

Turkish Journal of GERIATRICS

Volume: 25 • Number: 3 • Year: 2022



The Official Scientific Journal of Turkish Geriatrics Society

e-ISSN: 1307-9948

www.turkgeriatri.org

www.turkgeriatri.org

e-ISSN: 1307-9948

The official scientific journal of Turkish Geriatrics Society

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Published four times (March, June, September, December) a year

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Date of Publication: 30 September 2022

Turkish Journal of
GERIATRICS
Volume: 25 • Issue: 3 • Year: 2022

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From The Editor In Chief

The 7th edition of the **SCIENTIFIC RESEARCH COURSE IN THE FIELD OF GERIATRICS**, which is regularly organized by the Turkish Geriatrics Society, will be held on-line on 24-26th Nov, 2022.

Course topics include: Scientific researches on elder persons, Aging and evidence-based medicine practice, Rules to be considered in the planning of scientific research, Types of researches; general information and approaches, Observational studies, Experimental studies, Clinical drug researches, Animal researches, Clinical research on Aging in primary care, Validity and reliability studies, Preparing an application file for the ethics committee, How to read a scientific article? The mission of the editor and the referees, Journal selection for your article, Common problems and recommendations to authors, Special agenda: Current global health problems and old age research (COVID-19, Monkey Pox, etc.).

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Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2022.293
2022; 25(3): 347-350

■ Alfonso J. CRUZ-JENTOFT[1]

EDITORIAL

INTRODUCING SARCOPENIA IN CLINICAL PRACTICE IN TURKEY

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Received : Aug 15, 2022
Accepted : Aug 15, 2022

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Research on sarcopenia has grown in recent years in such an explosive manner that no practicing geriatrician is now unfamiliar with the term. However, this explosion is not yet translated, in most cases, into better patient care and improved outcomes, including falls, fractures, physical function, hospitalizations and mortality (1-3). In order to improve the clinical uptake of sarcopenia some organizations fostered coding of this condition in the clinical modification of the international classification of diseases (ICD-10-CM, code M62.84) (4), the newest definitions have incorporated simplified algorithms to be used in clinical practice (5,6), clinical guidelines have been developed (7,8) and research on screening tools is growing (9).

However, sarcopenia seems to be yet far for mainstream. A survey of healthcare professionals working in the national health system of the United Kingdom showed than only half of the respondents organizations identified sarcopenia, but most did not use any formal criteria to diagnose the condition and only one of the surveyed centres reported using a code for the disease (10). A similar survey in Australia and New Zealand found that less than 15% of the practitioners reported making the diagnosis of sarcopenia in their patients, and this situation was unchanged by an educational intervention (11). The situation seemed to be slightly better in the Netherlands, were 21% of the respondents of a survey reported to know how to diagnose sarcopenia and up to 82% had treated patients with the condition, but most were unaware of diagnostic tools and instruments (12). There are no similar surveys in Turkey, but there is no hint that the global picture will be different.

The prevalence of sarcopenia in Turkey has been well studied in most clinical settings. It seems to be low in the community, ranging

from 0.8% to 5.2% , depending on the instrument used to diagnose it and population characteristics (13, 14), but prevalence raises to some 14% in older inpatients (15) and can be as high as 29% to 85% in older people living in nursing homes (16,17). As sarcopenia carries a risk of impaired outcomes, including mortality, there is an evident need to detect and intervene, and Turkey seems to be better prepared than other countries to incorporate sarcopenia screening, diagnosis and treatment into mainstream practice, as has been claimed for long (18,19). This country is well represented in sarcopenia research, with several active groups in different universities (20, 21). There is plenty of information on the validity of screening tools in Turkish (22, 23), that have showed that many patients can be detected when at risk, before they develop the full condition. In fact, sarcopenia risk is also associated with unfavourable health care outcomes including dependency, malnutrition, and dysphagia (24, 25).

There is also plenty of information on cut-off points for different measures of muscle mass and muscles strength in Turkish population, based on studies in healthy young populations, that allow for a better detection and to adjust for height, weight or body mass index (24-26). A measure of sarcopenia-related quality of life (SARQOL) has also been translated and validated in Turkish (27).

Many things can be done to improve diagnosis and management of sarcopenia. Some depend on advances in research and consensus or in political decision making. For instance, a worldwide initiative to agree on a global definition of sarcopenia is ongoing (28) and updated clinical guidelines are needed. Also, sarcopenia needs to be included in the WHO International Classification of Diseases – at present it is only listed in the version named Clinical Modification and the latest version ICD-11 does not properly include sarcopenia. Implementation of ICD in Turkey is, however, still low.

Many other initiatives may be performed locally. Better education and training of healthcare professionals, routine screening in high risk settings, improved availability of diagnostic tools (bioimpedance, DXA, dynamometers) and of referral centres for sarcopenia, local clinical guidelines with well-defined clinical pathways for patients, and availability of nutritional and exercise advice that can deliver interventions that have been shown to reduce disability (29) would be steps in the right direction. Doctors who treat older patients should consider if their practices on the diagnosis and management on sarcopenia are appropriate to current knowledge or need rethinking and new training, turning their eyes back on patients (30).

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RESEARCH

COMPARISON OF SPINOPELVIC PARAMETERS AMONG OLDER ADULTS WITH LUMBAR SPONDYLOSIS, LUMBAR FRACTURES AND LUMBAR SPINAL STABILIZATION

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2022.294
2022; 25(3): 351-357

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Received : Jun 02, 2022
Accepted : Aug 04, 2022

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Abstract

Introduction: In elderly individuals, sagittal plane deformities may be iatrogenic due to aging. Fractures due to osteoporosis, as well as previous surgeries, can cause resistant lower back pain. As a result of pathologies, degeneration can occur in the spinal joints, excessive tension in the paravertebral muscles, and compensatory changes occur in the pelvis respectively. These changes were evaluated with spinopelvic parameters. Our aim was to compare the spinopelvic parameters in patients over 65 years of age who presented to the clinic with lower back pain.

Materials and Methods: Measurements of the angles for spinopelvic parameters characterizing the alignment of the sacrum (sacral slope), the pelvis (pelvic tilt, pelvic incidence) and the lumbar lordosis were calculated based on X-ray imaging analysis.

Results: The records of 122 patients were included. Their mean age was 73.5 ± 5.70 years. Patients were divided into three groups: as those with spondylosis, lumbar fractures and lumbar stabilization. While a significant decrease was observed in lumbar lordosis in the group with lumbar vertebral fractures ($p = 0.019$), no significant difference was observed between the groups in pelvic incidence, sacral slope and or pelvic tilt ($p > 0.05$). No gender differences in spinopelvic parameters was observed. No differences were detected in spinopelvic parameters between age groups below and above 75 years.

Conclusion: A remarkable decrease in lumbar lordosis was seen in patients with lumbar fractures. Careful evaluation of spinopelvic parameters before planning the treatment can increase the probability of successful treatment of resistant lower back pain in the elderly.

Keywords: Geriatrics; Spinal Curvatures; Spinal Fractures; Fracture Fixation; Spondylosis.

INTRODUCTION

An ideal spinal alignment allows for standing independently with minimal muscular energy expenditure. Pathologies occurring in the frontal and sagittal plane increase the energy used by the spine to maintain its posture together with the load on the vertebrae, muscles and ligaments (1). As a result, degeneration occurs in the spinal joints, excessive tension in the paravertebral muscles, and compensatory changes in the pelvis. These changes were evaluated with spinopelvic parameters (2). The pelvic tilt (PT) angle, which is closely related to pain and disability, is an indicator of the degree of retroversion of the pelvis (3). The PT and sacral slope (SS) are positional parameters that vary according to the position of the pelvis. SS is measured as the angle of the sacral plateau to the horizontal plane, which determines the position of the lumbar spine. Pelvic incidence (PI), called an anatomic parameter, plays a key role in achieving sagittal balance; it determines the relative position of the sacral plateau in relation to the femoral heads and does not change with the presence of fractures, degenerative changes or aging (1, 3-4).

