0.022 | 0.139 | 0.890 |
| SpO2 | 0.038 (-0.240-0.316) | 0.137 | 0.037 | 0.275 | 0.785 |
| Insomnia | -0.841 (-2.569-0.888) | 0.853 | -0.145 | -0.986 | 0.331 |
| Agitation | -3.113 (-6.228-0.003) | 1.538 | -0.513 | -2.024 | 0.050 |
| Sedation | 0.509 (-0.898-1.916) | 0.694 | 0.160 | 0.733 | 0.468 |
| CPOT | -1.190 (-3.794-1.414) | 1.285 | -0.193 | -0.926 | 0.360 |
| RSS | 1.461 (0.409-2.513) | 0.519 | 0.407 | 2.813 | 0.008 |

**Tablo 4.** *devamı*

| | B (95% CI for B) | SE | β | t | *p* |
|---|---|---|---|---|---|
| **Day seven** (R = 0.828, R2 = 0.686, F= 7.332, p < 0.01) | | | | | |
| SBP | 0.008 (-0.025-0.042) | 0.016 | 0.055 | 0.502 | 0.618 |
| DBP | 0.049 (-0.018-0.115) | 0.033 | 0.155 | 1.481 | 0.147 |
| Respiratory rate | 0.044 (-0.093-0.180) | 0.067 | 0.073 | 0.648 | 0.521 |
| Pulse rate | 0.019 (-0.014-0.052) | 0.016 | 0.117 | 1.184 | 0.244 |
| WBC | -0.080 (-0.192-0.032) | 0.055 | -0.153 | -1.439 | 0.159 |
| SpO2 | 0.170 (-0.045-0.386) | 0.106 | 0.191 | 1.603 | 0.118 |
| Insomnia | -1.051 (-2.801-0.699) | 0.864 | -0.177 | -1.217 | 0.231 |
| Agitation | -0.035 (-2.117-2.047) | 1.028 | -0.006 | -0.034 | 0.973 |
| Sedation | 0.766 (-0.177-1.710) | 0.466 | 0.250 | 1.645 | 0.108 |
| CPOT | -3.711 (-5.942-1.481) | 1.101 | -0.599 | -3.371 | 0.002 |
| RSS | 0.824 (0.093-1.555) | 0.361 | 0.267 | 2.284 | 0.028 |

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, WBC: White Blood Cell, SpO2: Oxygen Saturation, CPOT: Critical-Care Pain Observation Tool, RSS: Ramsay Sedation Scale, B: Unstandardized coefficient, SE: Standard Error, β: Standardized coefficient, CI: Confidence Interval

### Physiological variables

The difference between the insomnia and agitation frequencies and the sedative drug use of patients with and without delirium was at the level of statistical significance ($p < 0.01$). The difference between spontaneous breathing, mean systolic and diastolic blood pressures, respiratory and pulse rates, WBC, and $SpO_2$ levels of the patients with and without delirium was similar between groups ($p > 0.05$) (Table 3).

### Predictors of delirium

In the multiple regression model, independent variables (systolic blood pressure, diastolic blood pressure, respiratory rate, pulse rate, WBC, SpO2, insomnia, agitation, sedation, CPOT, and RSS measures) explained approximately 80% of the variance for delirium in elderly inpatients on Day 1 ($p<0.01$). Delirium was predicted by RSS (β=0.869), agitation (β=-0.582), and diastolic blood pressure (β=0.258, Table 4). Independent variables explained approximately 65% of the variance for delirium in elderly inpatients on Day 3 ($p<0.01$). Delirium was predicted by agitation (β=-0.661) and RSS (β=0.612, Table 4). In the evaluation on the third day, delirium was associated with agitation and sedation. Independent variables explained approximately 57% of the variance for delirium in elderly inpatients on Day 5 ($p<0.01$). Delirium was predicted by agitation (β=-0.513) and RSS (β=0.407, Table 4). In the evaluation performed on the fifth day, delirium was associated with agitation and sedation. Independent variables explained approximately 69% of the variance for delirium in elderly inpatients on Day 7 ($p<0.01$). The most important predictors of delirium on the seventh day were CPOT (β=-0.599) and RSS (β=0.267, Table 4). In the last evaluation, delirium was associated with pain and sedation.

### The effects of mortality, frailty index, and hospitalization on delirium

The mortality, frailty index, and hospitalization statistics explained 5% of the variance for delirium in elderly inpatients ($p > 0.05$) (Table 5). The 90-day

**Table 5.** The effects of mortality, frailty index, length of intensive care unit stay, and length of hospitalization statistics on delirium.

| | B (95% CI for B) | SE | β | t | *p* |
|---|---|---|---|---|---|
| **Model 1** (R = 0.543, R2 = 0.295, F= 11.727, p = 0.002) | | | | | |
| Frailty index | 0.987 (0.396-1.577) | 0.288 | 0.543 | 3.425 | 0.002 |
| **Model 2** (R = 0.221, R2 = 0.049, F= 2.404, p = 0.128) | | | | | |
| 90-day mortality | -1.335 (-3.067-0.397) | 0.861 | -0.221 | -1.550 | 0.128 |
| **Model 3** (R = 0.221, R2 = 0.049, F= 2.404, p = 0.128) | | | | | |
| Frailty index | 0.988 (-0.358-1.618) | 0.307 | 0.544 | 3.223 | 0.003 |
| Length of intensive care unit stay | 0.038 (-0.117-0.194) | 0.076 | 0.295 | 0.509 | 0.615 |
| Length of hospitalization | -0.035 (-0.182-0.113) | 0.072 | -0.280 | -0.480 | 0.635 |

B: Unstandardized coefficient, SE: Standard Error, β: Standardized coefficient, CI: Confidence Interval

mortality, length of intensive care unit stay, and length of hospitalization were not associated with delirium ($p > 0.05$). But the frailty index was the most important predictor of delirium and it explained approximately 30% of the variance for delirium in elderly inpatients with COVID-19 ($p = 0.002$).

## DISCUSSION

This study aimed to evaluate the risk of delirium in elderly inpatients in COVID-19 intensive care units. We demonstrated that the risk of delirium increased from Days 1 to 7 in elderly patients with COVID-19. Early risk factors for delirium in elderly patients with COVID-19 were sedation, agitation, and diastolic blood pressure. Late risk factors of delirium were sedation, agitation, and pain.

In this study, one of the early and late risk factors of delirium was sedation. In a study of COVID-19 patients, 86.4% of those with delirium had evidence of excessive sedation. In addition, the use of high doses of sedation was associated with the frequency of delirium in these patients, increased deaths in intensive care, and prolonged length of stay in intensive care (15). Another study on COVID-19 patients found a relationship between the proportion of days with delirium symptoms and the level of sedation (16). The use of sedative drugs, particularly sedative-hypnotics and anticholinergic agents, has been associated with the development of delirium in intensive care unit patients (17). Delirium in intensive care patients may be related to sedative use. Sedative-induced delirium is associated with high mortality and prolonged hospitalization (18). In our study, an increase in delirium level may have increased the use of sedatives and, therefore, the level of sedation.

Agitation was one of the most important predictors of early and late delirium in the present study. During COVID-19 infection, delirium and psychomotor agitation were associated conditions that occurred in intensive care patients (19). The hyperactive type of delirium was most common in patients with COVID-19. It causes agitation, which is difficult to control and increases with age. Patients with COVID-19 were more agitated than patients with influenza (20). Our study sample consisted of elderly patients with COVID-19. Agitation is an important predictor of delirium in elderly patients with COVID-19. Therefore, agitation in elderly needs to be well evaluated and managed to prevent delirium in intensive care units.

Another important risk factor for early delirium in this study was diastolic blood pressure. Most

studies of elderly patients with COVID-19 had not found blood pressure to be a risk factor (8–9, 21). The blood pressure values in elderly COVID-19 patients with and without delirium did not differ (8). The incidence of hypertension in adult COVID-19 patients with and without cognitive impairment did not differ (9). Further studies should be conducted to evaluate the effects of systolic and blood pressure in elderly patients with COVID-19. In this study, diastolic blood pressure in the early period was an important risk factor for delirium. In future studies, whether patients are using drugs for blood pressure should also be evaluated.

In this study, the pain was one of the most important predictors of last delirium in elderly patients with COVID-19. The high incidence of delirium in COVID-19 patients was associated with some factors, such as fear, anxiety, insomnia, and pain. Most patients in intensive care units experience pain during treatment and care interventions such as respiratory interventions, invasive strategies, nursing interventions, and trauma (22). One symptom of the novel coronavirus (SARS-CoV-2) is pain. After exposure to SARS-CoV-2, patients with COVID-19 experienced varying degrees of headache, muscle and/or joint pain, sore throat, chest pain, and abdominal pain. The virus affects the nervous system, digestive system, and cardiovascular system due to infection (19). This study also showed that pain is a significant risk factor for elderly COVID-19 patients. Therefore, pain assessment and management should be performed correctly in these patients to reduce or eliminate the risk of delirium.

The frailty index was one of the most important predictors of last delirium in elderly patients with COVID-19. The 90-day mortality, length of intensive care unit stays, and length of hospitalization were not associated with delirium. In one study, delirium was associated with frailty index, length of hospital stay, and 30-day mortality (23). In another study, the frailty index and clinical frailty scale were able to predict an acute delirium episode in patients in intensive care (24). In another study, it was reported that elderly patients with a high frailty index had a high risk of delirium, long hospital stays, and high hospital mortality (25). Therefore, frailty index is important in terms of delirium in elderly patients with COVID-19 in intensive care.

### Limitations

This study has some limitations. In the context of risk factors affecting delirium, the scope of the questionnaire can be expanded, and different scales can be used in future studies. The study was conducted in a single center. Therefore, the results of the study cannot be generalized to all elderly patients with COVID-19. Conducting similar and subsequent meta-analysis studies may contribute to forming an opinion on this subject.

## CONCLUSION

We suggested that the longer a patient stays in the intensive care unit, the higher the risk of developing delirium regarding COVID-19 patients hospitalized in ICU. The patient's pain, sedation, insomnia, and agitation levels were found to be important risk factors for delirium. Agitation and diastolic blood pressure were the most important predictors of early delirium. The incidence of delirium increases with age.

Delirium is a significant health concern for elderly patients with COVID-19, increasing the length of hospital stay and mortality. To reduce the risk of delirium in elderly patients, it is necessary to identify and eliminate risk factors. Nurses who provide uninterrupted care to patients have a great responsibility. Nurses should take active responsibility in identifying and managing the pain of elderly patients with COVID-19, assessing sedation levels and physiological parameters, such as diastolic blood pressure, agitation, pain, and insomnia, planning appropriate nursing

interventions, and providing medical treatment. Additionally, frailty indexes of elderly patients in intensive care should be evaluated and studies should be conducted to reduce the fragility of patients.

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ORIGINAL ARTICLE

# THE ROLE OF ENDOSCOPY-INDEPENDENT GASTROINTESTINAL BLEEDING SCORES IN PREDICTING 30-DAY MORTALITY IN AGED OVER 65

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## Abstract

**Introduction:** The aim of this study was to assess the power of clinical findings and scoring systems to predict mortality in patients over 65 years of age with non-variceal upper gastrointestinal bleeding.

**Materials and Method:** Data on demographic profiles and risk estimation scores were retrospectively extracted from electronic hospital medical records and other electronic databases using a standard data extraction form. The AIMS65, pre-Rockall, modified Glasgow-Blatchford, T, and Baylor bleeding scores were calculated to estimate the 30-day mortality risk. The inclusion criteria were patients aged 65 and over who presented with active bleeding symptoms and had been diagnosed with acute upper gastrointestinal bleeding by the gastroenterology department.

**Results:** The mean age was 75.23 years, and 23.6% of the patients died within 30 days. The 30-day mortality was associated with albumin levels, malignancy, and intensive care unit hospitalization. An inverse relationship was found between the albumin level and mortality, whereas the presence of cancer and the need for intensive care were associated with 2.8-fold and 2.2-fold increases in the risk of death, respectively. The AIMS65 score (AUC: 0.794) had the highest discriminative ability to predict 30-day mortality among all risk scores.

**Conclusion:** Albumin levels, malignancy presence, and ICU admission were indicators of mortality risk in elderly patients with upper gastrointestinal bleeding. Calculating all the scores, excluding the Baylor Bleeding score, is beneficial for assessing the risk of mortality associated with upper gastrointestinal bleeding. The AIMS65 score demonstrates the highest discriminative ability. However, using these risk-scoring systems necessitates additional data.

***Keywords:*** Gastrointestinal Hemorrhage; Mortality; Aged.

## INTRODUCTION

Upper gastrointestinal bleeding (UGIB) is associated with a broad clinical spectrum of symptoms ranging from occult bleeding leading to iron deficiency anemia to shock and death. It constitutes a significant cause of hospital admission (1), with an incidence ranging from 48 to 160 cases per 100,000 adults per year and mortality rates ranging from 2% to 8%. (2,3). UGIB can arise from various lesions of varying prognostic importance in the esophagus, stomach, or duodenum. Peptic ulcer diseases are the leading causes of acute UGIB, accounting for approximately 50–60% of global admissions (4,5).

Recent guidelines have recommended the use of risk scores in patients with upper gastrointestinal bleeding. However, uncertainty remains regarding their precise application and significance in clinical practice (6-9). Commonly used endoscopy-independent scoring systems include the Rockall pre-endoscopy score (pRS), modified Glasgow-Blatchford score (mGBS), T score, Baylor bleeding score (pre-endoscopy), and AIMS65 score (7,8). Elderly UGIB patients represent a unique subgroup requiring careful management due to often significant comorbidities, higher medication usage, and an increased risk of complications. With the growing elderly population and the rising incidence of gastrointestinal bleeding among them, understanding the prognosis and management of UGIB in older adults has become paramount.

Several studies have associated increasing age with adverse clinical outcomes in patients with UGIB (10,11). For example, a retrospective study in China emphasized that mortality is higher in elderly patients with UGIB than in younger individuals, thereby highlighting the need for closer monitoring of the elderly (8). For this reason, investigating the effectiveness of risk assessment scores in predicting outcomes in elderly patients has become crucial for making informed decisions and implementing optimized care strategies. The aim of the present retrospective study was to assess the effectiveness of five pre-endoscopic risk assessment scores for predicting 30-day mortality in patients over 65 years of age with non-variceal UGIB.

## MATERIALS AND METHOD

### Setting and Design

In this retrospective study, we evaluated patients aged 65 and older who were admitted to a university hospital presenting with active bleeding symptoms between January 1, 2012, and December 31, 2021. These patients were diagnosed with acute UGIB by the gastroenterology department. Data pertinent to their demographic profiles and risk prediction scores were extracted from the hospital's electronic medical records and relevant electronic databases by the department's faculty members utilizing a standardized data extraction form.

Comorbidities were categorized into diabetes mellitus, hypertension, chronic heart disease, chronic liver disease, chronic kidney disease, chronic neurological diseases, and malignancy. Mortality was defined as death within 30 days following the first bleeding. These data were utilized to calculate the AIMS65 system, pRS, mGBS, T, and Baylor bleeding scores for each patient, and these scores were then used to predict the 30-day mortality risk.

### Selection of Participants

Patients who underwent emergency upper gastrointestinal endoscopy based on the primary diagnosis of International Classification of Diseases (ICD) codes K92.0 Haematemesis, K92.1 Melena, and K92.2 Gastrointestinal Haemorrhage and who showed evidence of active bleeding were retrospectively analyzed. A patient presenting with new-onset UGIB was considered hemorrhagic, and bleeding was confirmed by endoscopy. Only patients with overt endoscopic stigmas of UGIB were included in the study. Exclusion criteria included age below 65 years, post-endoscopic retrograde cholangiopancreatography (ERCP), and

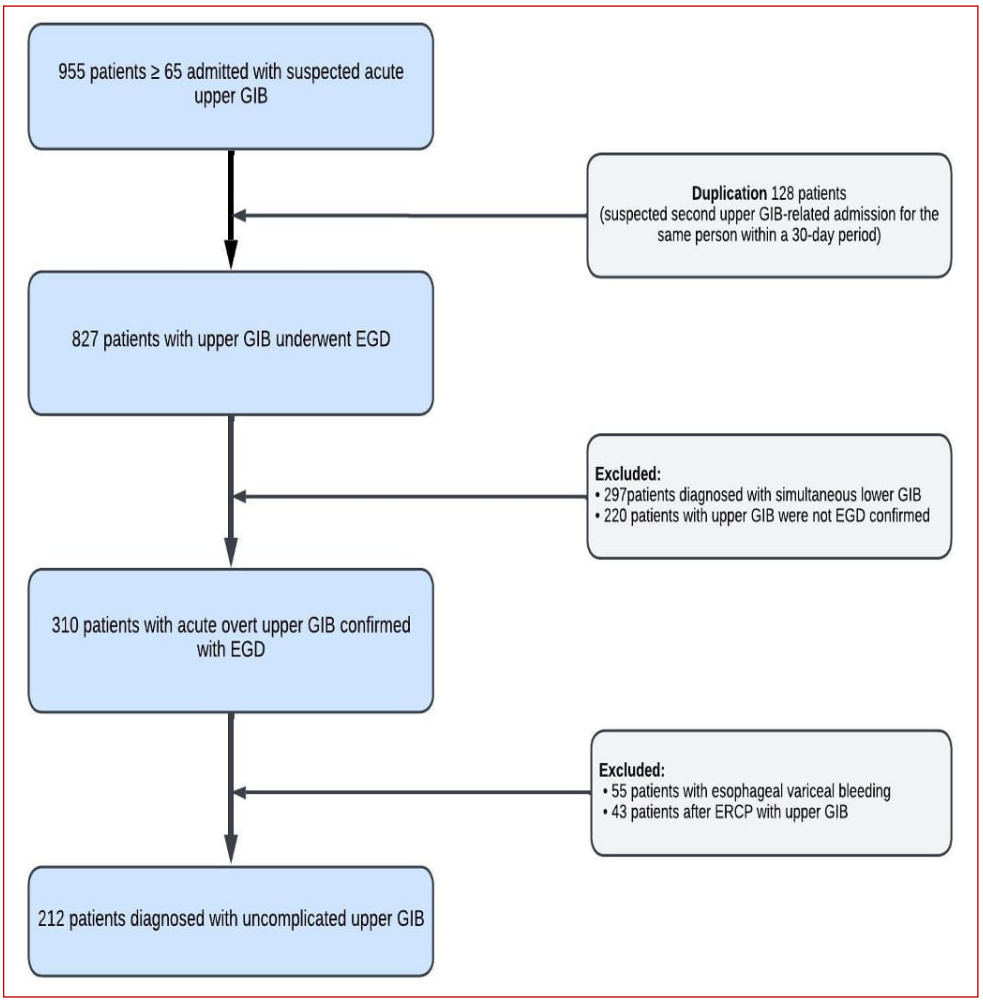


**Figure 1.** Flowchart of patient selection.

GIB: Gastrointestinal Bleeding, EGD: Esophagogastroduodenoscopy, ERCP: Endoscopic Retrograde Cholangiopancreatography

esophageal variceal bleeding. After applying these exclusion criteria, 212 patients were included in the study (Figure 1).

### Clinical Scores

This study employed five pre-endoscopic UGIB scoring systems: the mGBS, AIMS65 score, T-score, Baylor bleeding score, and pRS score. The mGBS consists of five parameters: pulse, systolic blood pressure (SBP), blood urea nitrogen (BUN), and hemoglobin (Hb) (7). The AIMS65 score is a composite of five variables: age over 65 years, systolic blood pressure lower than 90 mmHg, altered level of consciousness, serum albumin lower than 3 g/dL, and international normalized ratio (INR) higher than 1.5. Patients can be assigned 1 point for each criterion (11). The T-score encompasses the following variables: the patient's general appearance, number of comorbid diseases, pulse

rate, systolic blood pressure, and hemoglobin level. Unlike other scoring systems, the T-score is associated with a decreasing mortality risk as the score increases (12). The Baylor Bleeding Score, developed by Saeed et al. in 1993, consists of age, acute and chronic illness (13). The pRS estimates the risk of rebleeding and mortality in patients with UGIB using data on age, vital signs (heart rate and systolic blood pressure), and comorbidities (14).

### Data Collection

A thorough analysis was conducted based on the patients' anamnesis, curriculum vitae, and laboratory and imaging results. We recorded demographic data, hemodynamic parameters at admission, and biochemical parameters, such as leukocyte count, hemoglobin, hematocrit value, albumin, creatinine, blood urea nitrogen, international normalized ratio (INR), and comorbidities. Other parameters examined included recurrent bleeding, intensive care unit stay, and 30-day mortality. Pre-endoscopic UGIB assessment scores were calculated using this information.

### Statistical Analysis

Statistical analysis was performed using SPSS version 15.0. To determine whether the data distribution was normal, skewness and kurtosis values were analyzed, and values between -2 and +2 were accepted as indicating a normal distribution. Statistical comparisons of continuous variables were performed using either parametric or nonparametric tests. Logistic regression models were used to describe the effects of characteristic variables on mortality.

MedCalc Version 12.0 (free trial version, access date 16.02.2024) was used to construct receiver-operating curves (ROCs) to assess the prognostic value of each scoring system, and the area under the curve (AUC) for each of the five scoring systems was calculated for mortality. The Delong test was used to compare different AUCs among the five scoring systems. The AUC is widely used to measure the accuracy of diagnostic tests. For a diagnostic test to be meaningful, the AUC must be greater than 0.5. Generally, an AUC ≥ 0.8 is considered acceptable (15). The statistical significance level was accepted as $p<0.05$.

### Ethical Considerations

Approval for the study was obtained from the local university ethics committee. The study was conducted according to the principles of the Declaration of Helsinki (Ethics Committee No: 23.02.2022/1193). Informed consent was not obtained from the patients, as the study was conducted through a file review. However, additional permission was obtained from the university hospital administration to use the data after the ethics committee approved it. Any involvement of the patients or the public in our research study's design, conduct, reporting, or dissemination plans was deemed inappropriate or impossible.

## RESULTS

The study sample consisted of 212 patients aged 65 and over. The mean age was 75.23 years (min. 65; max. 92). Of the 212 patients, 53.8% had hypertension, 28.9% had chronic heart disease, and 20.7% had malignancy. A total of 50 patients (23.6%) died within 30 days of diagnosis. The mean survival time of the mortality group was 13.4 days. Of the 212 patients, 143 (67.5%) were followed up in the gastroenterology service, and 69 (32.5%) were admitted to the intensive care unit.

Table 1 shows the comparison of baseline characteristics and patient status at the end of the 30-day follow-up period. In comparing comorbidities and laboratory findings with 30-day mortality, the presence of malignancy was significantly greater in the non-survival group than

**Table 1.** The characteristics of the 212 study participants

| Variabiles | Survivors (n=162) | Nonsurvivors (n=50) | p |
|---|---|---|---|
| **Demographic data** | | | |
| Age[β] | 74.8±7.4 | 76.2±8.6 | 0.39 |
| Women/Men[β] | 57/105 | 20/30 | 0.53 |
| **Previous Medical History** | | | |
| Diabetes mellitus[β] | 45 (%27.8) | 12 (%24.0) | 0.59 |
| Hypertension[β] | 75 (%46.3) | 23 (%46.0) | 0.97 |
| Chronic heart disease[β] | 51 (%31.5) | 9 (%18.0) | 0.064 |
| Chronic neurological disease[¥] | 15 (%9.3) | 6 (%12.0) | 0.591 |
| Chronic renal failure[¥] | 10 (%6.2) | 6 (%12.0) | 0.218 |
| Chronic liver failure[¥] | 8 (%4.9) | 4 (%8.0) | 0.483 |
| Malignancy[β] | 26 (%16.0) | 18 (%36.0) | **0.002** |
| **Hemodinamic parameters at presentation** | | | |
| Systolic blood pressure[β] (mm/Hg) | 118.51±21.3 | 113.42±20.4 | 0.14 |
| Diastolic blood pressure[β] (mm/Hg) | 71.06±12.3 | 67.68±13.9 | 0.1 |
| Heart rate[β] (beats/min) | 88.17±16.1 | 95.32±20.4 | 0.11 |
| **Labaratory results** | | | |
| White blood cell[¥] (x103 /µL) | 9.85±4.4 | 12.4±6.1 | 0.07 |
| Hemoglobine[β] (g/dL) | 9.5±2.2 | 8.7±1.7 | **0.021** |
| Hct[β] (%) | 31.4±6.2 | 29.8±6.1 | 0.10 |
| Albumin[β] | 3.19±0.72 | 2.5±0.64 | <0.001 |
| BUN[¥] (mg/dL) | 31.7±24.6 | 50.9±33.9 | <0.001 |
| Urea[¥] (mg/dL) | 65.64±50.3 | 103.66±73.13 | **0.01** |
| Creatinine[¥] (mg/dL) | 1.07±0.7 | 1.6±1.1 | **0.03** |
| INR[¥] | 1.29±0.6 | 2.11±2.35 | 0.18 |
| **Secondary Outcomes** | | | |
| ICU admisson[β] | 44 (%27.2) | 25 (%50.0) | **0.03** |

Hct: Hematocrit, INR: International Normalised Ratio, ICU: Intensive Care Unite, BUN: Blood Urea Nitrogene
[β] Student's T test, [¥] Mann-Whitney U test analysis was used.

in the survival group (p=0.002). The hemoglobin and albumin levels were lower (p=0.021, p<0.001, respectively), while the BUN, urea, and creatinine values were higher (p<0.001, p=0.01, and p=0.03, respectively), in the non-survival group than in the survival group. In total, 50% of the non-surviving patient cohort underwent treatment in the intensive care unit (p=0.03) (Table 1).

Logistic regression analysis of the variables of albumin, presence of neoplasm, and intensive care hospitalization resulted in a value of $R^2$=0.299 for mortality. A low albumin level was identified as a significant mortality risk factor (p < 0.001). The presence of malignancy (2.8-fold) and the necessity for intensive care (2.2-fold) were also linked to an elevated risk of mortality (Table 2).

**Table 2.** Univariate and multivariate analysis of predictors of 30 day mortality in studied patients

| | Univariate | | Multivariate | |
|---|---|---|---|---|
| | Adjusted OR (95 %CI) | p | Adjusted OR (95 %CI) | p |
| **Age** | 1.026 (0.985-1.069) | 0.212 | 1.027 (0.979-1.078) | 0.275 |
| **Malignancy** (1 = Those with malignancy) | 2.942 (1.441-6.007) | 0.003 | 2.837 (1.266-6.359) | **0.011** |
| **Hemoglobine** (For every 1 unit increase) | 0.833 (0.712-0.975) | 0.023 | 0.903 (0.746-1.093) | 0.295 |
| **Albumin** (For every 1 unit increase) | 0.253 (0.146-0.436) | 0.000 | 0.297 (0.166-0.533) | **<0.001** |
| **BUN** | 1.022 (1.010-1.033) | 0.000 | 1.004 (0.990-1.018) | 0.582 |
| **Creatinin** | 1.926 (1.303-2.846) | 0.001 | 1.453 (0.977-2.160) | 0.065 |
| **ICU** (1 = with an inpatient stay) | 2.682 (1.395-5.156) | 0.003 | 2.212 (1.056-4.634) | **0.035** |

OR:Odd ratio, CI: Confidence interval, BUN: Blood urea nitrogen ICU: Intensive care unit.

* Backward LR analysis was used. *Nagelkerke R square value was 0.299.

**Tablo 3.** The ability of risk scoring systems to predict 30-day mortality.

| Risk Scoring Systems | Cut off | AUC (%95 CI) | Sensitivity (%) | Specifity (%) | p |
|---|---|---|---|---|---|
| **AIMS65** | ≤1 | 0,794 (0,733-0,846) | 52,47 | 94.00 | **<0,001** |
| **pRS** | ≤3 | 0,713 (0,647- 0,773) | 54,32 | 82,00 | **<0,001** |
| **mGBS** | ≤8 | 0,705 (0,638-0,765) | 60,49 | 72,00 | **<0,001** |
| **T-Score** | >8 | 0,682 (0,615-0,745) | 72,84 | 56,00 | **<0,001** |
| **Baylor Bleeding Score** | ≤10 | 0,584 (0,515-0,651) | 66,67 | 54,00 | 0,055 |

*MedCalc analysis was used

**Table 4.** Comparison of AIMS65, pRS, mGBS, T-score, and Baylor bleeding score's ability to predict mortality.

| | AUC (%95 CI) | AIMS65 p (%95 CI) | pRS p (%95 CI) | mGBS p (%95 CI) | T-Score p (%95 CI) | Baylor Beeding Score p (%95 CI) |
|---|---|---|---|---|---|---|
| **AIMS65** | 0,794 (0,733-0,846) | - | 0,073 (0,007-0,170) | **0,025** (0,010-0,168) | **0,004** (0,034-0,189) | **<0,001** (0,106-0,314) |
| **pRS** | 0,713 (0,647- 0,773) | 0,073 (0,007-0,170) | - | 0,874 (-0,094-0,111) | 0,540 (-0,066-0,128) | **0,014** (0,025-0,233) |
| **mGBS** | 0,705 (0,638-0,765) | **0,025** (0,0108-0,168) | 0,874 (-0,094-0,111) | - | 0,505 (-0,043-0,087) | **0,039** (0,005- 0,235) |
| **T-score** | 0,682 (0,615-0,745) | **0,004** (0,034-0,189) | 0,540 (-0,066-0,128) | 0,505 (-0,043-0,087) | - | 0,119 (-0,025-0,222) |
| **Baylor Bleeding Score** | 0,584 (0,515-0,651) | **<0,001** (0,106-0,314) | **0,014** (0,025-0,233) | **0,039** (0,005-0,235) | 0,119 (-0,025-0,222) | - |

*MedCalc analysis was used

The ability of the different scoring systems to predict mortality based on cut-off values is depicted in Table 3. The sensitivity and specificity of the scores, except for the Baylor bleeding score, showed statistical significance. The highest specificity for mortality prediction was observed with the AIMS65 score (94%), while the most heightened sensitivity was found with the T-score (72.84%).

Table 4 compares the areas under the curve of all five scoring systems for predicting 30-day mortality. The AIMS65 score (AUC: 0.794, 95% CI: 0.733–0.846) had the highest discriminative ability at predicting 30-day mortality among all risk scores. Compared to the other four scoring systems, the AIMS65 score was significantly superior to the mGBS, T-score, and Baylor Bleeding score evaluations for predicting mortality. The pRS (AUC: 0.713, 95% CI: 0.647-0.773) had the second highest discriminatory ability; however, it showed significant superiority only over the Baylor's Bleeding score (p=0.014). No significant difference was detected between the mGBS score and the other scores, except for the Baylor bleeding score, in terms of the AUCs (p=0.039) (Table 4).

## DISCUSSION

Our findings indicated that three parameters; malignancy, albumin levels, and admission to the intensive care unit, were associated with mortality in patients with UGIB. The AUROC analysis indicated that AIMS65 exhibited the highest discriminative ability among other scoring systems in predicting 30-day mortality.

A previous multinational multicenter study, which included 2868 patients with UGIB (aged 24 to 90 years), determined a malignancy rate of 14% and a mortality rate of 7% (16). In a study conducted in China, stratification of patients with UGIB into a younger age group and an elderly age group (mean age 72.9 years) revealed a malignancy rate of 8.7% and a 30-day mortality rate of 8.3% in the elderly group (8). A similar study conducted in patients aged over 80 years with UGIB reported a malignancy rate of 7.7% and a 30-day mortality rate of 16% (17). The elevated mortality rate observed in our study could therefore be attributed to the inclusion of patients aged 65 and above, coupled with the high prevalence of malignancy (20.7%) in our patients.

Some studies have demonstrated a higher mortality rate in patients with hypoalbuminemia than with normal albumin levels (18,19). For example, a retrospective study observed lower mean albumin levels in their non-surviving group of patients with UGIB than in the surviving group (20). Another study conducted in patients over 80 years of age with non-variceal UGIB also revealed a correlation between lower albumin levels and higher 30-day mortality rates (17). In the present study, we also identified an association between low levels of albumin and an increased risk of mortality. Therefore, we believe that the albumin level could be a crucial factor in identifying high-risk patients in clinical practice.

In the present study, the AIMS65 score was the best-performing scoring system for predicting mortality (AUC: 0.794), as it exhibited superior performance compared to other scoring systems, except for the pRS score. A previous retrospective study also confirmed the reliable predictive capability of the AIMS65 score for determining in-hospital mortality, as well as superior performance compared to the GBS (9). In this study, the AIMS65 score also demonstrated higher specificity than the other evaluated scoring systems, whereas the T-score exhibited greater sensitivity. A previous systematic review comprising 16 studies concluded that higher sensitivity and specificity for predicting 30-day mortality were achieved with the GBS score than with either the pRS score or the AIMS65 score (21).

A previous international multicenter study of patients ranging in age between 24 and 90 years found that mortality prediction was better with the AIMS65 score (AUROC 0.77) than with either the GBS or the pRS score (16). In a study conducted in

Turkey, the AIMS65 score (AUC: 0.877) was found to be superior to the GBS score (AUC: 0.695) in predicting 30-day mortality in their study group aged over 80 years (17). Another prospective multicenter study conducted in China reported a 90-day mortality rate of 10.9% in patients with a mean age of 61 and concluded that the pRS system was superior to the GBS and AIMS65 scores for predicting mortality (22).

While no clear consensus exists across the existing studies, the AIMS65 scores appear to effectively determine the risk of in-hospital and 30-day mortality. Based on our findings, we conclude that the AIMS65 score may be helpful in predicting mortality in patients aged 65 and older. Altered mental status, which is a component of the AIMS65 score, is frequently observed in elderly UGIB patients. The age of our study cohort, at 65 years and above, therefore inherently fulfilled another criterion of the AIMS65 score. All of these factors may explain the superior performance of the AIMS65 score in predicting mortality in this elderly cohort.