Recent research has emphasized the key role of spinal sagittal balance and investigated spinopelvic parameters in healthy volunteers (5-9). Aging is an important factor that affects lumbosacral alignment (5-6, 10). Age-related changes in the vertebra, degeneration of disks and ligaments, and weakness of back muscle strength contribute to these variations (1, 10-11).

In elderly individuals, sagittal plane deformities may be iatrogenic due to aging; fractures due to osteoporosis, as well as previous surgeries, can cause resistant lower back pain (1, 10, 12-13). Additionally, patients change their postures while trying to cope with back pain (6, 10, 12).

The aim of the present study was to compare the spinopelvic parameters of geriatric patients with lower back pain due to posterior instrumentation, lumbar spinal spondylosis and/or lumbar fractures.

MATERIALS AND METHOD

Sample and study design

This retrospective cross-sectional study was approved by the Institutional Review Board (IRB approval no. 2018/218). The number of patients for the research—which had three independent groups, 80% strength, type 1 error (alpha) 0.005, and effect size 0.290—was calculated as a total of 120 samples. The records of 122 patients over the age of 65 who applied to a polyclinic with lower back pain between May 2018 and September 2018 were reviewed. The patients were divided into three groups: those with lumbar spondylosis, lumbar vertebral fracture and lumbar stabilization. Standing lateral lumbar radiographs were obtained from the electronic hospital database for the calculation of spinopelvic parameters. Patients who had a congenital spinal deformity, total hip arthroplasty, ≥ 2 lumbar fractures, or long-level spinal fusion (>4), scoliosis, who were below the age of 65, or who had inappropriate radiographs were excluded from the study.

The spinopelvic parameters (LL, PT, PI, SS) were calculated as shown in Figure 1. All measurements were carried out with the same angle meter by two experienced researchers.

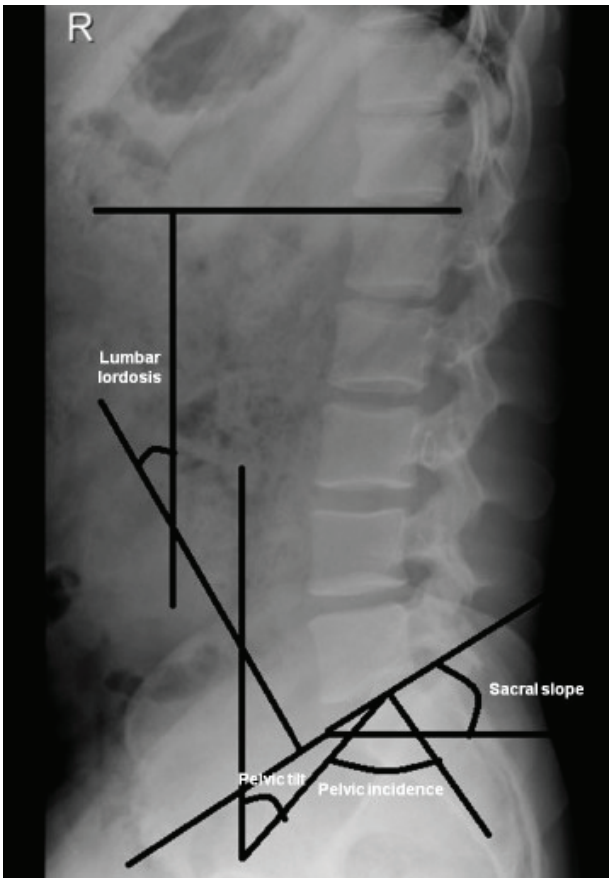
LL is defined as the angle between the line that passes through the upper-end plaque and the line drawn perpendicularly to the line that passes through the sacral-end plaque. The normal lumbar lordosis is between 40° and 70° when a distance of L3–4 is taken as the peak.

PI is the angle between the perpendicular line that passes through the midpoint of the upper sacral end-plaque and connects the femur head axis to this midpoint.

SS is the angle between the line that is drawn from the sacral-end plaque and the horizontal line that is drawn from the midpoint of the upper sacral-end plaque.

PT is the angle between the vertical line that passes through the femur head axis and the line

Figure 1. Radiographic image showing the reference line for measuring pelvic incidence (PI).



pelvic tilt (PT), lumbar lordosis (LL), sacral slope (SS)

that connects the sacral end-plaque midpoint of the femur head axis.

Ethical approval

This study was conducted in compliance with the principles of the Declaration of Helsinki. It was approved by the Institutional Review Board (IRB approval number, 2018/218)

Statistical analysis

Statistical analysis was performed using IBM SPSS 22.0 software. Descriptive statistics were calculated for age, gender, PI, SS, PT and LL [frequencies, percentages, mean ± SD, median (25^{th}%–75^{th}%)]. The normality of the data was evaluated using the Shapiro–Wilk and Kolmogorov–Smirnov tests. The Chi-square test was used to compare the qualitative data of gender and age in those over 75 years and those below. In comparing the quantitative data, to compare the lumbar spondylosis, lumbar vertebral fracture and lumbar stabilization groups for a normally distributed pelvic incidence, a one-way analysis of variance (ANOVA) test was employed. The Kruskal–Wallis test was employed to make the comparison among the parameter groups for non-normally distributed SS, PT and LL; the Tukey HSD test was used to determine the group that caused the difference and to compare gender and age in those above 75 and younger groups. Student's t-test was used for normally distributed PI, and the Mann–Whitney U test was used for non-normally distributed SS, PT and LL. A p value < 0.05 was considered statistically significant.

RESULTS

A total of 357 patients aged 65 years and above were examined. The records of 122 patients (89 females, 33 males) were included. The mean values of PI, SS, PT and LL were 56.40 ± 14, 38.84 ± 11, 17.41 ± 9.2 and 39.84 ± 15.9, respectively (Table 1).

No differences were detected between genders in the measurements of PI, SS, PT and LL values (p

Table 1. Demographic data of the patients

	N = 122
Age	73.53 ± 5.70; 73 (69–77)
Gender (F/M) (%)	89/33 (73/27)
Pelvic Incidence (PI)	56.40 ± 14; 57 (46–65)
Sacral Slope (SS)	38.84 ± 11; 40 (32–46)
Pelvic Tilt (PT)	17.41 ± 9.2; 16 (10–23)
Lumbar Lordosis (LL)	39.84 ± 15.9; 43 (30–51.3)

Values presented in mean ± SD, median (25th–75th%)

values: 0.458, 0.621, 0.793 and 0.084, respectively) (Table 2).

No differences were detected in spinopelvic parameters between the age groups below and above 75 (Table 3).

When the three groups were compared, the median age of those who had fractures was significantly higher (p = 0.007). There were no differences between PI, SS and PT measurements in the three groups (p > 0.05). Statistically significant differences were detected between the LL measurements (p = 0.019), and the angle of LL was significantly lower in the group with lumbar vertebral fracture (Table 4).