### Strengths and Limitations

The present study included patients with UGIB diagnoses confirmed by endoscopy to evaluate the effectiveness of endoscopy-independent risk scores in predicting mortality. This assessment of the efficacy of using endoscopy-independent risk scores in patients with an endoscopy-confirmed diagnosis is a notable strength of this study. Thus, an attempt was made to reveal the discriminative capabilities of different risk scores for the evaluation of patients with UIGB in institutions where endoscopy is impossible. However, the study's limitations must also be acknowledged. This was a single-center, retrospective study; thus, the results may not be generalizable to all patient populations. Therefore, multicenter studies should be conducted using larger samples to enable generalization of the results found in this study for this age group. This would overcome the potential limitations in terms of external validity, thereby providing results with greater transparency.

## CONCLUSION

Our study findings suggest that serum albumin levels, the presence of malignancy, and admission to the ICU are significant factors associated with mortality in patients aged 65 and over with UGIB. These parameters should be considered when triaging elderly patients for close observation and early intervention. The calculations performed for all the scores, but excluding the Baylor Bleeding score, were beneficial in assessing the risk of mortality associated with UGIB. The high discriminative ability of the AIMS65 score suggests its potential utility in older patients with UGIB. Nevertheless, these risk-scoring systems require further data and optimization in future endeavors, particularly when considering elderly patients.

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ORIGINAL ARTICLE

# WHAT AWAITS US AFTER COVID-19? MUSCULOSKELETAL SYSTEM INVOLVEMENT IN THE ELDERLY POPULATION IN TÜRKİYE AND ITS AFTERMATH

## Abstract

**Introduction:** Although COVID-19 primarily affects the respiratory system, one of the most frequently effected areas is the musculoskeletal system. COVID-19 associated musculoskeletal problems can cause disability in patients ≥65 years. The aim of the study was to define the musculoskeletal problems after the COVID-19 infection and to examine the relationship with the accompanying comorbidities in geriatric population.

**Materials and Method:** The study was conducted by the members of Geriatric Rehabilitation Study Group of Turkish Physical Medicine and Rehabilitation Society at 11 different hospitals from 7 provinces (Ankara, İstanbul, İzmir, Gaziantep, Adana, Bursa, and Kırıkkale) of Türkiye. Individuals aged 65 years and over who had a history of COVID-19 within the last 12 months and experienced persistent/continuous musculoskeletal complaints were included into the study. COVID-19 diagnoses were confirmed from electronic hospital records and the e-Nabız system. Data were collected by face-to-face interviews and after recruiting the first 50 patients from each center, patient recruitment was terminated.

**Results:** A total of 457 cases in which all questions were answered completely (without any missing data) were included in this observational study. The cases were mainly 65-75 years old, married, and non-smoking women. The most common musculoskeletal involvement was widespread pain (81%), followed by myalgia (63.7%) and arthralgia (44.4%). Other rare involvements (osteonecrosis, myositis, steroid myopathy, arthritis) were significantly more frequent in patients older than 75 years, regardless of gender. Analysis showed that musculoskeletal pain immediately after infection is observed more in cases with comorbid diseases ($p<0.001$), hypertension ($p<0.001$), pulmonary involvement ($p=0.002$) and hospitalization due to COVID-19 ($p<0.001$). It was determined that the incidence of pain seen immediately after infection increased as the number of comorbidities increased ($p<0.001$). In conjunction with this, persistent pain after COVID-19 infection were more common in those with osteoarthritis ($p=0.039$).

**Conclusion:** Elderly patients may develop musculoskeletal pain in multiple body sites after COVID-19, which is primarily related to presence and number of comorbidities, hospitalization and pulmonary involvement. The long-term consequences of COVID-19 on musculoskeletal health are still being studied, and further research is needed to fully understand the extent and duration of these effects.

***Keywords:*** Aged; COVID-19; Arthralgia; Musculoskeletal Pain.

## INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronovirus (SARS CoV-2), primarily targeting the pulmonary system. However, it can also affect the musculoskeletal, cardiovascular, gastrointestinal, and neurological systems. Post-infection period poses challenges for both patients and physicians, with ongoing issues that require management even after one year. These include musculoskeletal (myalgia, arthralgia, etc.), pulmonary (e.g., dyspnea), and cardiovascular (hypertension, arrhythmia, etc.) complications. Therefore, a comprehensive rehabilitation program is crucial for patients to achieve a healthy well-being (1). Concerning the musculoskeletal system, the first step is to be aware of symptomatology during the post-COVID period (2).

Musculoskeletal system involvement in older adults can manifest in muscles (myalgia, muscle weakness, myosis, rhabdomyolysis, necrotizing autoimmune myonecrosis, myopathy, sarcopenia), joints (arthralgia, virus-induced arthritis, inflammatory arthritis), nerves (peripheral neuropathy, Guillain-Barré Syndrome and its variants - Miller Fisher's syndrome, critical illness polyneuropathy), and/or bones (osteoporosis, osteonecrosis) (3). Additionally, pre-existing neuromuscular, muscular, and/or autoimmune conditions can contribute to disability in older adults (4).

The COVID-19 pandemic has been on the world's agenda for nearly four years, causing millions of infections, hospitalizations, weanings, and disabilities. In Türkiye, as of November 2022, 17.042.722 people have been infected, and 101.492 people have died. Unfortunately, no published data is available since then (5). A study by Ek et al., analyzing global data, revealed that deaths due to COVID-19 in individuals over 60 years of age were 35.93% in countries with characteristics similar to Türkiye (6). It can be estimated that the infected elderly population in Türkiye is approximately 6 million people. Considering a mortality rate of 1%, an estimated 60,000 people have died, and the remaining have experienced various degrees of post-COVID symptoms.

Knowledge regarding COVID-19-associated musculoskeletal system involvement in the geriatric population is limited. The present study aims to define musculoskeletal problems related to COVID-19 in patients aged 65 years and older, as well as to identify confounders of musculoskeletal issues. Data obtained from the study may increase awareness on this matter and pave the way for better management of COVID-19-associated musculoskeletal system problems in older adults.

## MATERIALS AND METHOD

### Study design and settings

This multi-center cross sectional study was conducted by the Geriatric Rehabilitation Study Group of the Turkish Physical Medicine and Rehabilitation (PMR) Society. An invitation letter was sent to all members of the Study Group and PMR departments of eleven hospitals from seven provinces of Türkiye (Ankara, Istanbul, Izmir, Gaziantep, Adana, Bursa, and Kırıkkale) have informed that they want to participate in the study. Afterwards the study protocol was approved by the Clinical Research Ethics Committee of the Hacettepe University Medical Faculty (Date: 19.04.2022, No: 16969557750).

A comprehensive patient registration form has been created and a consortium was formed to produce the final version of the questionnaire by all centers. Patients who applied to the PMR clinics (after having COVID-19) were evaluated in the scope of the study and recruited by the sequential method. Only older adults who had the history of COVID-19 and meeting the following criteria were included in the study: a-Aged 65 years or older, b-Diagnosed with COVID-19 within

the last 12 months, c-Individuals with persistent/continuous musculoskeletal complaints, and d-Those who agreed to participate in the study. COVID-19 diagnoses were confirmed by electronic hospital records and the e-Nabız system and all the interviews were conducted in the hospital. A written informed consent was obtained from each patient. All data were collected face-to-face and deposited using a web-based method. Patient recruitment was terminated at each center after reaching 50 patients meeting the acceptance criteria.

Musculoskeletal complaints were differentiated and listed, including widespread pain, arthralgia, arthritis, myalgia, myositis, myopathy, neuropathy, osteonecrosis, and falls.

Pain was divided into different categories such as pre existing pain, immediate pain after infection (lasting around seven days), pain lasting from 1-3 weeks, 4-8 weeks, 8 weeks to 3 months, 3-6 months, 6-9 months, 9-12 months, and persistent pain (lasting more than three months) after infection. The analysis of pain was based on its presence, duration, and location.

### Assessment procedure

Survey questions were asked face-to-face by the specialists at the PMR clinics. Completed questionnaires were transferred to electronic media. A total of 550 patients from 11 centers were collected within the scope of the study, and 457 patients in which all questions were answered completely (without any missing data) were included and analyzed.

### Statistical analysis

The data were entered into and analyzed by the SPSS software version 28.0.1.1 (IBM Corp., Armonk, NY, USA). All categorical variables were given as number and percentage values. Chi-squared test was used to compare categorical variables. Significance level was set at $p<0.05$.

## RESULTS

A total of 457 patients from 11 centers were included in this observational study. Majority of the cases were female, aged 65-75 years, vaccinated, married, primary school graduates, and had at least one chronic disease. They were non-smokers and living with their families/spouses. The demographic characteristics of the cases are given in Table 1.

Among the cases included in the study, 91 (19.9%) of them were hospitalized during the COVID-19 course. Of the hospitalized patients, 77% were admitted for pulmonary problems, 60% (52) had a hospitalization duration of less than 2 weeks, and 12 (10.2%) patients were hospitalized for more than 4 weeks. It is noteworthy that 174 (38.1%) patients did not take medication at the time of infection, and fifty-four patients (11.8%) took medication without a prescription. The COVID-19 related data of signs and symptoms and medication satatus are presented in Table 2.

Overall 94.1% of the patients had comorbidities and the most common comorbidity was hypertension (73.1%), followed by osteoarthritis (32.6%), diabetes mellitus (27.8%), and coronary artery disease (24.5%) (Table 3). Four hundred and thirty-eight (96.7%) patients were taking medication for these diseases. Of 162 (35.44%) patients taking medications, 47 (10.2%) taking more than 5 medications per day had polypharmacy (Table 2).

Pain was present in 370 (81%) of the cases included in the study. In 95 (25.67%) of these cases, pain lasted longer than six months. The most common sites of pain were the spine (48.9%) including the lumbar and thoracic regions and the lower extremities including the hip and knee. In 261 (80.6%) of the patients with pain, pain was present prior to COVID-19 and increased in terms of value. Arthralgia was present in 203 (44.4%) cases and was most common in the knee (60.6%) and hip (40.9%). Post COVID pain and its characteristics are shown in Table 4. Post-infection 123 cases (26.9%)

**Table 1.** The demographic data of the patients (n=457)

| Data | | Number (n) | Percentage (%) |
|---|---|---|---|
| Gender | Women | 296 | 64.8 |
| | Men | 161 | 35.2 |
| Age group | 65-75 | 294 | 64.3 |
| | 76-85 | 126 | 27.6 |
| | >86 | 37 | 8.1 |
| Marital status | Single/Divorced/Widowed | 155 | 31.7 |
| | Married | 312 | 68.3 |
| Education level | Illiterate | 78 | 17.1 |
| | Primary school | 226 | 49.4 |
| | High school | 74 | 16.2 |
| | University | 79 | 17.3 |
| Working status | Retired | 213 | 46.7 |
| | Housewife | 207 | 45.3 |
| | Still working | 37 | 12.5 |
| Life style | With family/spouse | 365 | 79.9 |
| | Caregiver/Nursing home/Other relatives | 35 | 7.6 |
| Cigarette status | Alone | 57 | 12.5 |
| | Non-smoking | 336 | 74 |
| | Smoking | 119 | 26 |

**Table 2.** The data of COVID-19 related signs and symptoms (n=457)

| | | Number (n) | Percentage (%) |
|---|---|---|---|
| Time after COVID-19 infection | <1 month | 25 | 5.5 |
| | 1-3 months | 38 | 8.3 |
| | 3-6 months | 66 | 14.4 |
| | 6-9 months | 75 | 16.4 |
| | 9-12 months | 89 | 19.5 |
| | >12 months | 164 | 35.9 |
| Vaccination status | No vaccination / Didn't want to specify | 137 | 19.3 |
| | Inadequate / Insufficient vaccination | 58 | 17.4 |
| | Full vaccination | 262 | 63.3 |
| Hospitalization for COVID-19 | Yes | 91 | 19.9 |
| | No | 366 | 80.1 |
| Medication at the time of infection | With prescription | 229 | 50.1 |
| | Without prescription | 54 | 11.8 |
| | No medication | 174 | 38.1 |
| Medication during COVID-19 | Anticoagulation | 259 | 56.7 |
| | Antiviral | 246 | 53.8 |
| | Corticostreroid | 68 | 14.8 |
| | Biological agent | 22 | 4.8 |

Inadequate/insufficient vaccination: 1 dosage of sinovac/1 dosage of biontech/ 2 dosage of sinovac/1 dosage of sinovac+1 dosage of biontech vaccination

Full vaccination: 3 dosage of sinovac/3 dosage of biontech/ 2 dosage of sinovac+2 dosage of biontech/3 dosage of sinovac+2 dosage of biontech vaccination

**Table 3.** The comorbidities of the patients (n=457)

| Comorbidities | Number of Patients (n) | Percentage (%) |
|---|---|---|
| **Overall** | 430 | 94.1 |
| **Hypertension** | 334 | 73.1 |
| **Osteoarthritis** | 149 | 32.6 |
| **Diabetes mellitus** | 127 | 27.8 |
| **Coronary artery disease** | 112 | 24.5 |
| **Osteoporosis** | 78 | 17.1 |
| **Gastro-intestinal diseases** | 59 | 12.9 |
| **Depression** | 33 | 7.2 |
| **Obesity** | 31 | 6.8 |
| **Chronic kidney disease** | 26 | 5.7 |
| **Stroke** | 25 | 5.5 |
| **Movement disorders** | 22 | 4.8 |
| **Thyroid diseases** | 22 | 4.8 |
| **Chronic obstructive pulmonary diseases** | 16 | 3.5 |
| **Asthma bronchiale** | 12 | 2.6 |
| **Liver diseases** | 9 | 2 |

**Table 4.** Post-COVID pain and its characteristics (n=457)

| | | Yes number (n) | Yes percentage (%) | No number (n) | No percentage (%) |
|---|---|---|---|---|---|
| **Presence of pain after infection** | | 370 | 81 | 87 | 19 |
| Duration of pain after infection | <1 week | 39 | 8.5 | | |
| | 1-3 weeks | 80 | 17.5 | | |
| | 4-8 weeks | 68 | 14.8 | | |
| | 8 week- 3 months | 38 | 8.3 | | |
| | 3-6 months | 50 | 10.9 | | |
| | 6-9 months | 95 | 20.7 | | |
| | 9-12 months | 27 | 5.9 | | |
| Localization of pain after infection | Backbone/lomber spine | 181 | 48.9 | | |
| | Dorsal | 162 | 43.8 | | |
| | Hip | 119 | 32.2 | | |
| | Knee | 118 | 31.9 | | |
| | Shoulder | 99 | 26.8 | | |
| Characteristic of prior pain | Prior pain and increase in | 261 | 80.6 | 63 | 19.4 |
| | Prior treatment for pain | 229 | 70.7 | 95 | 29.3 |
| Disability impact | Difficulty of walking | 123 | 26.9 | 334 | 73.1 |
| | Device usage | 76 | 16.6 | 381 | 83.4 |
| | Cane | 46 | 60.5 | | |
| | Walker | 22 | 28.9 | | |
| | Wheelchair | 15 | 19.7 | | |

**Table 5.** Post-COVID musculoskeletal system problems (n=457)

| | Number of Patients (n) | Percentage (%) |
|---|---|---|
| **Widespread pain** | 370 | 81 |
| **Myalgia** | 291 | 63.7 |
| **Arthralgia** | 203 | 44.4 |
| **Arthritis** | 15 | 3.3 |
| **Muscle weakness** | 74 | 16.2 |
| **Myositis** | 2 | 0.4 |
| **Steroid myopathy** | 6 | 1.3 |
| **Falls** | 53 | 11.6 |
| **Osteoporosis (detected in post-COVID period)** | 93 | 20.4 |
| **Osteonecrosis** | 1 | 0.2 |
| **Neuropathy** | 38 | 8.3 |
| **Peripheral** | 9 | 1.9 |
| **Polyneuropathy** | 29 | 6.3 |

had difficulty of walking and 76 (16.6%) patients felt the need to use an assistive device and the most commonly used device was a cane in 46 (60.5%) cases.

The most prevalent complaint, observed in 457 cases, was widespread pain (81%), followed by myalgia (63.7%) and arthralgia (44.4%). Post-COVID musculoskeletal system problems are presented in Table 5. The most rare involvements were osteonecrosis (1 patient, 0.2%) and myositis (2 patients, 0.4%).

Chi-squared test was used to compare categorical variables (significance level was set at $p<0.05$) (Table 6). According to the results of the analysis carried out, it was found that musculoskeletal pain immediately after infection is observed more frequently in cases with comorbid diseases ($p<0.001$), hypertension ($p<0.001$), and hospitalization due to COVID-19 ($p<0.001$). It was determined that the incidence of pain seen immediately after infection increased as the number of comorbidities increased ($p<0.001$). In conjunction with this, persistent pain after COVID-19 infection were more common in those with osteoarthritis ($p=0.039$).