Table 2. Spinopelvic parameter measurements with respect to gender

	Female (N = 89)	Male (N = 33)	p
PI	59.98 ± 4.36	54.85 ± 13.04	0.458
SS	39.15 ± 11.20	38.03 ± 10.57	0.621
PT	16.0 (10.0–24.0)	16.0 (10.0–20.0)	0.793
LL	43.0 (32.0–51.5)	34.0 (17.0–51.0)	0.084

Values presented in mean ± SD, median (25–75), Significance of p < 0.05, Simple T test
PI (pelvic incidence), SS (sacral slope), PT (pelvic tilt), LL (lumbar lordosis)

Table 3. Spinopelvic parameter measurements with respect to age groups

	Age < 75 (N = 76)	Age ≥ 75 (N = 46)	p
PI	56.56 ± 13.95	56.13 ± 14.23	0.869
SS	39.13 ± 10.95	38.37 ± 11.19	0.712
PT	18.0 (12.0–22.8)	15.0 (10.0–23.3)	0.659
LL	43.0 (32.3–50.8)	38.0 (23.8–52.0)	0.420

Values presented in mean ± SD, median (25-75), Significance of p < 0.05, Simple T test
PI (pelvic incidence), SS (sacral slope), PT (pelvic tilt), LL (lumbar lordosis)

Table 4. Spinopelvic parameter measurements of the groups

	Spondylosis	Those with fractures	Those undergoing stabilization	p
N (%)	57 (46.7)	31 (25.4)	34 (27.9)	
F/M(%)	44/13 (77.2/22.8)	19/12 (61.3/38.7)	26/8 (76.5/23.5)	0.238
Age	73.0 ± 6.13;71 (68–77)	76.16 ± 5.25; 74 (72–81)	72.03 ± 4.58; 71.5 (68–76.3)	0.007*^{K}
PI	57.14 ± 15.36; 59 (44–68)	55.96 ± 13.2; 55 (48–64)	55.56 ± 12.6; 55 (47.5–65)	0.858
SS	39.0 ± 11.42; 40 (30–47)	37.84 ± 10.14; 37 (31–44)	39.5 ± 11.3; 40 (33.5–45.3)	0.825
PT	18.14 ± 9.12; 16 (11–24)	17.55 ± 9.57; 18 (10–20)	16.06 ± 9.12; 15 (9.5–20.8)	0.599^{K}
LL	42.23 ± 15.27; 43 (32–52)	32.38 ± 17.9; 30 (20–48)	42.62 ± 13.2; 44.5 (37.5–51.3)	0.019*^{K}

Values presented in mean ± SD, median (25th–75th%), *Significance of p < 0.05; K: Kruskal–Wallis Test
PI (pelvic incidence), SS (sacral slope), PT (pelvic tilt), LL (lumbar lordosis)



DISCUSSION

The present study represents a retrospective, cross-sectional analysis of spinopelvic alignment in older adults as studied through lateral standing lumbosacral radiographs. Based on our findings, a remarkable decrease in LL was seen in the lumbar fracture group. Gender differences were not detected in the measurements of spinopelvic parameters.

Few studies have been conducted on the spinopelvic parameter assessment of adults aged above 50 years. Most studies so far have been conducted on the surgical correction of spinal deformities in younger populations. LL is effective in maintaining a straight posture. Young adults decrease the thorasic kyphosis to compensate for changes in LL. As a result of non-flexible columns in older adults, this compensation is not sufficient and contributes to sagittal imbalance (10). In our study with a geriatric population, the LL values were significantly lower in the fracture group. Dai's study showed that those with low LL have a higher risk of vertebral fracture, and LL was determined to be low in postmenopausal women with fractures (14). Since the previous radiographs of the patients were not evaluated in our study, a low LL value may be a risk factor for lumbar fracture as well as a result of lumbar fracture.

Flatback syndrome is a postural disorder of the spine due to the loss or decrease in LL. Although generally defined as post-fusion LL loss, it may also be seen in pathologies such as ankylosing spondylitis without surgery, diffuse idiopathic skeletal hyperostosis and Scheuermann's disease (15). Although lumbar fusion relieves resistant lower back pain, it may cause acceleration in the degeneration in the segments that are adjacent to the segments fixed after instrumentation and may lead to flatback syndrome (16). Indeed, a study by Gottfried et al. found a reduction in LL in patients with iatrogenic flat backs (17). In our study, on the other hand, a significant decrease in LL was detected not in those who underwent stabilization but in the group with fractures. This may be because of the inclusion of patients who had short segment fusion in our study.

Different results were reported in previous studies that examined the relationship between age and spinopelvic parameters. In a study to describe changes in spinopelvic parameters in 132 Korean adult male volunteers over 50 years of age, similar spinopelvic parameters were observed, with a tendency for thoracic kyphosis to increase with age (18). Similarly, a study investigating age-related changes in spinal alignment in asymptomatic Japanese individuals found no correlation between lumbosacral parameters and aging (19). On the contrary, Kobayashi et al. reported a decrease in LL with age (20). Yukawa et al. showed that there was a decrease in LL with advancing age, while there was a remarkable decrease in LL from the 7th to the 8th decade (6). Ethnicity and different measurement methods and sample sizes may lead to these different results (13).

We found no relationship between gender and spinopelvic parameters. Similarly, few studies have found any differences in lumbosacral parameters between female and male asymptomatic volunteers (7-8). Contrary to our results, some studies have reported that female patients had higher lumbar lordosis (21, 22). These conflicting results may be a result of different sample sizes or selection bias.

The PT angle varies between 12.1–13.2° in the healthy population (9, 23). When LL decreases, an increase occurs in PT because of the backward rotation of the pelvis, and an increase in PT might occur as a compensatory mechanic to maintain sagittal balance (6). In our study, consistent with the literature, the mean value of PT was 17.41 ± 9.2.

Preoperative measurement of the spinopelvic parameters of patients who will undergo surgery for spinal deformity is particularly important. Lafarge et al. stated that patients who had high PI values had negative results following pedicle extraction osteotomy for thoracic kyphosis restoration and that patients who had low PI values were likelier to

be satisfied compared to patients who had high PI values (24). Since this is a retrospective study, the lack of preoperative spinopelvic parameters and the inability to question the postoperative satisfaction of the patients are the limitations of this study. Geometrically, PI is equal to the sum of PT and SS. PT changes inversely to SS, while PI remains constant and does not change with age. In a study that included an adult population over 60 years of age, the PI, PT and SS values were calculated as 51 ± 9, 16 ± 9 and 36 ± 9, respectively (25). In our study, PI was measured as 56.40 ± 14. This may be due to ethnic differences. The PI is considered to be an inherent value. A pelvis with a higher PI has a large anteroposterior axis; it is a large horizontal pelvis with a higher possibility of retroversion (1).

There were several limitations to our study. The body mass index affecting the lumbosacral alignment cannot be taken into account, since the study is based on retrospective records. Only symptomatic elderly patients were enrolled in this study. The fact that the female patients outnumbered the male patients presented a potential bias. We could not assess the clinical impacts of lumbosacral parameters. It seems that more attention being paid to other factors, such as the duration of symptoms, comorbidities and environmental or physical exposures could increase the value of the study's results.

Despite the aforementioned limitations, this study revealed the importance of sagittal alignment differences in geriatric populations for degenerative spinal disease, lumbar fracture or posterior fusion. A marked decrease in LL was seen in the lumbar fracture group. A recent meta-analysis demonstrated a strong relationship between lower back pain and decreased LL, especially when compared to age-matched healthy controls (12). Lumbosacral alignment, particularly LL, which affects sagittal balance, is pivotal to sustaining proper upright posture and reducing fall risk in elderly populations. For this reason, spinopelvic parameters should be evaluated carefully in older adults with lower back pain, and those with lumbar fractures should be referred to a surgeon in light of their medical condition.

In conclusion**,** a remarkable decrease in lumbar lordosis was seen in elderly individuals with lumbar fractures. Degenerative processes, iatrogenic causes and vertebral fractures affect spinal sagittal alignment. Patients with impaired sagittal alignment spend a lot of energy to stand up, and they also fight pain. Careful evaluation of spinopelvic parameters before planning the treatment can increase the probability of successful treatment of resistant lower back pain in the elderly.

Conflict of Interest

The authors declare that they have no conflicts of interest.

Funding

The authors declare that this study received no financial support.