## DISCUSSION

This study reveals that musculoskeletal involvement during the post-COVID period in older adults referred to PMR clinics is an important issue. In the scope of our study patients who applied to the PMR clinics were evaluated by the sequential method. The predominant involvements include widespread pain (81%), myalgia (63.7%) and arthralgia (44.4%). Majority of the cases were female (64.8%). The reason for this situation may be due to the fact that our sample in which the survey was conducted consisted of more women and also women may had more persistent pain. But it can't be claimed that the percentage of women infected with COVID-19 was higher. However, rarer involvements, such as osteonecrosis, myositis, steroid myopathy, and arthritis, were more common in patients older than 75 years, irrespective of gender.

In terms of pain and its determinants, the study

**Table 6.** The relationship between comorbidities and musculoskeletal pain and persistent pain

| | | Musculoskeletal pain immediately after infection (lasting about 7 days) | | Persistent pain (that lasts for more than three months) after infection | |
|---|---|---|---|---|---|
| | | Number (%) | p | Number (%) | p |
| **Presence of comorbidities** | No | 41 (56.9%) | <0.001 | 47 (65.3%) | 0.602 |
| | Yes | 361 (83%) | | 270 (62.1%) | |
| **Hypertension** | No | 88 (71%) | 0.001 | 68 (54.8%) | 0.086 |
| | Yes | 286 (84.6%) | | 215 (63.6%) | |
| **Chronic liver disease** | No | 369 (81.5%) | 0.072 | 279 (61.6%) | 0.318 |
| | Yes | 5 (55.6%) | | 4 (44.4%) | |
| **Osteoarthritis** | No | 247 (79.2%) | 0.199 | 181 (58%) | 0.039 |
| | Yes | 127 (84.7%) | | 102 (68%) | |
| **Number of comorbidities** | No | 13 (48.1%) | <0.001 | 13 (48.1%) | 0.311 |
| | Only 1 disease | 94 (76.4%) | | 74 (60.2%) | |
| | 2 or 2 < diseases | 267 (85.6%) | | 196 (62.8%) | |
| **COVID vaccination** | No | 8 (61.5%) | 0.163 | 11 (84.6%) | 1.000 |
| | Yes | 255 (79.2%) | | 264 (82%) | |
| **Pulmonary involvement** | No | 270 (77.6%) | 0.002 | 219 (62.9%) | 0.196 |
| | Yes | 104 (91.2%) | | 64 (56.1%) | |
| **Hospitalization due to COVID** | Yes | 88 (94.6%) | <0.001 | 50 (53.8%) | 0.097 |
| | No | 286 (77.5%) | | 233 (63.1%) | |

finds that musculoskeletal pain immediately after infection is observed more in cases with comorbid diseases, hypertension, pulmonary involvement and hospitalization due to COVID-19. It was determined that the incidence of pain seen immediately after infection increased as the number of comorbidities increased. And persistent pain after COVID-19 infection were more common in those with osteoarthritis.

Over the approximately four-year duration of the COVID-19 pandemic, which infected millions worldwide, the infection posed challenges to the musculoskeletal system. The primary aim of this descriptive study was to examine post-COVID musculoskeletal involvement in older adults. The characteristics of the study population align with those of previous studies from Türkiye, with the majority being women, married, housewives, and having at least one medical comorbidity (7).

Myalgia, rhabdomyolysis, myositis, rarely necrotizing autoimmune myositis, and critical illness myopathy may be observed as post-COVID muscle involvement. In the current study, myalgia (63.7%) and muscle weakness (16.2%) were the most reported complications, with myopathy (1.2%) and myositis (0.4%) were being very rare. Patel et al. stated that among persistent symptoms, myalgia (23.14%) had a higher prevalence (8). In this review where long-term COVID effects were analyzed, the authors specified the long COVID period as around the first 70 days after infection.

Jacobs et al. reported that symptoms associated with the infection, particularly joint pain, myalgia and generalized pain, tended to disappear around

the 4th week (9). However, our observations suggest a fluctuating course, with a tendency to decrease towards the end of the first month, followed by an increase afterwards. Karaaslan et al conducted a single-center cohort study, comprising 300 participants, with phone interviews and found 21% arthralgia and 22% myalgia after the first month of infection (10). In the study carried out as a continuation of the first research, the rates of myalgia and arthralgia were 18.6 % and 15.1 %, respectively in the sixth month (11). It is also higher than Wang's medical chart review of post-acute sequela of COVID-19 (19%) and similar to the rate (64%) in Lippi et al.'s article on long-term sequelae of COVID-19 published in 2023 (12, 13). In a study designed as a cross-sectional, single-center case series, the rate of myalgia and arthralgia were 68.0% and 43.3% respectively in hospitalized adults (14). The disparity in results compared to Karaaslan, Patel, and Wang may arise from the methodology implemented in our study, involving face-to-face interviews by a medical doctor during the long COVID period (9-12 months).

Joint involvement is another condition that is as common as myalgia. In the systematic review by Claffi et al., only one study focussing on arthralgia was found and the rate was mentioned to be 2.5% (15). Joints were the third most frequent site of involvement and was observed in 44.4% of cases in our study. This rate is higher than the study by Wang et al, which assessed post-acute sequela of COVID-19 (21%), and the study by Moreno-Pérez et al, which evaluated up to 14 weeks (19.2%) (12,16). However, it is also lower than the rate in the study of Lippi et al. (13).

This study's findings on joint involvement differ from previous studies, suggesting diverse post-COVID presentations, possibly influenced by variant differences, emphasizing the importance of specialized evaluations, as symptoms of COVID-19, especially musculoskeletal symptoms, exhibit a diverse and fluctuating course. Arthritis has been reported in various studies (16-18) and on careful diagnosis, viral arthritis and arthritis in particular can be distinguished by the quick response to nonsteroidal anti-inflammatory drugs (3). In our study, the rate of arthritis was 3.3%, which was not very rare. None of our patients with arthritis had a background of chronic inflammatory arthritis. The presenting pictures might be post-viral arthritis. Yet, we do not have information on their follow-up.

Nerve involvement includes peripheral neuropathy, critical illness polyneuropathy, and Guillan-Barré syndrome and its variants (3). In this study, neuropathy was observed in 8.3% of the patients, and most of them were diagnosed with polyneuropathy. Two patients (0.4%) had Guillan Barré Syndrome, one patient had transverse myelitis (0.2%), and 13 patients (2.8%) were diagnosed with sensorimotor polyneuropathy during COVID-19 infection. It is noteworthy that there were 16 (3.5%) patients who developed sensorimotor polyneuropathy after that period. Although the frequency of neurological involvement is quite high in the early period, nerve involvement can also occur in the post-COVID period (19).

It seems that the post-COVID era will never be the same. The infection, which has been on the global agenda for the past four years or so, is difficult to characterize because of the variety of systems involved, the differences in age, sex, and presentation, and the wide range of co-morbidities in patients. The involvement of the musculoskeletal system can lead to disability and mobility during the post-COVID period (20). An analysis of these characteristics; female gender, age between 65-75 years, and presence of at least one comorbidity are predisposing factors for post-COVID syndrome. Older individuals have to deal with more severe pain, especially in the presence of concomitant osteoarthritis. However, this study finds encouraging evidence of pain reduction after the 12th month of treatment.

Aspects that need to be improved: In this observational study we evaluated the first 12 months after infection. This period, referred to as post-COVID in the literature, could have been extended to examine long symptoms. Additionally, it would have been beneficial to analyze these three periods separately, providing detailed insights into the musculoskeletal involvement of patients during the primary infection. Given the known differences between variants, these symptoms could have been investigated in cases with genetic analysis. However, the study was conducted during a time when the concept of post-COVID was just established, and the details of musculoskeletal involvement were still being determined, making it challenging to address all these questions. Nonetheless, it is essential to conduct future studies incorporating these characteristics for both the older population and all other age groups.

Positive aspects: To the best of our knowledge, our study represents the first descriptive analysis of musculoskeletal disorders in older people in our country, even though it was conducted when information about musculoskeletal disorders was limited. This study marks the face-to-face investigation in Türkiye with patients over 65 years of age at PMR clinics. The results encompass data from eleven PMR clinics across seven provinces in the country, spanning the Aegean, Marmara, Central Anatolia, Mediterranean, and Southeastern Anatolia regions. In this regard, it stands out as the study with the broadest range of known characteristics.

## CONCLUSION

There are potential musculoskeletal effects of COVID-19 in older adults. Arthralgia and myalgia are common symptoms associated with COVID-19. Elderly patients with pre-existing musculoskeletal conditions, such as osteoarthritis, may experience exacerbated symptoms during or after a COVID-19 infection. Also, factors such as the presence and number of other comorbidities, hospitalization and pulmonary involvement play considerable roles. The long-term consequences of COVID-19 on musculoskeletal health are still under investigation, and further research is necessary to fully comprehend the extent and duration of these effects.

**Ethics Committee Approval:** The study protocol was approved by the University of Hacettepe Clinical Research Ethics Committee (Date: 19.04.2022, No: 16969557750). The study was conducted under the principles of the Declaration of Helsinki.

**Patient Consent for Publication:** A written informed consent was obtained from each patient.

**Data Sharing Statement:** The data that support the findings of this study are available.

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ORIGINAL ARTICLE

# SARCOPENIA, AND CHRONIC PAIN IN PATIENTS WITH PSEUDOEXFOLIATION SYNDROME

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## Abstract

**Introduction:** We aimed to investigate whether the rate of sarcopenia is higher in patients with pseudoexfoliation syndrome and if an association exists between pseudoexfoliation syndrome, sarcopenia parameters, and chronic musculoskeletal pain.

**Materials and Method:** A total of 96 enrolled patients were divided into two equal groups: "pseudoexfoliation syndrome group" and "no pseudoexfoliation syndrome group". The variables were demographic characteristics, sarcopenia parameters (SARC-F, hand-grip strength, chair-rise test, gait speed), and pain parameters (having any chronic musculoskeletal pain, pain regions, and Visual Analog Scale-pain).

**Results:** Comparison of sarcopenia and pain parameters between the two groups showed that SARC-F (all groups:p<0.001, 65-74 years:p<0,001, 75-84 years:p=0,015), chair rise test (all groups:p<0.001, 65-74 years:p=0,002, 75-84 years:p=0,003), and Visual Analog Scale-pain (all groups:p<0.001, 65-74 years:p=0,007, 75-84 years:p=0,003) scores were statistically significantly higher, while the gait speed (all groups:p<0.001, 65-74 years:p=0,004, 75-84 years:p=0,007) score was significantly lower in "pseudoexfoliation syndrome group" than in "no pseudoexfoliation syndrome group". 60.4% of patients with pseudoexfoliation syndrome had probable sarcopenia, and 83% had chronic musculoskeletal pain. A comparison of the two groups showed that the rate of sarcopenia (all groups:p<0.001, 65-74 years:p<0,001, 75-84 years: p=0,014) and the rate of having chronic musculoskeletal pain (all groups, 75-84 years: p=0.002) was significantly higher in patients with pseudoexfoliation syndrome.

**Conclusion:** Our study results showed that most patients with pseudoexfoliation syndrome had chronic musculoskeletal pain and probable sarcopenia. Although pseudoexfoliation syndrome and sarcopenia are problems of aging, further research is needed to explain the pathogenetic mechanisms underlying the high rate of sarcopenia and chronic pain in patients with pseudoexfoliation syndrome. ClinicalTrials.gov Identifier: NCT06121154

***Keywords:*** Chronic Pain; Exfoliation Syndrome; Sarcopenia.

## INTRODUCTION

Sarcopenia is defined as decreased muscle mass, muscle strength, and muscle function, which leads to lower physical performance, disability, and a reduced quality of life. The European Working Group on Sarcopenia in Older People (EWGSOP) produced a consensus paper, EWGSOP2 (1). In that consensus, muscle strength was the key parameter of sarcopenia; following SARC-F, low muscle strength was enough to screen for causes and start clinical intervention (2). The prevalence of sarcopenia reported in a study in Turkey was 5.2% (3). The prevalence of sarcopenia and chronic musculoskeletal pain problems increases with age. Bakılan et al. (4) reported a noteworthy correlation between sarcopenia and chronic musculoskeletal pain.

Pseudoexfoliation syndrome (PEX) is an age-related, genetic, and systemic disease characterized by abnormal extracellular fibrillar material accumulation in many ocular and extraocular tissues (5). In a biomicroscopic examination, PEX can be easily diagnosed by observing anterior segment changes characterized by white deposits on the pupillary border and anterior lens (6). PEX has been reported to have a high frequency in Scandinavian countries, Türkiye, Greece, and Saudi Arabia. Yildirim et al. (7) reported the frequency of PEX as 5% in people >40 years old in the Central Anatolia region. In addition to the ocular tissues, exfoliating material has been shown to accumulate in the connective tissue layers of the skin and visceral organs, the periphery of blood vessels, and both the smooth muscle layers of the visceral organs. Previous studies have demonstrated the accumulation of cross-linked polyethylene (PEX) materials within the striated muscle layers of visceral organs and cardiac muscles, leading to impaired systolic function of the heart (8,9). On the other hand, sarcopenia affects the striated muscles and decreases muscle mass and function. Sarcopenia and PEX are aging disorders affecting striated muscles and connective tissues. Although the relationship between PEX and systemic diseases such as coronary artery disease, stroke, and sensorineural hearing loss has been extensively researched in the literature (6,10), to the best of our knowledge, the relationship between PEX and sarcopenia has not been investigated. Other studies investigating musculoskeletal system problems associated with PEX are also limited. In a study, sensorial nerve latency was reported to be longer, and sensorial nerve conduction amplitude and velocity were reported to be lower in patients with PEX. The sensory nerves also play a role in the pain mechanism (11). The other study reported the relationship between PEX and calcium channels (12). These calcium channel problems were also detected in chronic pain conditions such as migraine (13). Only one study was found concerning the relationship between PEX and chronic musculoskeletal pain. Ucar et al. (14) reported a possible relationship between osteoarthritis and PEX. Patients with PEX had higher knee pain scores and this finding has been reported to be associated with disturbance of connective tissue metabolism. To the best of our knowledge, despite the existence of such common mechanisms in PEX and pain, no study examining the relationship between PEX and chronic musculoskeletal pain, except for knee pain, has been identified in the literature.

Pseudoexfoliation syndrome, sarcopenia, and chronic pain are all aging disorders affecting connective tissue and striated muscles, PEX may contribute to sarcopenia and chronic musculoskeletal pain through common pathways. The first aim of this study was to investigate whether the rate of sarcopenia was higher in patients with PEX. The second aim was to investigate any association between PEX, sarcopenia parameters (SARC-F, chair rise test, grip strength, gait speed), and chronic musculoskeletal pain.

## MATERIALS AND METHOD

This case-control study involved 96 patients who were admitted to the Department of Physical Medicine and Rehabilitation Outpatient Clinic at

Eskişehir Osmangazi University Hospital, between March and August 2023. The inclusion criteria were being ≥60 years old and undergoing a detailed complete ophthalmic examination by an experienced physician within one month at the Department of Ophthalmology in the same hospital.

The exclusion criteria were having ophthalmic diseases that cause vision loss and reduce quality of life and mobility, including smoking, acute/subacute pain, amputation, infection, active arthritis, active cancer, having any prosthesis or surgery in the lower extremities and lower back, neurological disorders, malabsorption, weight loss, uncontrolled major systemic diseases, impaired cognitive function, and being immobilized.

The detailed complete ophthalmic examination included evaluations of refraction, visual acuity, intraocular pressure (Goldmann applanation tonometry), and anterior and posterior segment examinations.

The criteria to diagnose PEX were, after pupillary dilatation, white fluffy dandruff-like material on ≥1 anterior segment structures, including the pupillary margin, the anterior lens capsule, or the angle in the biomicroscopic examination. The patients were categorized into two groups according to their PEX-positive (n = 48) or PEX-negative (n = 48) status (7).

All patients were questioned on their age, gender, weight, height, drug usage, cane usage, educational/employment status, family type, and systemic diseases.

A physiatrist carried out a detailed musculoskeletal examination. Chronic musculoskeletal pain was accepted as persistent pain for >3 months, and the pain regions (upper extremity/cervical region, lower extremity/lumbar region, and the whole body) were recorded. The Visual Analog Scale (VAS) was used to measure general body pain severity, with assessments ranging from "zero" (indicating no pain) to "ten" (worst conceivable pain) (15).

The SARC-F is recommended in the EWGSOP2 to determine sarcopenia patients in usual geriatric practice. The SARC-F has five questions evaluating strength, assistance in ambulation, chair rise, climbing stairs, and falls. The cut-off point for predicting sarcopenia is a score of 4; "4 and more" means there is a risk of sarcopenia. Low gait speed is characterized by walking slower than 0.8 meters per second. Low muscle strength was evaluated with the "chair rise test" and the "grip strength". The EWGSOP2 recommends using the chair rise test to assess the strength of leg muscles. This test measures the time taken to rise from the sitting position without using the upper extremities five times, and the strength of the muscles is defined as "low" when the time taken is more than fifteen seconds (1). Grip strength was assessed using a hand-held dynamometer (Baseline, White Plains, New York, USA), and the cut-off thresholds were 32 kg for males and 22 kg for females. "Probable sarcopenia" was defined according to the EWGSOP2 algorithm as having a "4 and more" score in SARC-F with low muscle strength (1).

The Physical Activity Scale for the Elderly (PASE) is a questionnaire, comprising 12 questions concerning the frequency and duration of various activities conducted during the preceding week. These activities encompass leisure pursuits, household chores, and occupational tasks. The questionnaire employs diverse scoring methods: leisure and strengthening activities are graded based on frequency (ranging from "never" to "often") and duration (categorized into different time intervals), while household and work-related activities are simply marked as "yes" or "no." In the case of work-related activities, the duration was quantified in hours per week, regardless of whether the work was paid or unpaid. The final PASE score is calculated by assigning empirically derived weights to each activity and summing up the scores obtained from all activities (16).

Written informed consent was obtained from all patients. This study was performed in line with the principles of the Declaration of Helsinki. Ethics approval was granted by the Local Ethics Committee, with the date and number 21/02/23-22.

### Statistical Analysis

A total of 96 patients were determined as the required sample size (48 patients allocated to each group) with a sufficient statistical power 0.80 and a moderate effect size (0,52) using G*Power software package (version 3.1.9.4) (Franz Faul, Universität Kiel, Düsseldorf, Germany). Furthermore, the power of our study, calculated based on the SARC-F outcome (alpha = 0.05), was determined to be 0.99. The distribution of each continuous variable was assessed for normality using the Shapiro-Wilk test. Normally distributed variables were compared using the t-test and expressed as mean ± standard deviation (SD). Non-normally distributed variables were compared using the Mann-Whitney U test and presented as median values (25%-75%). Categorical variables were conveyed as frequencies and percentages and were compared using the Chi-square test. A p-value less than 0.05 was considered statistically significant. All analyses were performed using the SPSS version 21.0 software (SPSS Inc., Chicago, IL, USA).

## RESULTS

A total of 96 patients (51 female, 45 male) (mean age: 71.18 ± 6.93) were included in the study. The demographic characteristics of the two groups were statistically similar (Table 1).

**Table 1.** Comparison of demographic characteristics between PEX-positive and PEX-negative patients

| | | PEX-positive (n=48) | PEX-negative (n=48) | p value |
|---|---|---|---|---|
| **Age** (25-75%) | | 73,0 (66,25-76,0) | 69,50 (64,0-73,75) | 0,076 |
| **Gender (female/male)** n (%) | | 25 (52,1%) / 23 (47,9%) | 26 (54,2%) / 22 (45,8%) | 0,838 |
| **Body Mass Index** (mean±SD) | | 28,86±4,59 | 27,43±4,14 | 0,114 |
| **Chronic diseases** (yes) n (%) | | 40 (83,3%) | 41 (85,4%) | 0,416 |
| DM (yes) | | 19 (39,5%) | 23 (47,9%) | 0,411 |
| Cardiac Disease (yes) | | 18 (37,5%) | 12 (25,0%) | 0,186 |
| COPD (yes) | | 8 (16,6%) | 9 (18,7%) | 0,789 |
| Hipertension (yes) | | 30 (62,5%) | 34 (70,8%) | 0,386 |
| **Employment status n (%)** | Working | 1 (2,0%) | 3 (6,3%) | 0,369 |
| | Never worked | 17 (35,5%) | 21 (43,7%) | |
| | Retired | 30 (62,5%) | 24 (50%) | |
| **Educational status n (%)** | Lower than high school | 32 (66,7%) | 38 (79,2%) | 0,251 |
| | High school and higher | 16 (33,3%) | 10 (20,8%) | |
| **Family status n (%)** | Alone | 7 (14,6%) | 11 (22,9%) | 0,576 |
| | Nuclear family | 34 (70,8%) | 31 (64,6%) | |
| | Extended family | 7 (14,6%) | 6 (12,5%) | |
| **Cane usage** (yes) n (%) | | 1 (2%) | 2 (4,1%) | 0,557 |

(PEX: pseudo-exfoliation syndrome, SD: Standard deviation, DM: Diabetes mellitus, COPD: Chronic obstuctive pulmonary disease, Most of the patients had more than one chronic diseases)

**Table 2.** Comparison of ophtalmologic characteristics between PEX-positive and PEX-negative patients

| | | PEX-positive (n=48) | PEX-negative (n=48) | p value |
|---|---|---|---|---|
| **PEX** n(%) | Unilateral | 38 (79,2%) | | |
| | Bilateral | 10 (20,8%) | | |
| **Refraction errors** (yes) n (%) | | 25 (89,3%) | 28 (58,3%) | 0,583 |
| **Glaucoma** n (%) (yes) | | 44 (91,7%) | 22 (45,9%) | <0,001 |
| **Maculopathy** n (%) (yes) | | 17 (35,4%) | 16 (33,3%) | 0,830 |
| **Cataract** n (%) (yes) | | 33 (68,7%) | 29 (60,4%) | 0,393 |

(PEX: pseudoexfoliation syndrome)

**Table 3.** Comparison of pain, sarcopenia parameters and PASE scores between PEX-positive and PEX-negative patients according to age groups

| | | | All patients (n=96) | | | 65-74 years (n=46) | | | 75-84 years (n=27) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | PEX-positive (n=48) | PEX-negative (n=48) | p value | PEX-positive (n=21) | PEX-negative (n=25) | P value | PEX-positive (n=18) | PEX-negative (n=9) | p value |
| **Sarcopenia parameters (mean±SD)** | **SARC-F score** | | 4,29±2,56 | 1,52±1,84 | **<0,001** | 3,90±1,92 | 1,44±1,75 | **<0,001** | 5,38±3,10 | 2,44±1,81 | **0,015** |
| | **Gait Speed** | | 0,84±0,28 | 1,05±0,18 | **<0,001** | 0,87±0,19 | 1,04±0,17 | **0,004** | 0,72±0,24 | 1±0,19 | **0,007** |
| | **Grip Strength** | | 23,10±8,41 | 25,39±6,72 | 0,144 | 23,33±8,47 | 23,68±6,37 | 0,875 | 21,16±8,67 | 24,11±5,92 | 0,370 |
| | **Chair Rise Test** | | 17,71±5,95 | 12,54±3,15 | **<0,001** | 15,63±3,70 | 12,38±2,62 | **0,002** | 20,82±6,27 | 15,38±2,15 | **0,003** |
| **Pain parameters** | **Chronic musculoskeletal pain (yes) n(%)** | | 40 (83,3%) | 26 (54,1%) | **0,002** | 17 (80,9%) | 15 (60%) | 0,124 | 18(100%) | 5 (55,5%) | **0,002** |
| | **Pain Regions n(%)** | **Upper extremity and cervical region** | 2 (5,0%) | 3 (11,5%) | 0,582 | 2 (11,8%) | 2 (13,3%) | 0,981 | 0 (0%) | 1 (20%) | 0,142 |
| | | **Lower extremity and lumbar region** | 28 (70%) | 16 (61,5%) | | 10 (58,8%) | 9 (60%) | | 15 (83,3%) | 3 (60%) | |
| | | **Whole body** | 10 (25,0%) | 7 (27,0%) | | 5 (29,4) | 4 (26,7%) | | 3 (16,7%) | 1 (20%) | |
| | **VAS (25-75%)** | | 5,0 (2,25-6,75) | 1,0 (0-3,0) | **<0,001** | 5 (1,5-7) | 2 (0-3) | **0,007** | 5 (3,75-7) | 2 (0-3,5) | **0,003** |
| **PASE score (25-75%)** | | | 31,5 (28-44,25) | 30 (20-50) | 0,298 | 31 (20-35,75) | 30 (28-46,50) | 0,575 | 27 (17,5-55) | 25 (15-60) | 0,909 |

(PEX: pseudoexfoliation syndrome, VAS: Visual analog scale, PASE: the Physical Activity Scale for the Elderly)

**Table 4.** The relation between PEX and sarcopenia according to age groups

| | All patients (n=96) | | | 65-74 years (n=46) | | | 75-84 years (n=27) | | |
|---|---|---|---|---|---|---|---|---|---|
| | PEX-positive (n=48) | PEX-negative (n=48) | P value | PEX-positive (n=21) | PEX-negative (n=25) | P value | PEX-positive (n=18) | PEX-negative (n=9) | P value |
| **No sarcopenia n (%)** | 19 (39,6%) | 42 (87,5%) | **<0,001** | 8 (38,1%) | 22 (88,0%) | **<0,001** | 5 (27,8%) | 7 (77,8%) | **0,014** |
| **Sarcopenia n (%)** | 29 (60,4%) | 6 (12,5%) | | 13 (61,9%) | 3 (12,0%) | | 13 (72,2%) | 2 (22,2%) | |

(PEX: pseudoexfoliation syndrome)

The ophthalmologic characteristics of the patients are given in Table 2.

The patients were evaluated according to age groups (all patients, 65-74 years, 75-84 years). The PASE scores were similar between PEX-positive and PEX-negative patients in all age groups. The evaluation of all patients showed that 83% of the PEX-positive patients had certain chronic musculoskeletal pain, while this rate was 54% in PEX-negative patients. SARC-F score (all groups: p <0.001, 65-74 years: p<0,001, 75-84 years: p=0,015) chair rise test (all groups: p <0.001, 65-74 years: p=0,002, 75-84 years: p=0,003) and VAS scores (all groups: p <0.001, 65-74 years: p=0,007, 75-84 years: p=0,003) were significantly higher in PEX-positive patients than in PEX-negative patients while gait speed (all groups: p <0.001, 65-74 years: p=0,004, 75-84 years: p=0,007) were significantly lower in PEX-positive patients than in PEX-negative patients. The rate of having chronic musculoskeletal pain (all groups: p=0.002, 75-84 years: p=0,002) were statistically significantly higher in PEX-positive patients than in PEX-negative patients. However, grip strength (p>0,005) and pain regions (p>0,005) were statistically similar between the PEX-positive and PEX-negative in all age groups. (Table 3).

The evaluation of all patients showed that probable sarcopenia was identified in 29 (60.4%) patients in the PEX-positive group and 6 (12.5%) patients in the PEX-negative group. A comparison of the two groups showed that the rate of sarcopenia was significantly higher in the PEX-positive group (all groups: p <0.001, 65-74 years: p<0,001, 75-84 years: p=0,014). In patients aged between 65 and 74 years, 13 (61,9%) of 21 PEX-positive patients had probable sarcopenia while 3 (12%) of 25 PEX-negative patients had probable sarcopenia (p<0.001) Also in patients aged between 75 and 84 years, 13 (72,2%) of 18 PEX-positive patients had probable sarcopenia while 2 (22,2%) of 9 PEX-negative patients had probable sarcopenia. (p=0.014) (Table 4).

## DISCUSSION

To the best of our knowledge, in the existing literature, there was no study examining the relationship between PEX and either sarcopenia or chronic pain. Our study was conducted in the geriatric population according to age groups and the findings of this study indicated that in the aging population, most patients with PEX had certain chronic musculoskeletal pain and probable sarcopenia.

Our results showed that the VAS-pain scores were higher in patients with PEX in all three age groups. Besides that, only the rate of chronic musculoskeletal pain showed statistically higher rates in PEX-positive patients compared to PEX-negative patients in all group analyses and the 75-84 years age group. However, despite chronic

musculoskeletal pain being present in 80% of PEX-positive patients and 60% of PEX-negative patients in the 65-74 years age group, no statistical difference was observed.

Only one other study was observed evaluating VAS-pain scores in patients with PEX. Ucar et al. (14) reported a probable relationship between osteoarthritis and PEX. Similar to our study, pain scores were evaluated using the VAS, and the VAS values of patients who were PEX-positive were significantly higher than those of patients who were PEX-negative. Thus, these two studies observed a similar result that patients with PEX had higher musculoskeletal pain scores. In the literature, we could not identify any study regarding the relationship between chronic pain and PEX. One possible underlying mechanism may be that PEX affects peripheral nerves, especially sensorial nerve fibers. Coban et al. (11) compared electroneuromyographic findings between patients who were PEX-positive and PEX-negative, and sensorial nerve latency was observed to be longer. In contrast, sensorial nerve conduction amplitude and velocity were lower in patients who were PEX-positive.

Taner et al. (17) reported that PEX is associated with atrial electromechanical delay. Additionally, myocardial systolic velocities were observed to be lower in patients with PEX. The risk of arrhythmia was reported to be higher in PEX and a decreased global arousal threshold may be associated with a decreased arousal threshold of sensory nerves that cause pain.

Aung et al. (12) reported a significant relationship between the *CACNA1A* rs4926244 locus and increased susceptibility to the development of PEX. *CACNA1A* encodes the alpha 1A subunit of the type P/Q voltage-gated calcium channel, which involves multiple processes, such as neurotransmitter release and is widely expressed throughout the central nervous system. In addition, *CACNA1A* mutations are observed in a few patients with craniofacial pain, such as migraine (13). The relationship between calcium channels and pain, decreased thresholds, and sensory nerve fiber involvement in PEX may explain the relationship between PEX and chronic pain. Further studies are needed to explain the exact underlying mechanisms.

Our results showed that 60.4% of all our patients who were PEX-positive had probable sarcopenia, this rate was 61% in patients aged between 65-74 and 72% in patients aged between 75-84. Moreover, their SARC-F scores and chair rise test scores were higher, while gait speed was lower in patients who were PEX-positive than in patients who were PEX-negative. A literature review reveals no study evaluating a relationship between PEX and sarcopenia. Possible mechanisms underlying this association are described below.

In previous studies, PEX material has accumulated in the striated muscle layers of the visceral organs and cardiac muscle (8,9). In addition to the involvement of the cardiac muscle, the systolic function of the heart was observed to be impaired in previous studies (17). Sarcopenia affects the striated muscles and decreases muscle mass and function. The detection of sarcopenia in most patients with PEX here made us contemplate that PEX might affect striated muscles in the musculoskeletal system, including cardiac muscle. Further studies are needed in this area.

Vascular disorders are more common in patients with PEX and those with sarcopenia. Lower basal capillary perfusion in the fingers of patients who were PEX-positive and histological microvascular changes (8) have been reported previously. Earlier studies have reported that sarcopenia is known to aggravate vascular disorders such as atherosclerosis. This association was explained as being due to the alteration of intracellular mechanisms caused by changes in myokine secretion and poor vascular hemostasis (18).

The skeletal muscle extracellular matrix comprises collagen and other connective tissue proteins, such as elastin. Fibrosis is the key mechanism in sarcopenia pathogenesis, and overexpression of TGF-β1 promotes fibrosis around myofibers and activates myofibroblasts to produce collagen and fibronectin (19). In PEX cases, Mastronikolis et al. (20) reported that overexpression of TGF-β induces the expression of LOXL1 (lysyl oxidase-like 1), belonging to the lysyl oxidase (LOX) family. LOXL1, LOXL2, LOXL3, and LOXL4 are extracellular copper-dependent enzymes that play an important role in cross-linking of the extracellular matrix. LOXL1, which catalyzes the first step in collagen and elastin cross-linking in connective tissues, was identified as a strong genetic risk factor for PEX (20). In addition, a recent study highlighted that treatment with a LOXL2 inhibitor reduced skeletal muscle fibrosis and increased muscle mass and strength in mice (21). TGF-β and LOX family members affect connective tissue in PEX and seem to affect sarcopenia.

From the above data, a relationship between sarcopenia and PEX can be inferred. Both conditions could result from chronic inflammation and an imbalance between oxidants and antioxidants. The pathogenesis of sarcopenia is multifactorial and is usually related to oxidative stress (22), systemic inflammation, endocrine function changes, immobility, mitochondrial dysfunction, and malnutrition (23). Most of these factors do not act in isolation and intersect or overlap in relation to oxidative stress. Sullivan-Gunn et al. (24) reported that hydrogen peroxide, catalase, and glutathione peroxidase play key roles in the onset of sarcopenia in an aging mouse model. Similarly, Yaz et al. (25) reported that serum malondialdehyde levels, superoxide dismutase, catalase enzymic activities, and glutathione levels significantly differ in patients who were PEX-positive compared to those in patients who were PEX-negative.

Both sarcopenia and PEX have similar pathogenetic pathways, including increased oxidative stress and vascular disorders, dysregulation of LOX family members, and altered function of calcium transport.

The main limitation of this study is not adopting a definitive diagnosis of pain conditions, such as disc herniation or osteoarthritis. The other limitations were the small number of patients and not evaluating chronic pain with an objective parameter. A strength of this study is that it excluded patients with ophthalmic diseases that cause vision loss and reduce quality of life and mobility because vision impairment in older adult patients can lead to physical inactivity and inappropriate nutrition. Although PEX and sarcopenia are both prevalent problems in the aging population, additional studies are needed to explain the pathogenetic mechanisms responsible for the elevated occurrence of sarcopenia and chronic pain among PEX patients.