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RESEARCH

EVALUATING THE SYSTEMIC IMMUNE-INFLAMMATION INDEX FOR ADVERSE OUTCOMES IN ELDERLY ACUTE CORONARY SYNDROME PATIENTS

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2022.295
2022; 25(3): 358-366

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Received : Jul 18, 2022
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Abstract

Introduction: Acute coronary syndrome is a fatal clinical manifestation of coronary artery disease. A newly defined index—Systemic Immune–Inflammation Index—has recently been reported to have prognostic value in patients with cardiovascular disease. This investigation was aimed at evaluating the systemic immune-inflammation index predictive value for in-hospital and 1-year follow-up clinical outcomes in elderly patients with acute coronary syndrome.

Materials and method: We retrospectively enrolled 910 consecutive patients in the study. We divided the patients into two groups: young patients with acute coronary syndrome (Group 1) and elderly patients with acute coronary syndrome (Group 2). The patients were followed up on for one year. We compared the two groups' systemic immune-inflammation index results, neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio.

Results: The neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and systemic immune-inflammation index were significantly higher in Group 2. According to multivariate logistic regression analyses, systemic immune-inflammation index, and platelet-to-lymphocyte ratio ($p < 0.001$, and $p = 0.013$, respectively) emerged as independent predictors of in-hospital mortality in Group 2. Group 2 had significantly worse in-hospital mortality rates than those of Group 1. However, the groups' long-term outcomes were similar.

Conclusion: High systemic immune-inflammation index values were independently associated with an elevated risk of in-hospital mortality in Group 2. This investigation may be the first to demonstrate that this index is independently linked with in-hospital and long-term mortality in elderly acute coronary syndrome patients. It could be used as an easy, inexpensive, and practical predictor to identify high-risk elderly patients with acute coronary syndrome.

Keywords: Acute Coronary Syndrome; Inflammation; Aged.

INTRODUCTION

Cardiovascular disease is one of the most common causes of morbidity and mortality around the world and was responsible for approximately 17.7 million deaths in 2017 (1). Acute coronary syndrome (ACS) is an acute and lethal clinical manifestation of extensive coronary artery disease (CAD) that causes more than one-third of all deaths in developed nations annually (2). Advances in primary and secondary prevention have helped reduce disease incidence rates. However, compared to younger patients, elderly patients with ACS have a higher risk of death, complications, and decreased functional capacity (3).

Inflammation plays a key role in the formation and progression of atherosclerosis (4). Moreover, a correlation has been found between the inflammatory markers of this process and the high severity of and poor prognosis related to CAD. The vascular bed's inflammatory and immune cells, such as white blood cells and white blood cell subtypes (e.g., neutrophils, monocytes, and lymphocytes), reflect systematic inflammation severity and play an important role in AMI's mortality and morbidity (5). Therefore, in addition to the traditional risk factors, the distribution of cells in the complete blood count has begun to be evaluated among CAD's predictors in the interventional cardiology era.

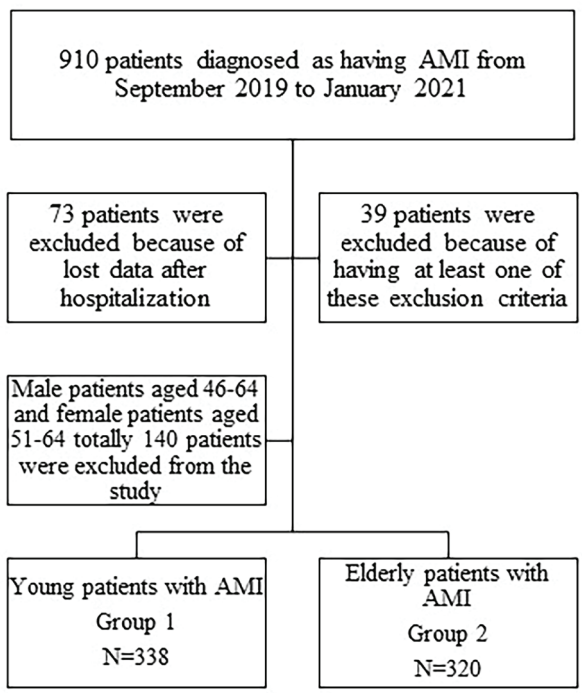
Recently, the Systemic Immune–Inflammatory Index (SII), derived from the distribution of blood cells, was developed. The SII is used to determine prognosis in various cardiovascular diseases and cancer types (6). It is based on platelet, neutrophil, and lymphocyte counts (7). Studies on cardiovascular diseases are a good predictor of in-hospital and long-term clinical outcomes in patients with chronic heart failure, CAD, and ACS (8,9). Nevertheless, the SII's prognostic role related to morbidity and mortality in elderly patients with ACS has not yet been evaluated. In our study, we examined the SII's prognostic value in young and elderly ACS patients during one year of follow-up.

MATERIALS AND METHOD

Study population

Between September 2019 and January 2021, we retrospectively enrolled 910 patients (aged 18–80 years) in our study. All patients were diagnosed with acute myocardial infarction (AMI) and underwent coronary artery angiography (CAG). We excluded 39 patients according to the exclusion criteria. We excluded 73 patients because some of their data were lost after hospitalization. We excluded male patients aged 46–64 years and female patients aged 51–64 years from the study. Finally, we included 658 patients in this study. We divided the patients into two groups: young patients with AMI (Group 1) and elderly patients with AMI (Group 2; Figure 1). We included male patients up to 45 years old and female patients up to 50 years old in the young AMI group. We included patients 65–80 years old in the elderly AMI group. We defined AMI according to

Figure 1. Study flow diagram



the diagnostic criteria of the European Society of Cardiology's non-ST-elevation myocardial infarction (NSTEMI) guidelines published in 2020 and the ST-elevation myocardial infarction (STEMI) guidelines published in 2017 (10,11).

We obtained the study population's demographic characteristics from their hospital records. The exclusion criteria were being aged under 18 years or over 80 years, experiencing changes in inflammatory or immune markers other than AMI (e.g., autoimmune diseases, sepsis, trauma, recent major surgery, and active malignancy), having a glomerular filtration rate of less than 30 ml/min, having severe hepatic failure, receiving thrombolytic therapy, and being pregnant. The local ethics committee approved the current study, and we conducted the research in compliance with the Declaration of Helsinki.

Blood sample test analysis

Fasting blood samples were obtained from the participants' peripheral veins. Their fasting glucose levels, cholesterol panels, and renal function tests were measured using a Roche Cobas 6000 analyzer. Blood samples were obtained for the calculation of SII values upon participants' admission to the hospital. Complete blood count parameters were measured using an auto hematology analyzer (BC 6800 Mindray Medical Electronics Co. Shenzhen, China). The participants' SII values were calculated according to the following formula at admission: SII = platelet count × neutrophil count ÷ lymphocyte count. Platelet–lymphocyte ratios (PLR) were calculated according to the following formula: platelet count ÷ lymphocyte count (12). Neutrophil–lymphocyte ratios (NLR) were calculated according to the following formula: neutrophil count ÷ lymphocyte counts (12).

Coronary artery intervention

According to Judkins' technique, coronary artery interventions were performed via the patients' femoral arteries. Based on the current guidelines, all the patients received aspirin (300 mg), clopidogrel (300–600 mg), ticagrelor (180 mg), and prasugrel (60 mg) as antiplatelet therapy before coronary intervention (10,11). Heparin and, if necessary, tirofiban therapy were administered during the perioperative period. According to the patients' angiography results and clinical findings, the doctors selected current practice guidelines.

Transthoracic echocardiography

Echocardiographic measurements were performed using the Philips Affinitti 70 ultrasound system (Medical Healthcare Solutions, Inc.; Andover, MA, USA) with an S4-2 transducer probe. Transthoracic echocardiographic analyses were performed by two cardiologists who were blinded to the study groups. Single-lead echocardiographic recordings were simultaneously obtained during the echocardiographic recordings. Two-dimensional, M-mode, and color-flow Doppler echocardiography were performed according to the current guidelines (13). Left ventricular (LV) end-diastolic dimensions, interventricular septum, and left ventricular posterior wall thicknesses were measured from the parasternal-long-axis and apical four- and five-chamber views and averaged. LV ejection fractions were measured using the Biplane Simpson method in the apical four-chamber view.

Follow-up and study end points

The study's clinical end points included all-cause mortality and major adverse cardiovascular events. We assessed in-hospital mortality (during the participants' hospital stays) and long-term mortality (up to one year of follow-up). All-cause mortality was the study's primary end point. The major adverse cardiovascular events included rehospitalization for severe heart failure, nonfatal myocardial infarction (MI), and nonfatal stroke. We defined severe heart failure according to the New York Heart Association (NYHA) Classification Class IV. We defined ischemic stroke as obstruction within a blood vessel supplying blood to the brain evidenced by either magnetic resonance imaging (MRI) or computed tomography

(CT) scans and a new neurologic deficit lasting for at least 24 hours. We defined all-cause mortality as death from any cause during the one-year follow-up period. We reviewed the participants' medical records to confirm their primary clinical outcomes and mortality statistics. The patients were followed up on from September 2019 to January 2022.

Statistical analysis

We used IBM SPSS Statistics for Windows, version 18.0 (IBM Corp., Armonk, NY, USA), to perform the statistical analysis. We used the Kruskal–Wallis test to assess the normality of the variables' distributions. We expressed each quantitative variable with a normal distribution as its mean ± standard deviation, and we expressed each abnormally distributed variable as its median (25th–75th percentile). We expressed categorical variables as numbers and percentage values. We assessed the abnormally distributed variables using the Mann–Whitney U test, whereas we assessed the normally distributed variables with independent samples t-tests. We analyzed the categorical variables using chi-square tests. We obtained the survival curve using Kaplan–Meier analysis and the log-rank test. Logistic univariate regression and multivariate regression analysis identified factors related to clinical end points.

RESULTS

Our study population's basal demographic characteristics, laboratory results, and transthoracic echocardiographic findings are presented in Tables 1 and 2. There was no difference between the two groups in terms of basal demographic characteristics. Decisions of PCI occurred more often in Group 1 than in Group 2 ($p < 0.001$). The in-hospital mortality, first month mortality rate, the six-month mortality rate, and the first-year mortality rate were higher in Group 2 than in Group 1 ($p = 0.025$; $p = 0.032$, $p= 0.028$, and $p= 0.032$, respectively). The two groups' fasting glucose, high-density lipoprotein, triglycerides, and serum creatinine levels were similar. Group 1's total cholesterol and low-density lipoprotein levels and its neutrophil, lymphocyte, and platelet counts were significantly higher than those of Group 2. Group 2's median NLR and PLR values were significantly higher than those of Group 1. Moreover, Group 2's SII values and C-reactive protein (CRP) levels were higher than those of Group 1 ($p < 0.001$ and $p < 0.001$, respectively).

The logistic regression analysis results we achieved using one model, including continuous SII, PLR, CRP, serum creatinine, and categorical HT values, to detect dependent and independent predictors of in-hospital mortality in the elderly are presented in Table 3. According to multivariate logistic regression analyses, SII and PLR values ($p < 0.001$) were independent predictors of in-hospital mortality in elderly patients.

Twenty-two (3.34%) patients died during hospitalization in this study population, and 11 (1.6%) died during follow-up. Group 2 had significantly worse in-hospital mortality than Group 1 (Figure 2; logrank test $p = 0.013$).

Figure 2. The comparison of both groups Kaplan-Meier cumulative survival curves for in-hospital mortality

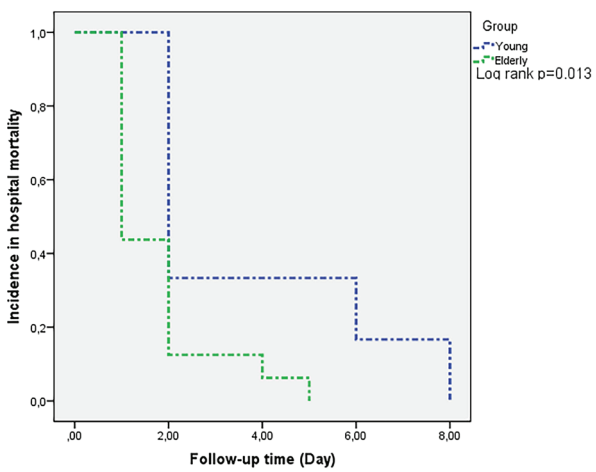


Table 1. Demographic and clinical characterictics of the groups

	Group 1 (n=338)	Group 2 (n=320)	*p**
Male	277 (82.7%)	264 (82.5%)	0.809*
Age	41.62 ±4,82	70.52±4.1	<0.001**
Type of ACS	STEMI=174 (51.5%)	STEMI=176 (55%)	0.377*
History of CAD	38 (11.2%)	36 (11.3%)	0,548*
HT	52 (15,6%)	46 (14.4%)	0.375*
HL	8 (2.4%)	4 (1.3%)	0.213*
DM	60 (18%)	64 (20%)	0.286*
Smoking	210 (62.9%)	194 (60.6%)	0.301*
Decision of PCI	PCI= 304 (91%)	PCI =246 (76.9%)	<0.001*
In hospital mortality	6 (1.8%)	16 (5%)	0.025*
Days of in hospital mortality	5.33 ±1.94	2±0.68	0.001**
Mortality rate of first month	0 (0%)	2 (0.62%)	0.032*
Mortality rate of 6. Month	2 (0.59%)	5 (1.56%)	0.028*
Mortality rate of first year	0 (0%)	2(0.62%)	0.032*
MACE of first month	16 (5.2%)	19 (5.8%)	0.528*
MACE of sixth month	21 (6.31%)	25 (7.81%)	0.253*

ACS:Acute coronary syndrome ; CAD: Coronary artery disease; PCI: Percutaneous coronary intervention; DM: Diabetes mellitus; HL: Hyperlipidemia; HT: Hypertension; MACE: Major advers cardiovascular event; STEMI: ST elevation myocard infarctus

*: Fisher's Exact Test.

**: Independent sample Student t test

DISCUSSION

This study revealed that SII and PLR values are independent predictors of in-hospital mortality in elderly patients. To our knowledge, this study is the first in the literature to investigate the SII's predictive value in elderly patients with ACS.

Inflammation plays a highly important role in the development of many diseases, such as malignancy, metabolic diseases, and cardiovascular diseases. The determination of inflammation's active role in the development of atherosclerosis has drawn researchers' attention. Neutrophils, lymphocytes, and platelets also play significant roles in this process (14,15).

Neutrophil infiltration into endothelial tissue is associated with the initiation and progression of atherosclerosis, which causes damage to the endothelium. Moreover, neutrophils secrete inflamma-

Table 2. Laboratory tests and transthoracic echocardiography results of the groups

	Group 1 (n=338)	Group 2 (n=320)	*p*
Glucose (mg/dL)	106 (88.25-130.75)	109 (102.5-130)	0.181 **
Total cholesterol (mg/dL)	193.5 (163.25-227.5)	181 (150-212)	<0.001**
LDL (mg/dL)	120 (97.3-151)	114.2 (84.05-114.7)	<0.001**
HDL (mg/dL)	36 (31-43)	37 (34-42)	0.095**
Triglycerides (mg/dL)	165 (114-279.7)	146 (87-184)	0.129**
Serum creatinine (mg/dL)	0.91 (0.73-1.01)	0.98 (0.81-1.13)	0.251**
Neutrophil (N) count ($\times 10^3$/µL)	9.08 ±3.67	8.33±3.77	0.004*
Lymphocyte (L) count ($\times 10^3$/µL)	2.49 (1.81-3.3)	1.84 (1.3-2.54)	<0.001**
Platelets (P) ($\times 10^3$/µL)	264.85±79.83	248.77±70.57	0.022*
N/L ratio	2.96 (2.13-5.29)	3.92 (2.35-6.93)	<0.001**
P/L ratio	97.15 (72.19-150.81)	133.16 (92.59-178.67)	<0.001**
SII index	1134.77±284.09	1500.48±353.74	<0.001*
C – reactive protein (mg/dL)	0.83 (0.22-4.15)	1.92 (0.5-5.59)	<0.001**
Ejection Fraction (%)	50.97±10.75	49.48±10.58	0.103*

dL: deciliter;; HDL: High density lipoprotein; ıqr: Interquartile range; LDL: Low density lipoprotein; mg:Miligram; uL: microliter; SII: Systemic immune-inflammation index.