Previous studies primarily focused on visceral organs, the heart, and the central nervous system, however, limited literature focused on the musculoskeletal system. The advantage of our research over other previous studies is that it is the first which evaluate the musculoskeletal system in terms of the relationship between PEX and either sarcopenia or chronic musculoskeletal pain. Most of the patients with PEX had probable sarcopenia and chronic musculoskeletal pain in our study. Based on our findings, it can be concluded that patients with PEX should be evaluated by a physiatrist for chronic pain and sarcopenia. PEX is most commonly diagnosed in the ophthalmology department, and increasing awareness among ophthalmologists about sarcopenia and chronic musculoskeletal pain may lead to early referral for physiatrist consultation, which can significantly improve the quality of life for these patients.

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ORIGINAL ARTICLE

# COMPARISON OF CLINICAL FRAILTY SCALE AND EDMONTON FRAIL SCALE IN OLDER ADULTS PRESENTING TO THE EMERGENCY DEPARTMENT

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## Abstract

**Introduction:** This study aimed to compare the prognostic values of Edmonton Frail Scale and Clinical Frailty Scale in the emergency department and determine their suitability for patient management.

**Materials and Method:** This study was conducted as a single-center prospective observational study. Patients aged 65 and older who presented to the emergency department were included. Clinical Frailty Scale and Edmonton Frail Scale scores, the emergency department outcomes, length of stay in the emergency department, 30-day mortality, and 30-day readmission data of the patients were recorded. ROC analysis was performed to examine the predictive values on outcomes. DeLong Test was used to compare the predictive values.

**Results:** This study included 400 patients. Intensive care unit admission was significantly more frequent in the frail group according to both Edmonton Frail Scale and Clinical Frailty Scale. The length of stay in the emergency department was significantly longer in the frail group in both classifications. The mortality rate was significantly higher in the frail group in both classifications. The optimal cut off value for predicting mortality was found to be 9 for Edmonton Frail Scale and 7 for Clinical Frailty Scale. There was no significant difference between the predictive values of two scales.

**Conclusion:** We found that two frail scales have good predictive values for adverse outcomes, such as mortality and the need for Intensive care unit admission in the emergency department. We believe that both scores would be valuable in guiding decisions for the emergency department usage due to their similar predictive values.

***Keywords:*** Geriatrics; Emergency Service; Hospital; Frailty; Frail Elderly; Mortality.

## INTRODUCTION

Emergency departments (EDs) are medical units that typically serve as entry points to hospital systems or long-term care and provide vital services to older adults (1). Individuals ages 75 and older have the highest rates of ED visits, second only to infants (2). Furthermore, the global older adult population is increasing steadily, thereby necessitating EDs' growing importance in older-adult care. Frailty is a practical and unifying concept that directs attention toward a more holistic view of care for older adults, focusing on their overall condition, rather than organ-specific diagnoses. Frailty involves a state of vulnerability to stressors and is associated strongly with adverse outcomes. Therefore, differentiating frail older adults from non-frail ones, particularly in situations involving invasive procedures or potential exposure to harmful medications, constitutes a significant aspect of assessment.

Patients with frailty have longer hospital stays and experience higher rates of readmission and mortality (3). In EDs, the aim is to reduce adverse outcomes from treatment by assigning risk classifications to frail patients (4). However, comprehensive geriatric assessments are often not feasible in routine practice in EDs due to limited time available for each patient (5). Therefore, the use of shorter and validated scales has been recommended to identify these high-risk patients (6). However, a recent systematic review reported very low completion rates for frailty scales in critically ill patients presenting at EDs, and it was found that no studies covered over half (52%) of potentially eligible patients for screening (7). Among the reasons for this, factors such as dealing with more complex and challenging cases, as well as knowledge and training gaps, have been cited (8).

The Clinical Frailty Scale (CFS) and Edmonton Frail Scale (EFS) are practical scales suitable for assessing frailty in EDs. This study aims to compare CFS and EFS frailty scales' prognostic values for adverse outcomes, such as mortality and the need for intensive care unit (ICU) admission, contributing to the identification of scores suitable for use in EDs.

## MATERIALS AND METHOD

The study was conducted as a prospective observational study in the ED of a university hospital between March 1, 2021, and October 1, 2021.

### Study Population

Patients ages 65 and older who presented to the ED were included in the study (n = 429). Patients who were unable to communicate due to language barriers or sequelae (n=2); had cerebrovascular events (n=2), major trauma (n=17), or Alzheimer's disease (n=3); or were comatose or intubated (n=5) were excluded from the study.

In a review by Theuou et al., the prevalence of frailty among older adults presenting to the EDs ranged from 7% to 80% (9). The sample size was calculated using the confidence interval method for proportions. The largest sample size was taken as 0.50. It was found, through calculations, that a minimum of 371 volunteers would need to be included in the study to estimate the value of 0.50 in the population, with a 95% confidence interval of ± 0.05 (0.45; 0.55).

### Outcomes and data analysis

After patients presented at the hospital, the study team physician evaluated them, and their data were recorded in the case report form. ED outcomes, follow-up duration, 30-day readmission, and 30-day mortality data were monitored. The national health system database and phone interviews with patients and their caregivers were used for patient follow-up. No interventions were made regarding routine diagnosis, treatment, and testing practices that the responsible ED physician determined throughout the study.

Demographic information, vital signs, comorbidities, polypharmacy, and CFS and EFS scores were recorded. The ED follow-up duration, hospital admission status (discharge/general

ward/ICU), 30-day readmission rates, number of readmissions, and 30-day mortality data were tracked and recorded.

CFS evaluates fitness, active diseases, activities of daily living, and cognition. Patients with CFS scores of 1–4 were classified as non-frail; 5–6, mild to moderately frail; and 7-9, severely frail. The data then were compared between two categories: non-frail (CFS 1–4) and frail (CFS > 4) (10). Ozsurekci et al. conducted the Turkish validity and reliability of the CDS (11).

The EFS is a multidimensional scale comprising 10 domains and 17 potential deficits covering cognition, overall health status, functional independence, social support, medication use, nutrition, mood, continence, and functional performance. Patients were grouped into categories based on EFS scores: 0–5, non-frail; 6–11, mild frailty; and 12–17, severe frailty. The data then were compared between two categories: non-frail (EFS 0–5) and frail (EFS 6–17) (12). Aygör et al. conducted a validity study in the Turkish population and showed that the ECS is appropriate and valid for use in the Turkish population (13).

The study's primary outcome was determined through a comparison of the predictive values of CFS and EFS for 30-day mortality. Secondary outcomes were defined as determining the predictive value of CFS and EFS for length of stay (LOS) in the ED, hospital admission, and readmission to the ED within 30 days. Mortality and/or ICU admission were viewed as a composite outcome and were analyzed among secondary outcomes.

Statistical Package for the Social Sciences (SPSS) software, Version 25, was used for analysis. The normal distribution was determined through the Kolmogorov-Smirnov test and an examination of histograms. Normally distributed data were presented as mean ± standard deviation, and non-normally distributed data were presented as median (interquartile range [IQR] 25–75). For a comparison of continuous numerical variables, Student's t-test was used for normally distributed data, while the Mann-Whitney U test was used for non-normally distributed data. Categorical variables were compared using the chi-square test or Fisher's exact test. A receiver operating characteristic (ROC) analysis was conducted to examine predictive values. Area under the curve (AUC) values were examined, and optimal cutoff values were determined using Youden's index. Differences between ROC curves were analyzed using the DeLong test. A p-value < 0.05 was viewed as statistically significant.

### Ethical Considerations

Ethical approval was obtained from the Ege University Clinical Research Ethics Committee on February 19, 2021 (protocol number 21-2.1T/47). This study was conducted in accordance with Declaration of Helsinki principles. Informed consent was obtained from all patients or their legal guardians.

## RESULTS

Out of the 400 patients included in the study, 52.3% were female. The median age for all patients was 77 years (65–100). Patients' demographic characteristics, vital signs, and comorbidities are summarized in Table 1.

The median CFS score for the patients was 6 (1–9), and the median EFS score was 8 (0–15). A comparison of clinical parameters in EFS and CFS frailty groups is presented in Table 1.

Significantly higher ages were observed in the frail group, according to the EFS ($p < 0.001$). Both systolic blood pressure (SBP) and diastolic blood pressure (DBP), as well as $SpO_2$ and Glasgow Coma Scale (GCS) values, were significantly lower in the frail group, according to both EFS and CFS. Respiratory rate was higher in the frail group, according to both EFS and CFS. Coronary artery disease (CAD), chronic kidney disease (CKD), and cerebrovascular disease

(CVD) were significantly more common in the frail group (p=0.003, p=0.002, p=0.024, respectively). Polypharmacy was significantly more frequent in the EFS frailty group (p < 0.001).

In the comparison between CFS groups, age was significantly higher in the frail group (p<0.001). Female gender was significantly more common in the frail group (p<0.001). CKD and CVD were significantly more prevalent in the frail group, according to CFS (p=0.004 and p=0.020, respectively). Polypharmacy was more common in the CFS frail group (p=0.001). The patients' demographic and clinical characteristics, according to CFS and EFS groups, were compared and presented in Table 2.

The hospitalization rate (ward or ICU) was significantly higher in the EFS frail group (p=0.014), while no significant difference was found between CFS groups (p=0.131). ICU admission was significantly more frequent in both the EFS and CFS frail groups (p<0.001 and p=0.027, respectively). The LOS in the ED was significantly longer in the frail group in both classifications (both p<0.001). Mortality was observed in 63 patients in the EFS frail group and 61 in the CFS frail group. The mortality rate was significantly higher in the frail group in both classifications (both p< 0.001) (Table 3).

In the ROC analysis for predicting mortality, the optimal cutoff value for EFS was found to be 9 (AUC: 0.810 [0.754–0.866], p<0.001). According to this cutoff, the negative predictive value (NPV) for mortality was determined to be 95.4%. For CFS, the optimal cutoff was found to be 7 (AUC: 0.783 [0.722–0.844], p<0.001). According to this cutoff, the NPV for mortality was determined to be 94.1%. No

**Table 1.** Demographic, clinical, and outcome characteristics of all patients

| Demographic and Clinical Data | | Outcome Data | |
|---|---|---|---|
| | **n (%) Total n = 400** | | **n (%)** |
| | | **EFS, median (IQR25-75)** | 8 (0-15) |
| **Age, year, median (IQR25-75)** | 77 (65-100) | Non-frail | 131 (32.8) |
| **Gender, Female, n(%)** | 209 (52.3) | Mildly-Moderate Frail | 195 (48.8) |
| **HT** | 257 (64.3) | Severe Frail | 74 (18.5) |
| **CAD** | 168 (42) | **CFS, median (IQR25-75)** | 6 (1-9) |
| **DM** | 151 (37.8) | Non-frail | 108 (27) |
| **Dementia** | 31 (7.8) | Mildly-Moderate Frail | 148 (37) |
| **CKD** | 39 (9.8) | Severe Frail | 144 (36) |
| **CVD** | 168 (42) | Hospital Admission | 150 (37.5) |
| **Malignancy** | 77 (19.3) | Service Admission | 65 (16.3) |
| **Hepatic Failure** | 15 (3.8) | ICU Admission | 98 (24.5)a |
| **Polypharmacy** | 210 (52.5) | ED Length of Stay (hours) | 13 (7-26) |
| | | 30-day ED readmission | 89 (22.3) |
| | | 30-day Mortality | 66 (16.5) |
| | | Composite Outcome | 123 (30.8) |

[a]Patients requiring transfer to the Intensive Care Unit (ICU) were also included during the service admission. IQR: Interquartile Range, HT: Hypertension, CAD: Coronasry Artery Disease, DM: Diabetes Mellitus, CKD: Chronic Kidney Disease, CVD: Cerebrovascular Disease, ICU: Intensive Care Unit, ED: Emergency Department, EFS: Edmonton Frailty Scale, CFS: Clinical Frailty Scale

**Table 2.** Comparison of clinical parameters in EFS and CFS frailty groups

| | | EFS Frail n = 269 | EFS Non-Frail n = 131 | P Value[a] |
|---|---|---|---|---|
| Age, year, median (IQR25-75) | | 78 (72-85) | 73 (70-77) | **<0.001[b]** |
| Gender, Female, n (%) | | 149 (55.4) | 60 (45.8) | 0.072 |
| **Median (IQR 25-75)** | SBP, mmHg | 133 (111-150) | 140 (124-163) | **0.003[b]** |
| | DBP, mmHg | 74 (63-87) | 77 (69-91) | **0.022[b]** |
| | Pulse rate, /min | 86 (74-101) | 89 (78-100) | 0.449[b] |
| | Temperature, C° | 36.5 (36.3-36.8) | 36.5 (36.3-36.8) | 0.874[b] |
| | $SpO_2$, % | 96 (94-97) | 96 (95-98) | **0.004[b]** |
| | GCS | 15 (15-15) | 15 (15-15) | **<0.001[b]** |
| | Respiratory Rate, /min | 17 (15-19) | 15 (15-17) | **<0.001[b]** |
| **N (%)** | HT | 172 (63.9) | 85 (64.9) | 0.853 |
| | CAD | 127 (47.2) | 41 (31.3) | **0.002** |
| | DM | 106 (39.4) | 45 (34.4) | 0.328 |
| | Dementia | 25 (9.3) | 6 (4.6) | 0.098 |
| | CKD | 35 (13) | 4 (3.1) | **0.002** |
| | CVD | 31 (11.5) | 6 (4.6) | **0.024** |
| | Malignancy | 58 (21.6) | 19 (14.5) | 0.093 |
| | Hepatic Failure | 12 (4.5) | 3 (2.3) | 0.218[c] |
| | Polypharmacy | 164 (61) | 46 (35.4) | **<0.001** |
| | | **CFS Frail n = 292** | **CFS Non-Frail n = 108** | **P Value[a]** |
| Age, year, median (IQR25-75) | | 77 (72-85) | 72 (69-77) | **<0.001[b]** |
| Gender, Female, N (%) | | 172 (58.9) | 37 (34.3) | **<0.001** |
| **Median (IQR 25-75)** | SBP, mmHg | 135 (114-151) | 137 (121-163) | **0.035[b]** |
| | DBP, mmHg | 74 (64-87) | 80 (67-92) | **0.041[b]** |
| | Pulse rate, /min | 86 (74-101) | 89 (78-100) | 0.599[b] |
| | Temperature, °C | 36.5 (36.3-36.8) | 36.5 (36.3-36.8) | 0.931[b] |
| | $SpO_2$, % | 96 (94-97) | 96 (95-98) | **0.039[b]** |
| | GCS | 15 (15-15) | 15 (15-15) | **0.001[b]** |
| | Respiratory rate, /min | 17 (15-19) | 16 (15-17) | **<0.001[b]** |
| **N (%)** | HT | 187 (64) | 70 (64.8) | 0.886 |
| | CAD | 130 (44.5) | 38 (35.2) | 0.093 |
| | DM | 107 (36.6) | 44 (40.7) | 0.453 |
| | Dementia | 27 (9.2) | 4 (3.7) | 0.066 |
| | CKD | 36 (12.3) | 3 (2.8) | **0.004** |
| | CVD | 33 (11.3) | 4 (3.7) | **0.020** |
| | Malignancy | 58 (19.9) | 19 (17.6) | 0.609 |
| | Hepatic Failure | 9 (3.1) | 6 (5.6) | 0.248[c] |
| | Polypharmacy | 168 (57.5) | 42 (39.3) | **0.001** |

[a]ChiSquareTest [b]Mann Whitney U test [c]Fisher Exact Test IQR: Interquartile Range, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, GCS: Glasgow Coma Scale HT: Hypertension, CAD: Coronary Artery Disease, DM: Diabetes Mellitus, CKD: Chronic Kidney Disease, CVD: Cerebrovascular Disease, EFS: Edmonton Frailty Scale, CFS: Clinical Frailty Scale

**Table 3.** Comparison of outcome measures in EFS and CFS frailty groups

| | EFS Frail n = 269 | EFS Non-Frail n = 131 | P Value* |
|---|---|---|---|
| **Hospital Admission** | 112 (41.6) | 38 (29) | **0.014** |
| **Service Admission** | 41 (15.2) | 24 (18.3) | 0.433 |
| **ICU Admission[c]** | 80 (29.7) | 18 (13.7) | **<0.001** |
| **ED Length of Stay (h)[b]** | 15 (8-28) | 9 (5-21) | **<0.001** |
| **30-day ED Readmission** | 60 (22.3) | 29 (22.1) | 0.970 |
| **Number of Readmissions[a,b]** | 1 (1-1) | 1 (1-2) | 0.416 |
| **30-day Mortality** | 63 (23.4) | 3 (2.3) | **<0.001** |
| | **CFS Frail n = 292** | **CFS Non-Frail n = 108** | **P Value*** |
| **Hospital Admission** | 116 (39.7) | 34 (31.5) | 0.131 |
| **Service Admission** | 44 (15.1) | 21 (19.4) | 0.292 |
| **ICU Admission[c]** | 80 (27.4) | 18 (16.7) | **0.027** |
| **ED Length of Stay (h)[b]** | 28 (16-57) | 18 (9-36) | **<0.001** |
| **30-day ED Readmission** | 65 (22.3) | 24 (22.2) | 0.994 |
| **Number of Readmissions[a,b]** | 1 (1-1) | 1 (1-2) | 0.540 |
| **30-day Mortality** | 61 (20.9) | 5 (4.6) | **<0.001** |