*: Independent sample T test

**: Mann Whitney U test

Table 3. Predictors of in-hospital mortality in elderly patients by logistic regression analysis

Variables	Univariate		Multivariate	
	OR (95 % CI)	*p* value	OR (95 % CI)	*p* value
HT	0.481 (0.148-1.561	0.250		
Serum creatinine (mg/dL)	5.808 (0.853-39.545)	0.072		
P/L ratio	0.993 (0.984-1.002)	0.044	0.975 (0.957-0.995)	0.013
SII	1 (1-2.801)	<0.001	1.005 (1.003-3.527)	<0.001
C-reactive protein (mg/dL)	0.890 (0.753-1.052)	0.173		

Nagelkerke R square= 0.809; -2 Log likelihood= 27.828; p= <0.001

dL: Deciliter; HT: Hypertension, mg: miligram; L: Lymphocyte; P: Platelet; SII: Systemic immune-inflammation index.

tory mediators, which are associated with acute inflammatory responses after tissue injury (16). Unlike neutrophils, a low lymphocyte count in a coronary artery patient is a poor prognostic indicator (17).

In this inflammatory process, lymphocytes are mostly associated with modulation of the immune system. Whereas neutrophils are associated with a destructive inflammatory response (18), platelets play an important role in inflammation, thrombosis, and atherogenesis. Additionally, platelets release various inflammatory mediators that can further activate platelets and create a vicious cycle (19,15).

After demonstrating that these cells may have a predictive role in the development of CAD, information such as NLR, PLR, and SII values has been brought to the forefront. It has been concluded that these ratios might be more valuable than evaluating cells alone. Therefore, many studies have been conducted on this subject. Sari et al. investigated the relationship among NLR, PLR, and CAD severity in patients undergoing coronary angiography and found that NLR and PLRs were significantly correlated with SYNTAX and Gensini scores (20). Another study, which contained 414 patients, revealed that the NLR is associated with CAD severity in patients with NSTEMI (21). In another study, admission NLR values were an independent predictor of all-cause mortality in patients with ACS (22).

Cicek et al. assessed the effectiveness of a combination of NLR and PLR values in predicting in-hospital and long-term mortality in patients with STEMI. They concluded that neither NLRs nor PLR alone were independent predictors of all-cause mortality. In contrast, the use of these ratios combined provided significant prognostic information (23). Our study's findings are supported by the abovementioned studies. In this study, the elderly patients' median NLR and PLR values were higher than those of the young patients. Additionally, PLR was an independent predictor of in-hospital mortality in the elderly group.

Thus far, inflammatory parameters, such as white blood cells, NLR, PLR, CRP, and some interleukins, have been reported to be associated with atherosclerosis (15,4). Seo et al. described the SII, which gathers neutrophil, lymphocyte, and platelet cell counts, as a prognostic marker in congestive heart failure (24). Yang et al. reported that the SII resulted in better risk prediction than traditional risk factors for death, congestive heart failure, and major adverse cardiovascular events in patients with CAD (25). Huang et al. evaluated 711 elderly AMI patients and found that the SII was a potential indicator for predicting all-cause mortality and major adverse cardiovascular events. Moreover, they discovered a significant correlation between SII values and cardiovascular-related variables, such as Gensini score. In our study, we compared the prediction abilities of the SII and some other parameters through univariate and multivariate logistic regression analyses (9). We adjusted all confounding factors and found that SII values had predictive ability regarding in-hospital mortality in elderly patients.

This study has some limitations. First, it was a single-center, retrospective cross-sectional study. Because of the study's nature, the patients did not undergo follow-up for more than one year, so no comments could be made regarding their long-term prognosis. The study had a relatively small sample size. The patients' medications were not taken into consideration. Therefore, prospective studies with larger populations are needed to validate our conclusions.

High SII values are independently associated with a high risk of in-hospital mortality in elderly patients with AMI. This index could be used as an easy, inexpensive, and practical predictor to identify high-risk elderly patients with AMI.



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RESEARCH

DO THE PERCEPTION OF BENEFITS OF AND BARRIERS TO EXERCISE AFFECT PHYSICAL PERFORMANCE IN THE ELDERLY?

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2022.296
2022; 25(3): 367-376

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Received : Jun 01, 2022
Accepted : Sep 20, 2022

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Abstract

Introduction: It is important to sustain mobility in order to maintain functionality and physical independence in the elderly. The aim was to evaluate the perception of exercise in the elderly in terms of the benefits of and barriers to exercise and determine the related factors.

Materials and Method: 138 elderly people aged 65 and over were included in the study. Demographics, ambulation status and duration, history of falls, spontaneous/low-energy fractures, exercise/walking activities were recorded. Depression states, benefits and barriers of exercise, risk of falling, balance and Daily activities were evaluated.

Results: The average age of the patients was 71.59±6.21 years and 52.2% were female. Only a quarter (24.6%) reported regular exercise, 50.7% had history of falling, and 18.8% had a fracture history. Only 24.6% of the patients walked for exercise purposes and 44.2% did exercise. The perception of exercise benefit was significantly higher in those with a history of falling ($p=0.012$) and significantly lower in those who walked for exercise purposes and did exercise ($p<0.001$ and $p<0.001$). Perception of exercise benefit was positively correlated with depression, negatively correlated with Lawton-Brody, and perception of obstacle was negatively correlated with balance ($r=0.333$, $r=-0.375$, $r=-0.383$, respectively). Depression level, perceived benefit of exercise, risk of falling were higher in women whereas balance disorder was higher in men ($p<0.001$, $p=0.049$, $p=0.004$, respectively).

Conclusion: In the elderly, exercise is associated with the perception of benefit/obstacle, depression, risk of falling/fracture, balance and functional dependence. Active life should be supported by strengthening the perception of benefit and reducing the perception of obstacles.

Keywords: Aged; Exercise; Health Promotion; Activities of Daily Living; Depression; Fall.

INTRODUCTION

The elderly population is increasing rapidly in today's world, and researchers have estimated that the number of people aged 60 years and over will reach 2.1 billion by 2050 (1). There is ample evidence that regular physical activity (PA) is the key to preventing chronic diseases in the elderly (2). In addition, maintaining physical function and mobility prevent and postpone the onset of disabilities (3). During the aging process, PA is reduced which decrease the aerobic and physical capacity of individuals (4) the independent and joint associations among fitness, adiposity, and mortality in older adults have not been adequately examined.\nOBJECTIVE: To determine the association among cardiorespiratory fitness (\"fitness\", thus, limiting the functional independence of the elderly who progressively have more difficulty to reach sufficient aerobic capacity and muscle strength by time (5)more attention is being given to geriatric healthcare needs and successful ageing is becoming an important topic in medical literature. Concept of successful ageing is in first line on a preventive approach of care for older people. Promotion of regular physical activity is one of the main non-pharmaceutical measures proposed to older subjects as low rate of physical activity is frequently noticed in this age group. Moderate but regular physical activity is associated with a reduction in total mortality among older people, a positive effect on primary prevention of coronary heart disease and a significant benefit on the lipid profile. Improving body composition with a reduction in fat mass, reducing blood pressure and prevention of stroke, as well as type 2 diabetes, are also well established. Prevention of some cancers (especially that of breast and colon. However, evidence shows that regular exercise reduces the risk of cardiovascular morbidity, diabetes, depression, falls, anxiety, and dementia in the elderly, and increases bone density, sleep quality, and cognitive and motor skills (5)more attention is being given to geriatric healthcare needs and successful ageing is becoming an important topic in medical literature. Concept of successful ageing is in first line on a preventive approach of care for older people. Promotion of regular physical activity is one of the main non-pharmaceutical measures proposed to older subjects as low rate of physical activity is frequently noticed in this age group. Moderate but regular physical activity is associated with a reduction in total mortality among older people, a positive effect on primary prevention of coronary heart disease and a significant benefit on the lipid profile. Improving body composition with a reduction in fat mass, reducing blood pressure and prevention of stroke, as well as type 2 diabetes, are also well established. Prevention of some cancers (especially that of breast and colon. Given the positive effects of exercise, the majority of the old aged avoids PA. The reports indicate that two most important barriers to the required PA in the elderly have been identified as a lack of self-confidence and lack of social support. The determining factors of the intention for exercise in the elderly include perceived chance of success, how strongly persons believe they can shape their own health, how confident they are about activity, past experiences, how much they believe in success, and perceived importance of the set goal (6). In the management of elderly exercise counseling, the identification of the perception of exercise and the major determining factors of the intention for exercise are of crucial importance. The perception of exercise basically consists of the barriers to and benefits of exercise. In this study, the aim was to evaluate the perception of exercise in the elderly in terms of the benefits of and barriers to exercise and determine the related factors.

MATERIALS AND METHOD

In February–June 2021, 138 elderly people aged 65 years and older who were able to walk and lacked cognitive impairment were included in the study. Immobilized patients with neurologic deficits including paraplegia, hemiplegia, amyotrophic lat-



eral sclerosis, multiple sclerosis, and Parkinson's disease were not included. Those with major organ failure, advanced heart failure, orthopedic surgery history, chronic obstructive pulmonary disease, any cancer, dementia and with active infectious disease were excluded from the study.

The sample size was calculated by the estimation of appropriate sample size for prevalence surveys formula "$n=(z^2)P(1-P)/d^2$ " (7). The letters; z stood for the coefficient (z=1.96), *P* for expected prevalence and *d* for allowable errors (*d*=0.05). Based on our physical therapy clinic records, the prevalence of the geriatric patients who were able to walk was 8.3%.

$n=(z^2)0.83(1-0.83)/0.05^2=117$

The result of the formula indicated that a minimum of 117 participants were enough to conduct the study.

Age, gender, occupation, height, weight, educational status, chronic diseases requiring continuous medical treatment, ambulation status (walking around independent or assisted), the daily mean duration of walking, history of falls and spontaneous or low-energy fractures in the last 6 months, and structured exercise or walking activities were recorded. Depression level was evaluated with the Geriatric Depression Scale Short Form (GDS), a 15-item scale developed by Burke et al. On this scale, a score of 0–4 indicates no depressive symptoms, scores of 5–8 indicate mild, scores of 9–11 indicate moderate, and scores of 12 and above indicate severe depressive symptoms. The Turkish validity and reliability study of the scale were assessed by Durmaz et al (8).

Perceptions of the benefits of and barriers to exercise were assessed using the Exercise Benefits/Barriers Scale. Consisting of 43 questions, the scale is rated on a 4-point Likert scale. It consists of two components, the Exercise Benefit Scale and Disability Scale, which are evaluated independently of each other. The benefit scale total score is between 29 and 116, and the disability scale total score ranges between 14 and 56. A high total value of the Exercise Benefit Scale indicates that the individual has a good perception of exercise benefit, whereas a high total value of the Exercise Barrier Scale indicates that the individual has a high perception of exercise disability. A Turkish validity and reliability study has been performed to evaluate this scale (9). Fall risk was assessed with the Five-Times Sit-to-Stand Test (5 X Sit–to-Stand Test). In this test, the person is asked to get up and sit down as quickly as possible from an armless chair at a height of 43 cm after hearing the command "start." The test score is obtained from an average of five repetitions. If the score is longer than 12 seconds, this indicates a risk of falling. The test has validity and reliability (10). Berg Balance Scale is designed for the assessment of balance in the elderly (11). Activities of daily living were evaluated using the Lawton–Brody Instrumental Activities of Daily Living Scale (IADL) (12). This scale assesses the state of using the phone, shopping, preparing meals, cleaning the house, doing laundry, mode of transportation, medication liability, and managing finances. Scoring ranges from 0 (low function, dependent) to 8 (high function, independent); a lower score indicates more disability.

Ethical Approval

Ethical approval was obtained for this study from the Clinical Research Ethics Committee (DATE 12.02.2021, NO. 51). The study was conducted according to the World Medical Association's Declaration of Helsinki. Each patient provided written informed consent before the evaluation.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation and categorical data as numbers and percentages. In the intergroup analysis of continuous variables, normality analyses were performed using the Kolmogorov–Smirnov Goodness-of-Fit Test. In the evaluation of continuous variables between the two groups, the t-test was used if the variable was in a normal distribution, and the

Mann–Whitney U test was used if it was not. For comparison of categorical data, the Pearson's Chi-Square Test (Fisher's Exact Test when necessary) was used. The linear relationship between continuous variables was tested with the Pearson correlation test. The analyses were performed with IBM SPSS version 22.0 (IBM Corporation, Armonk, NY, USA). The statistical significance level was accepted as $p<0.05$.

RESULTS

The total participant number was 138. The mean age was 71.59 ± 6.21 years and 52.2% of the participants were female. The majority, 83.3%, had at least one comorbidity. Moreover, 73.2% did not use walking assist devices, 50.7% had a fall, and 18.8% had a fracture history. Of the respondents, 24.6% walked for exercise and 44.2% for exercise. The mean scores of the GDS, the Benefits and Barriers of Exercise Scale, the 5 X Sit–to-Stand Test, the IADL Scale, and the Berg Balance Test (BBT) are presented in Table 1.

There were significant differences between men and women in terms of BMI, education status, occupation, walking for exercise, GDS, 5 X Sit-to-Stand Test, BBT, and Benefits of Exercise total scores ($p<0.001$, $p<0.001$, $p<0.001$, $p=0.026$, $p<0.001$, $p=0.002$, $p=0.004$, $p=0.353$, respectively). The results showed that 54.5% of the men and 34.7% of the women were walking for exercise ($p=0.026$). It was determined that GDS, Benefits of Exercise score, Benefit-Barriers total score, 5 X Sit–to-Stand Test scores in women and BBT scores in men were significantly higher ($p<0.05$) (Table 2). Benefits of Exercise mean score was higher in those with systemic disease and a history of falling ($p=0.025$ and $p=0.012$, respectively), was low in those with a high level of education, those who exercise, and those who walk for exercise ($p=0.002$, $p<0.001$ and $p<0.001$, respectively). Although the mean scores of Barriers to Exercise were high in those with a history of fractures ($p=0.015$), it was observed that they