[a]Evaluated among patients with readmissions.[b]Presented as Median (IQR25-75). Mann Whitney U test was applied. [c]Included patients requiring transfer to the ICU during service admission. *Chi Square Test IQR: Interquartile Range, ICU: Intensive Care Unit, ED: Emergency Department, EFS: Edmonton Frailty Scale, CFS: Clinical Frailty Scale

**Table 4.** Predictive values of CFS and EFS for mortality and composite outcome

| **ROC analysis results for 30-day mortality** | | | | | | | |
|---|---|---|---|---|---|---|---|
| | **Cut-off** | **Sensitivity** | **Specifity** | **PPV** | **NPV** | **AUC (%95CI)** | **P Value** |
| **EFS Total** | 9 | 83.3 | 67.7 | 33.7 | 95.4 | 0.810 (0.754-0.866) | **<0.001** |
| **CFS Total** | 7 | 77.3 | 72.2 | 35.4 | 94.1 | 0.783 (0.722-0.844) | **<0.001** |
| | | | | | | **De Long Test between CFS and EFS** | 0.159 |
| **ROC analysis results for composite outcome** | | | | | | | |
| | **Cut-off** | **Sensitivity** | **Specifity** | **PPV** | **NPV** | **AUC (%95CI)** | **P Value** |
| **EFS Total** | 9 | 64 | 70 | 49.1 | 82 | 0.702 (0.644-0.760) | **<0.001** |
| **CFS Total** | 7 | 60.2 | 74.7 | 51.4 | 80.9 | 0.698 (0.638-0.758) | **<0.001** |
| | | | | | | **De Long Test between CFS and EFS** | 0.820 |

ROC: Receiver Operating Characteristic, PPV: Positive Predictive Value, NPV: Negative Predictive Value, AUC: Area Under the Curve, IQR: Interquartile Range, EFS: Edmonton Frailty Scale, CFS: Clinical Frailty Scale

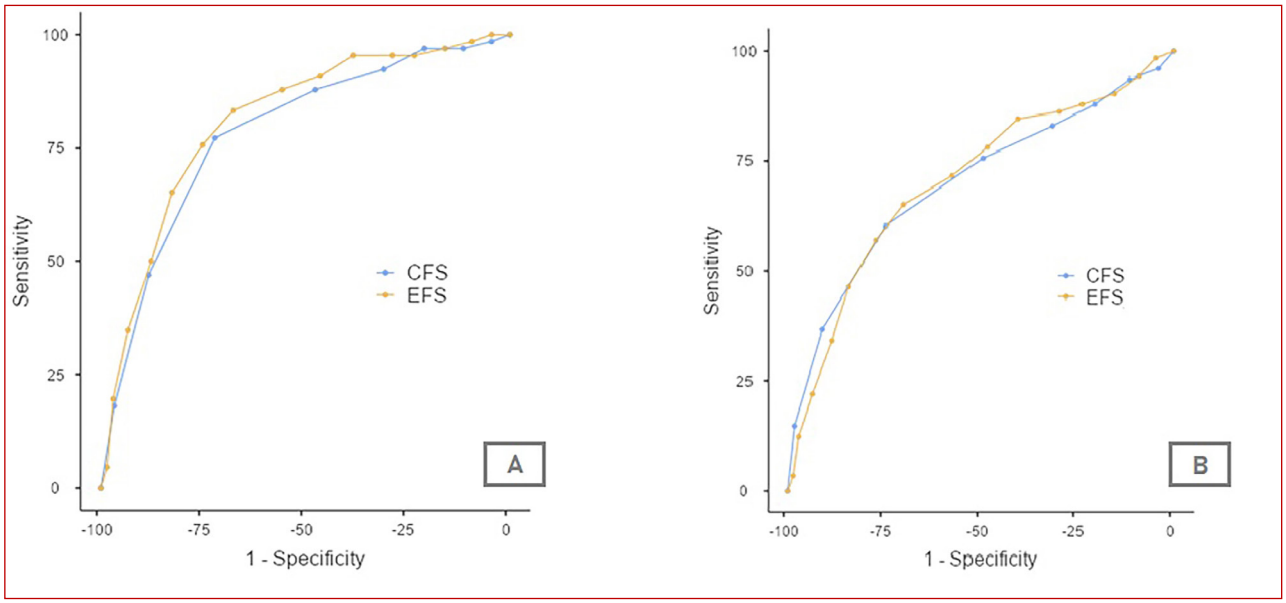


**Figure 1. A.** ROC analysis for 30-day mortality, **B.** ROC analysis for composite outcome.

significant difference in predictive values was found between EFS and CFS (p=0.159, DeLong Test) (Table 4, Figure 1).

In the ROC analysis for the composite outcome defined as mortality and/or ICU admission, the optimal cutoff for EFS again was found to be 9 (AUC: 0.702 [0.644–0.760], p<0.001). The optimal cutoff for CFS was 7 (AUC: 0.698 [0.638–0.758], p<0.001). No significant difference in predictive values was found between EFS and CFS for the composite outcome (p = 0.820, DeLong Test) (Table 4, Figure 1).

## DISCUSSION

In this study, in which we compared the predictive values of EFS and CFS frailty scales for adverse outcomes, such as mortality and ICU admission in EDs, we found that both EFS and CFS had significant predictive value, but neither displayed superiority over the other. According to both scales, mortality, ICU admission, and LOS in the ED were significantly higher in the frail group.

Joseph et al. found a frailty prevalence of 44% based on a 50-item frailty scale assessment among 250 older adults admitted to a Level 1 trauma center (14). Battagia et al. reported a frailty prevalence of 58.5% among 200 older adults presenting to the ED (15). In this study, we believe that the higher frailty rates according to both scales can be attributed to this study being conducted in a tertiary ED serving as a reference hospital in the region catering to the increasing geriatric population.

In this study, CAD, CKD, and CVD rates were significantly higher in the EFS frailty group. In the CFS frailty group, CKD and CVD were significantly higher. The association of frailty with many comorbidities has been examined previously in the literature. Sinclair et al. found a statistically significant association between frailty and diabetes mellitus (DM), suggesting that diabetes may accelerate the aging process and provide an early pathophysiological environment for frailty (16). Castrejón-Pérez et al. (17) found a statistically significant association between frailty and HT. This

systematic review demonstrated that frailty is a strong predictor of mortality, hospitalization, and falls resulting in injuries in hypertensive patients. In this study, no significant difference in HT and DM was found between the EFS and CFS frailty groups. However, considering that CAD, CKD, and CVD are well-established comorbidities similar to DM and HT, their contribution to frailty should be considered (18). We believe that these comorbidities may lead to this result through their impact on cardiac functions and sarcopenia.

Pulok et al. (19) reported a 17% 30-day mortality rate in patients identified as frail, according to the CFS score in their study of 808 ED patients. Kaeppeli et al. (20) found a 12% mortality rate in patients with a CFS score of 5 or higher. Chong et al. (21) reported a mortality rate of 4.7% in the frail group in their study of 210 patients. In this study, the mortality rate was 4.6% in non-frail patients and 20.9% in frail patients, according to the CFS assessment. We believe that the higher mortality rates in the frail group in this study, compared with similar studies in the literature, may be because the hospital where the study was conducted serves as a reference tertiary care center in the region. Furthermore, Kaeppeli et al. (20) reported an ICU admission rate of 16% in the frail group, according to CFS. They stated that CFS is a good scale for predicting ICU admission. In this study, ICU admission rates were significantly higher in the CFS frail group (27.4%). Therefore, we believe that CFS can be a useful predictor for both mortality and ICU admission in EDs.

In a study by Rose et al. (22) using EFS, it was found that frailty was associated with longer hospital stays and mortality. In this study, LOS in the ED was significantly longer in both frailty groups (both $p<0.001$). The longer LOS in the frail group in line with the literature may be attributed to the need for comprehensive evaluation of this patient group, rather than disease-specific management, and, therefore, the need for a more comprehensive assessment before making a safe discharge decision or determining the appropriate unit for admission, as well as the difficulties in determining patient needs.

Serina et al. (23) examined the predictive value of CFS for hospitalization, readmission within nine days, and readmission within 30 days in the ED, and found that higher CFS values were associated with increased hospitalization, and readmission within 30 days. However, the CFS did not indicate a significant predictive value for return visits within nine days (23). In this study, no significant difference in readmission within 30 days was found between frail groups, according to both EFS and CFS. However, as for hospitalization need, no significant difference was found between CFS groups, while hospitalization need was significantly higher in the EFS frail group. The lack of significance in the number of readmissions between groups may be attributed to multifactorial reasons that increase readmissions in both groups, such as deficiencies in the effective use of EDs in the region and attempts to resolve problems in the healthcare system through EDs. In terms of predicting hospitalization need, we believe that EFS may be a better scale than CFS.

Malstrom et al. (24) compared the predictive power of FRAIL, the Study of Osteoporotic Fractures frailty scale, Frailty Index (FI), and Cardiovascular Health Study frailty scale for nine-year mortality in a study conducted with African Americans using in-home assessments and found that the FRAIL and FI scales were stronger predictors. However, comprehensive extant studies evaluating other scores for predicting mortality in EDs and 30-day mortality are limited.

Nowak et al. (25) evaluated EFS, CFS, FRAIL, and Fried scale data on older adults with acute coronary syndrome admitted to a coronary ICU and found high concordance among the scales, but the FRAIL scale had the highest hazard ratio for mortality. EFS was found to be more successful in predicting readmission (25). In this study, no significant

difference in readmission rates was found between CFS and EFS frailty groups. However, this study was conducted among all ED visits without grouping according to specific presenting complaints. The frailty scales' success may vary depending on specific presenting complaints and diagnoses. For 30-day mortality, we found that EFS had an NPV of 95.4%, and CFS had an NPV of 94.1%. We believe that these rates can guide discharge and follow-up decisions in EDs. When comparing the predictive values of CFS and EFS for mortality and composite adverse outcomes, we found no significant difference for both. Therefore, we believe that both scales can be applied easily in EDs. However, the inclusion of more subjective assessments in CFS may lead to variations between studies, while EFS provides more objective results. As more studies are conducted and these scales are used effectively, we anticipate decreases in mortality, reductions in hospital costs, and shorter hospital stays.

### Limitations

This study used a single-center study approach, conducted at a tertiary referral hospital in the region; therefore, it may not fully reflect the general population. Due to the wide range of final diagnoses, subgroup analyses based on final diagnoses could not be conducted.

## CONCLUSION

In this study, in which we compared predictive values of the EFS and CFS scales for 30-day mortality, ICU admission, readmission, and LOS in EDs, we found that both scales have good predictive value, and no significant difference was found between them. We believe that both scales can be used safely in predicting poor outcomes and identifying frailty in older adults in EDs.

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ORIGINAL ARTICLE

# INTENSIVE CARE UNIT OUTCOMES AND MORTALITY IN ELDERLY ONCOLOGY PATIENTS

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## Abstract

**Introduction:** Rising life expectancy has increased elderly admissions to intensive care units. With age, comorbidity risks rise. Intensive care units' hospital mortality for elderly patients stands at 24% to 40%. Oncology patients often require intensive care units care, stemming from cancer-related conditions, treatment complications, or other health issues. However, intensive care units' mortality remains higher among cancer patients.

**Materials and Method:** Ethics committee-approved retrospective analysis covered oncology patients aged 65+ in intensive care units from Jan 2020 to Dec 2021. We categorized patients into two age groups, reviewing demographic data, admissions' reasons, cancer types, recent treatments, APACHE II and SOFA scores, ventilator use, renal replacement therapy need, intensive care units /hospital durations, mortality rates, primary diseases, and comorbidities.

**Results:** Among 706 intensive care units' patients, 25% were over 65 with similar mortality across age groups. Lung/colon tumors and acute leukemias were common. Hematological cancer had higher APACHE II scores but similar mortality. Vasoactive drugs and mechanical ventilation significantly affected intensive care units and hospital mortality. Mortality increased in patients without vasoactive drugs/ventilation during hospitalization. Recent surgery correlated with lower hospital mortality in cancer patients. Mechanical ventilation and vasoactive drugs doubled mortality risk. Surgical admissions showed lower mortality. Renal replacement therapy correlated with higher mortality. No significant survival difference existed between cancer types.

**Conclusion:** In conclusion, treatments impact elderly oncology patients' survival in intensive care units /hospitals. Intensive care units' care's effectiveness in older groups, especially those 75+, suggests potential benefits. Non-surgical admissions and life support contribute to higher mortality. Further studies on pre- intensive care unit treatment and admission timing are essential.

***Keywords:*** Neoplasms; Critical Care; Aged.

## INTRODUCTION

Due to increased life expectancy, the number of elderly patients taken to intensive care units (ICUs) is gradually increasing (1). As people get older, they have an increased risk of developing comorbidities (2). According to studies, the hospital mortality rate for elderly critically ill patients in ICUs was found to be between 24% and 40% (3). Cancer is a disease whose incidence increases with advanced age. According to UK data, 65.5% of newly diagnosed cancer patients are people over the age of 65, and people between the ages of 85 and 89 have the highest incidence of cancer (4).

Oncology patients may need care in ICUs for conditions caused by cancer, treatment-related conditions, or other health problems that occur. Cancer patients constitute 13.5% to 21.5% of all ICU admissions (5). A growing number of studies have shown that critically ill patients with cancer may benefit from ICU treatment (6). Nevertheless, ICU mortality is higher for cancer patients than for patients without cancer (7). Among the reasons for this are clinical conditions such as immunosuppression and neutropenia due to cancer or its treatment (8).

The aim of our study was to reveal the ICU outcomes and mortality rate for oncology patients over 65 years of age, to document the predisposing factors that cause mortality for these patients, and to discuss the measures that can be taken to improve their overall care and outcomes.

## MATERIALS AND METHOD

After approval from the ethics committee was obtained, the data of oncology patients over the age of 65 who were treated in the oncology hospital ICU between 1 January 2020 and 31 December 2021 were retrospectively analyzed. Patients were divided into two groups: a group with people 65–74 years of age and a group with people over 75 years of age. The demographic data of the patients, the reason for their admissions to the ICU, the types of cancer they had, whether they had received chemotherapy or radiotherapy within six months before the, their recent surgical status, their Acute Physiology and Chronic Health Evaluation II (APACHE II) and The Sequential Organ Failure Assessment (SOFA) scores, whether they were on mechanical ventilators, and whether they were receiving renal replacement therapy were examined. Their ICU and hospitalization days and mortality rates were also evaluated. Disease scores, ICU and hospitalization days, and mortality rates were examined based on the hematologic and solid tumor statuses of the patients. In addition, the patients' primary diseases and concomitant diseases were evaluated.

The data were evaluated with the Statistical Package for the Social Sciences version 24.0 on a personal computer. The normal distribution of continuous data was assessed using the Kolmogorov–Smirnov test, and homogeneity was assessed using the one-way ANOVA test. Independent t-tests and Mann–Whitney tests were applied for the analysis of independent variables. A chi-square test was used for categorical data. A p-value less than 0.05 was considered statistically significant for all tests.

## RESULTS

A total of 706 patients were treated in the ICU during the date range examined. Of these patients, 174 (25%) were oncology patients over 65 years of age. It was observed that the patients were admitted to the ICU mostly from the ward. The demographic data, concomitant diseases, APACHE II and SOFA scores, total ICU and hospitalization days, and mortality rates of the patients are shown in Table 1. There were 98 people (56.3%) in the 65-74 years of age range and 76 people over the age of 75 (43.7%). The differences in comorbidities, APACHE II and SOFA scores, ICU and hospitalization days, and mortality rates between these two age groups are shown in Table 2. The incidence of

**Table 1.** Demographic data, comorbidities, scores on day of admission and mortality.

| | | Total, n=174, (%), [SD] |
|---|---|---|
| **Gender** | **Male** | 112 (64.4) |
| | **Woman** | 62 (35.6) |
| **Comorbidity** | | 137 (78.7) |
| **Hypertension** | | 88 (50.6) |
| **Diyabetes mellitus** | | 55 (1.6) |
| **Coronary artery disease** | | 33 (19.0) |
| **COPD** | | 29 (16.7) |
| **Thyroid disease** | | 11 (6.3) |
| **Atrial Fibrillation** | | 6 (3.4) |
| **Heart failure** | | 7 (4.0) |
| **Psychiatric illness** | | 14 (8.0) |
| **Chronic kidney disease** | | 13 (7.5) |
| **Cerebrovascular event** | | 3 (1.7) |
| **Other** | | 20 (11.5) |
| **APACHE II** | | 26.1 [9.4] |
| **SOFA** | | 8.0 [3.6] |
| **ICU LOS** | | 14.1 [15.6] |
| **Hospital LOS** | | 24.3 [19.8] |
| **ICU mortality** | | 123 (70.7) |
| **Hospital mortality** | | 136 (78.2) |

COPD; chronic obstructive pulmonary disease, APACHE II; the acute physiology and chronic health evaluation, SOFA; sequential organ failure assessment, ICU; intensive care unit, LOS; length of stay

hypertension and chronic obstructive pulmonary disease increased with age. Although the APACHE II scores were slightly higher for patients over 75 years of age, their mortality rates were similar to those of patients under 75 years of age. When the distribution of cancer types was examined, it was found that the most common solid tumors were lung and colon tumors and that the most common hematologic tumors were acute leukemias (Table 3). The differences between ICU mortality rates and organ failure scores, ICU days and hospitalization days, and the mortality rates of solid cancers and the mortality rates of hematological cancers are shown in Table 4. Although the APACHE II scores were higher for patients with hematological cancers, both ICU and hospital mortality rates for these patients were similar to those for patients with solid tumors. Among the factors affecting ICU and hospital mortality rates, the most significant were the use of vasoactive drugs at any time and invasive mechanical ventilation support (Table 5). The average APACHE II score was calculated

**Table 2.** Comorbidity, disease scores, intensive care and hospitalization day, mortality according to age groups of patients

| | Age range | | p |
|---|---|---|---|
| | 65-74 years, n=98 (%), [SD] | >75 years n=76 (%), [SD] | |
| **Comorbidity** | 74 (75.5) | 63 (82.9) | 0.320b |
| **Hypertension** | 43 (43.9) | 45 (59.2) | 0.045b |
| **Diabetes mellitus** | 27 (27.6) | 28 (36.8) | 0.253b |
| **Coronary artery disease** | 15 (15.3) | 18 (23.7) | 0.229b |
| **COPD** | 11 (11.2) | 18 (23.7) | 0.047b |
| **Thyroid disease** | 7 (7.1) | 4 (5.3) | 0.429c |
| **Atrial fibrillation** | 3 (3.1) | 3 (3.9) | 0.533c |
| **Heart failure** | 2 (2.0) | 5 (6.6) | 0.131c |
| **Psychiatric illness** | 6 (6.1) | 8 (10.5) | 0.436b |
| **Chronic kidney disease** | 7 (7.1) | 6 (7.9) | 1.000b |
| **Cerebrovascular event** | 1 (1.0) | 2 (2.6) | 0.405c |
| **Other** | 15 (15.3) | 5 (6.6) | 0.121b |
| **APACHE II** | 24.9 [9.2] | 27.7 [9.3] | 0.051 |
| **SOFA** | 8.0 [3.7] | 8.0 [3.5] | 0.980 |
| **ICU LOS** | 13.4 [15.4] | 15.0 [16.0] | 0.526 |
| **Hospital LOS** | 24.1 [20.6] | 24.5 [18.8] | 0.883 |
| **ICU mortality** | 68 (69.4) | 55 (72.4) | 0.794b |
| **Hospital mortality** | 75 (76.5) | 61 (80.3) | 0.685b |

a; pearson chi-square, b; yates chi-square, c; fisher's exact

COPD; chronic obstructive pulmonary disease, APACHE II; the acute physiology and chronic health evaluation, SOFA; sequential organ failure assessment, ICU; intensive care unit, LOS; length of stay

as 26.82 for patients receiving vasoactive drugs and 23.47 for those not receiving them (p=0.018). Similarly, the mean SOFA score was 8.81 for patients receiving vasoactive drugs and 5.26 for those not receiving them (p<0.001).

While the ICU mortality rate for patients who neither received vasoactive drugs nor required invasive mechanical ventilator treatment ranged from 15.8% to 20.5%, the hospital mortality rate increased significantly to between 39.5% and 41.0% for these patients. Hospital mortality was found to be lower for cancer patients who had undergone surgery within six months before the study than for patients who had not undergone surgery. The average APACHE II scores of patients who underwent surgery and those who did not in the last six months were found to be 26.59 and 27.79, respectively, with a calculated p-value of 0.586. Similarly, the average SOFA scores of the same groups of patients were found to be 7.84 and 8.15, respectively, with a calculated p-value of 0.597.

**Table 3.** Distribution of cancer types

| | Age range | | |
|---|---|---|---|
| | **65-74 years n=98 (%)** | **>75 years n=76 (%)** | **Sum n=174 (%)** |
| **Solid tumor** | 80 (81.6) | 55 (72.4) | 135 (77.6) |
| **CNS** | 2 (2.0) | 1 (1.3) | 3 (1.7) |
| **Esophageal** | 4 (4.1) | 1 (1.3) | 5 (2.9) |
| **Stomach** | 9 (9.2) | 4 (5.3) | 13 (7.5) |
| **Liver** | 2 (2.0) | 2 (2.6) | 4 (2.3) |
| **Pancreas** | 4 (4.1) | 4 (5.3) | 8 (4.6) |
| **Lung** | 12 (12.2) | 11 (14.5) | 23 (13.2) |
| **Colon** | 10 (10.2) | 12 (15.8) | 22 (12.6) |
| **Bladder** | 6 (6.1) | 4 (5.3) | 10 (5.7) |
| **Prostate** | 1 (1.0) | 11 (14.5) | 12 (6.9) |
| **Renal** | 4 (4.1) | 1 (1.3) | 5 (2.9) |
| **Breast** | 4 (4.1) | 2 (2.6) | 6 (3.4) |
| **Gynecologic** | 6 (6.1) | 0 | 6 (3.4) |
| **ENT** | 10 (10.2) | 1 (1.3) | 11 (6.3) |
| **Skin** | 1 (1.0) | 0 | 1 (0.6) |
| **Malignant mesenchymal tumor** | 3 (3.1) | 1 (1.3) | 4 (2.3) |
| **Malignant melanoma** | 1 (1.0) | 0 | 1 (0.6) |
| **Gallbladder** | 1 (1.0) | 0 | 1 (0.6) |
| **Hematological** | 14 (14.3) | 20 (26.3) | 34 (19.5) |
| **AML-ALL** | 4 (4.1) | 9 (11.8) | 13 (7.5) |
| **KML-KLL** | 4 (4.1) | 2 (2.6) | 6 (3.4) |
| **NHL** | 3 (3.1) | 5 (6.6) | 8 (4.6) |
| **HL** | 1 (1.0) | 0 | 1 (0.6) |
| **MM** | 1 (1.0) | 4 (5.3) | 5 (2.9) |
| **MDS** | 1 (1.0) | 0 | 1 (0.6) |
| **Unknown** | 4 (4.1) | 1 (1.3) | 5 (2.9) |

CNS; central nervous system, ENT; otorhinolaryngology, AML; acute myeloid leukemia, ALL; acute lymphoblastic leukemia, CML; chronic myeloid leukemia, CLL; chronic lymphoblastic leukemia, NHL; non-Hodgkin lymphoma, HL; Hodgkin's lymphoma, MM; multiple myeloma, MDS; myelodysplastic syndrome

**Table 4.** Intensive care processes of solid and hematological cancers

| | **Solid tumor n=135 (%), [SD]** | **Hematological cancer n=34 (%), [SD]** | **p** |
|---|---|---|---|
| **APACHE II** | 25.4 [8.7] | 29.0 [9.7] | 0.037 |
| **SOFA** | 7.9 [3.6] | 8.8 [3.5] | 0.171 |
| **ICU LOS, days** | 14.5 [16.4] | 12.2 [12.8] | 0.445 |
| **Hospital LOS, days** | 23.6 [19.8] | 27.8 [20.7] | 0.269 |
| **Intensive care mortality, n** | 96 (71,1) | 22 (64,7) | 0.604b |
| **In-hospital mortality, n** | 104 (77,0) | 27 (79,4) | 0.947b |

a; pearson chi-square, b; yates chi-square, c; fisher's exact, APACHE II; the acute physiology and chronic health evaluation SOFA; sequential organ failure assessment, ICU; intensive care unit, LOS; length of stay

**Table 5.** Factors affecting intensive care and hospital mortality.

| | | Intensive care mortality, n (%) | p | RR | In-hospital mortality, n (%) | p | RR |
|---|---|---|---|---|---|---|---|
| **Gender, n (%)** | Male, 112 (64) | 77 (68.8) | 0.561[b] | 0.91 | 84 (75.0) | 0.244[b] | 0.84 |
| | Female, 62 (36) | 46 (74.2) | | | 52 (83.9) | | |
| **Comorbidity, n (%)** | Yes, 137 (79) | 99 (72.3) | 0.501[b] | 1.08 | 108 (78.8) | 0.851[b] | 1.04 |
| | None, 37 (21) | 24 (64.9) | | | 28 (75.7) | | |
| **Chemotherapy, radiotherapy treatment in the last 6 months, n (%)** | Yes, 66 (38) | 47 (71.2) | 1.000[b] | 1.03 | 55 (83.3) | 0.271[b] | 1.40 |
| | None, 108 (62) | 76 (70.4) | | | 81 (75.0) | | |
| **Surgery in the last 6 months, n (%)** | Yes, 64 (37) | 42 (65.6) | 0.344[b] | 0.79 | 43 (67.2) | 0.013[b] | 0.57 |
| | None, 110 (63) | 81 (73.6) | | | 93 (84.5) | | |
| **Vasoactive medication, any time of treatment in intensive care, n (%)** | Yes, 136 (78) | 117 (86.0) | <0.001[b] | 2.55 | 121 (89.0) | <0.001[b] | 2.25 |
| | None, 38 (22) | 6 (15.8) | | | 15 (39.5) | | |
| **Invasive mechanical ventilation, n (%)** | Yes, 135 (78) | 115 (85.2) | <0.001[b] | 2.38 | 120 (88.9) | <0.001[b] | 2.24 |
| | None, 39 (22) | 8 (20.5) | | | 16 (41.0) | | |
| **Renal replacement therapy, n (%)** | Yes, 35 (20) | 28 (80.0) | 0.252[b] | 1.66 | 29 (82.9) | 0.601[b] | 1.35 |
| | None, 139 (80) | 95 (68.3) | | | 107 (77.0) | | |

a; pearson chi-square, b; yates chi-square, c; fisher's exact

RR; relative risk

## DISCUSSION

In this retrospective study, it was found that the mortality rate among oncological patients over 65 years of age who were treated in the ICU was over 70%. The study revealed that the mortality risk of patients requiring invasive mechanical ventilation and vasoactive drugs was more than two times higher than those who had no such requirements. No difference in mortality rates was found between solid and hematological cancers.

Invasive mechanical ventilation therapy is a factor that increases mortality in patients with cancer. Although the overall mortality rate in elderly solid tumor patients in France was 33.6%, the mortality rate was 92.1% in patients treated with mechanical ventilation, and the 90-day mortality risk rate for those on mechanical ventilation was 5.96 (95% confidence interval [CI] [3.91–9.10]; p < 0.0001) (8). In another study in which solid and hematological tumors were evaluated together, the one-month mortality rate was 67.6% and the mortality risk rate for those on mechanical ventilation was 2.873 (95% CI 1.352–6.104, p=0.006) (9). Considering that the proportion of patients who underwent invasive mechanical ventilation was higher in our study, ICU and hospital mortality rates are expected to be higher than those reported in the literature.

The 90-day mortality risk ratio in oncology patients receiving vasopressor therapy ranges from 2.14 (95% CI 0.97–4.73, p=0.05) to 3.68 (95% CI 2.54–5.33, p<0.0001) (9,10). In one study, the odds ratio was 16.839 (95% CI 3.98–71.235, p=0001) (11). In the current study, 78% of the patients used vasopressors, and the contribution of vasopressor use to mortality was found to be significant. Additionally, in our study, the calculated APACHE

II and SOFA scores during ICU admission were found to be significantly higher in patients receiving vasoactive drugs compared to those not receiving them. The higher predicted mortality rates during ICU stay indicate an increased likelihood of mechanical ventilation and vasopressor use among these patients. Furthermore, the elevated APACHE II and SOFA scores in patients receiving vasoactive drugs underscore the severity of their condition and the need for intensive monitoring and management strategies. These findings highlight the importance of early identification and intervention in critically ill patients to optimize outcomes and reduce mortality rates in the intensive care setting.

The high mortality rate in patients undergoing mechanical ventilation or vasopressor therapy is an expected outcome. However, it was not feasible to assess the relationship between tumor stage and frailty scores in our study. A recent study revealed a high prevalence of frailty among patients aged 50 and older, with an increased frailty score associated with higher mortality within 30 days (12). A meta-analysis on frailty and ICU mortality showed an increase in intensive care unit mortality with increasing frailty scores among individuals aged 65 and older(13).

The contribution of anti-cancer treatment received by elderly cancer patients with solid tumors before they were admitted to the ICU mortality was not found to be significant (p=0.18), and the 90-day mortality risk ratio was calculated as 1.07 (10). In a study conducted by Xia assessing the prognosis in solid tumors, receiving chemotherapy and radiotherapy treatment before ICU did not make a difference in mortality (14). In our study, although the relative risk ratio for mortality in patients who underwent chemotherapy and radiotherapy in the last six months before ICU was 1.40, we did not find a significant difference.

Previous studies have shown that mortality is lower in patients admitted to the ICU for surgical reasons (15). In a study of elderly cancer patients, the odds ratio for hospital mortality in those admitted to the ICU due to emergency surgery was found to be 0.71 (95% CI 0.52–0.96) (16). In our study, we grouped patients with a history of surgery in the last six months before ICU admission and calculated the relative risk ratio for hospital mortality for these patients as 0.79. The average APACHE II scores were found to be similar between patients who underwent surgery and those who did not. While the estimated mortality rate for non-surgical patients with an APACHE II score between 25-29 was 55%, it was 35% for surgical patients (17). It is known that patients with a SOFA score between 7-9 have an expected mortality rate of 15-20% (18). The SOFA score in surgical patients was calculated to be lower compared to non-surgical patients. Although the lower mortality rate in surgical patients in our study was not statistically significant, we consider it to be consistent with the calculated APACHE II and SOFA scores. We lack sufficient data to assess the relationship between tumor type, origin, surgical resectability, and intensive care unit mortality, and this issue warrants further investigation with studies involving more comprehensive data.

The incidence of acute kidney injury in ICU ranges from 27% to 67% and is associated with increased mortality (19,20). Renal replacement therapy is one of the treatment options available for kidney injury, with an estimated 23.5% of patients with acute kidney damage potentially needing this treatment (21). Mortality was found to be higher in ICU patients who underwent renal replacement therapy (22). In our study, we observed that ICU and hospital mortality rates were higher in patients who underwent renal replacement therapy, similar to the findings in literature.

Some studies also indicate both similarities and differences in mortality rates between solid and hematological cancers. Studies by Na S et al. in Korea and Van Der Zee E et al. in the Netherlands found that ICU and hospital mortality were higher in hematological cancers than in solid tumors (23,24).

In the study conducted by Nassar A et al., hospital mortality odds ratios of metastatic solid tumors and hematological cancers were similar (16). In a review of studies on elderly cancer patients, the mortality rates of solid and hematological cancers in ICU processes were found to be similar (25). In our study, although the APACHE II score of hematological cancers was higher than that of solid tumors, there was no difference between ICU and hospital mortality. Additionally, the numerical distribution of solid tumors is not conducive to detailed analysis. Hematological tumors comprise only a quarter of the number and distribution of solid tumors. Due to the numerical discrepancy between the two groups, making a valid comparison is challenging. Therefore, this assertion remains open to discussion.

The fact that our study is a single-center retrospective study is regarded as an important limiting factor. Therefore, we think it would be inappropriate to generalize the results. Other limiting factors include the lack of cancer staging for the patients examined and the inability to obtain frailty score data, which is an important prognostic factor for the elderly.

In conclusion, the treatments administered can have a significant impact on the survival periods of elderly oncology patients in ICUs and hospitals. However, the number of patients who survive holds significant importance and should not be underestimated. Especially in patients aged 75 and older, their similarity in survival rates to those between 65 and 75 years underscores the effectiveness of intensive care treatment within this age group. Moreover, this information suggests that patients aged 75 and older may benefit from intensive care treatment, and avoiding treatment might not be appropriate. Non-surgical hospitalization and life-supporting treatments are factors that contribute to increased mortality. There is no significant difference in survival between hematological cancers and solid tumors. We advocate for studies that encompass pre-intensive care treatment options and underscore the importance of timely admission to the ICU to mitigate mortality in this patient group.

The authors of this study do not have any conflict of interest.

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