Table 1. Socio-demographic and clinical relationships

Parameters	Patient group (n = 138)
Age (years) (SD)	71.59 ± 6.21
BMI (kg/m^2) (SD)	28.56 ± 5.07
Ambulation time (hours/day) (SD)	2.57 ± 2.30
Gender (*n*, %) Female Male	 72 (52.2) 66 (47.8)
Education status (*n*, %) Primary school Secondary education University	 81 (58.7) 40 (29.0) 17 (12.3)
Job (n, %) Housewife/Working remotely Physical worker Dekstop Employee	 63 (45.7) 43 (31.2) 32 (23.2)
Systemic Disease (n, %) Exist None	 115 (83.3) 23 (16.7)
Walking aid device (n, %) Independent Walking stick Canedian Tripod Crutches	 101 (73.2) 29 (21.0) 3 (2.2) 4 (2.9) 1 (0.7)
History of falling (n, %) Exist None	 70 (50.7) 68 (49.3)
Fracture history (n, %) Exist None	 26 (18.8) 112 (81.2)
Exercise (n, %) Doing Exercises Not Exercising	 34 (24.6) 104 (75.4)
Walking for exercise purpose (n, %) Doing Not doing	 61 (44.2) 77 (55.8)
GDS point (SD)	10.07±5.99
Exercise Benefits point (SD)	50.07±18.37
Exercise Bariers point (SD)	44.06±18.67
Exercise benefit/bariers total point	94.23±16.49
5 X Sit–to-Stand Test	14.72±6.49
Lawton Brody Instrumental Activities of Dailiy Living	6.74±1.44
Berg Balance Test	42.17±10.32

GDS: Geriatric Depression Scale



Table 2. Gender relative demographic and clinical education planning

Parameter	Female (n=72)	Male (n=66)	*P*
Age (year) (SD)	71.50±6.75	71.69±5.62	0.853*
BMI (kg/m^2) (SD)	30.08±5.55	26.90±3.90	<0.001*
Ambulation Time (hour/day) (SD)	2.38±2.27	2.78±2.33	0.173**
Education Status (n, %) Primary school Secondery education Üniversity	 54 (75.0) 13 (18.1) 5 (6.9)	 27 (40.9) 27 (40.9) 12 (18.2)	<0.001***
Job (n, %) Housewife/ Working remotely Physical worker Dekstop employee	 61 (84.7) 2 (2.8) 9 (12.5)	 2 (3.0) 41 (62.1) 23 (34.8)	<0.001***
Systemic Disease (n, %) Exist None	 60 (83.3) 12 (16.7)	 55 (83.3) 11 (16.7)	>0.5***
Walking aid devise (n, %) Independent Walking Stick Canedien Tripod Crutches	 50 (69.4) 18 (25.0) 3 (4.2) 1 (1.4) 0 (0.0)	 51 (77.3) 11 (16.7) 0 (0.0) 3 (4.5) 1 (1.5)	0.168***
History of falling (n, %) Exist None	 42 (58.3) 30 (41.7)	 28 (42.4) 38 (57.6)	0.088***[a]
Fracture History (n, %) Exist None	 18 (25.0) 54 (75.0)	 8 (12.1) 58 (87.9)	0.080***[a]
Exercise (n, %) Doing exercise Not exercing	 14 (19.4) 58 (80.6)	 20 (30.3) 46 (69.7)	0.168***[a]
Walking for exercise purpose (n, %) Doing Not Doing	 25 (34.7) 47 (65.3)	 36 (54.5) 30 (45.5)	0.026***[a]
GDS point	12.01±5.61	7.95±5.69	<0.001*
Exercise Benefit point	53.01±19.68	46.86±16.37	0.049*
Exercise Barriers point	44.65±18.00	43.42±19.50	0.500**
Exercise Benefit/Barriers total point	97.63±15.35	90.51±17.00	0.011*
5 X Sit-to-Stand Test	15.74±6.25	13.61±6.61	0.002**
Lawton-Brody İnstrumental Activities of Daily Living	6.61±1.44	6.88±1.44	0.170**
Berg Balance Test	39.76±9.97	44.80±10.13	0.004*

GDS:Geriatric Depression Scale
* Student's t-test ** Mann Whitney U Test*** Pearson's Chi-Square Test ([a] Fisher's Exact test)

Table 3. Comparison of the Benefits of Exercise and the Barriers of Exercise according to socio-demographic and clinical parameters

Parameter	Exercise Benefit Point (SD)	*p*	Exercise Barriers Point(Ort±Ss)	*p*
Education Status				
Primary school	53.00±18.93	0.002*	45.39±17.59	0.138**
Secondery education	50.12±17.51		42.85±21.18	
University	36.00±9.81[a]		40.58±17.88	
Job				
Physical worker	53.38±18.66	0.148*	46.73±18.65	0.002**
Dekstop employee	46.83±17.30		46.39±19.57	
Housewife/Working remotely	47.90±18.65		35.68±15.24[b]	
Systemic Disease				
Exist	51.53±18.10	0.025***	42.03±17.93	0.011***
None	42.78±18.34		54.21±19.40	
Walking aid device				
Independent	48.80±18.39	0.081***	42.80±18.19	0.361***
Walking stick	55.89±17.80		47.13±20.81	
Canedien	32.00±3.60		60.00±6.92	
Tripod	48.00±17.06		43.75±20.03	
Crutches	72.00		36.00	
History of falling				
Exist	53.92±18.63	0.012****	44.10±17.74	0.498***
None	46.10±17.35		44.02±19.72	
Fracture History				
Exist	46.30±18.30	0.248****	51.42±17.73	0.015***
None	50.94±18.35		42.35±18.55	
Exercise				
Doing	39.79±14.72	<0.001***	48.41±18.13	0.203***
Not doing	53.43±18.25		42.64±18.72	
Walking for exercise purpose				
Doing	38.72±11.04	<0.001***	47.44±19.21	0.197***
Not doing	59.06±18.08		41.38±17.91	

* One Way ANOVA Test (Post hoc:[a]Bonferroni)

** Kruskal Wallis Test (Post hoc:Mann Whitney U Test)

*** Mann Whitney U Test

**** Student's t-test



were low in housewives and those with systemic disease (p=0.002 and p=0.011, respectively) (Table 3). The correlation between the scales applied to the geriatric patient group showed a positive, moderate and statistically significant correlation was found between the Geriatric Depression Scale and the Benefits and Barriers of Exercise Scale total scores (p=<0.001, r=0.597). There was a negative, statistically significant correlation between the 5 times Sit and Stand Test and Berg Balance Test scores (p=<0.001, r=-0.695) (Table4).

DISCUSSION

Exercise activity has many positive effects in the elderly in terms of improving physical functions, cardiovascular risk factors, all-cause mortality, and overall quality of life (13). In this study, which was conducted to determine the perception of exercise in terms of the benefits and barriers among the geriatric patient population and related factors, valuable results emerged regarding the effects of exercise habits, exercise perception, and gender on balance and activities of daily living of the elderly.

Perception of the benefits of exercise: Although those with systemic disease and a history of falling frequently perceived exercise to have benefits, such perception was found at a low level in those who exercise and walk. However, those with a history of fracture exhibited high perceptions of exercise obstacles, such perceptions were found to be low in those with systemic disease. In the study, it was observed that the average daily walking duration of the elderly during the day was quite short. In their study on elderly people aged 75 and over, Grossman et al. stated that the respondents viewed sedentary behavior as harmful and saw themselves as relatively active; yet, they needed more information about PA. In addition, their well-being in current state of

Table 4. Correlation between the scales applied to the geriatric patient group (n=138)

		GDS	Exercise Benefit point	Exercise Barriers point	Benefit Barriers Total point	5 X Sit-to-Stand Test	Laton Brody IADL
Exercise Benefit Point	**r**	0.333(**)					
	p	**<0.001**					
Exercise Barriers Point	**r**	0.198(*)	-0.603(**)				
	p	**0.020**	**<0.001**				
Benefit Barriers Total Point	**r**	0.597(**)	0.414(**)	0.472(**)			
	p	**<0.001**	<0.001	<0.001			
5 X Sit-to-Stant Test	**r**	0.376(**)	-0.095	0.443(**)	0.423(**)		
	p	**<0.001**	.269	**<0.001**	**<0.001**		
Lawton-Brody IADL	**r**	-0.471(**)	-0.375(**)	0.024	-0.390(**)	-0.386(**)	
	p	**<0.001**	**<0.001**	.776	**<0.001**	**<0.001**	
Berg Balance Test	**r**	-0.397(**)	0.062	-0.388(**)	-0.383(**)	-0.695(**)	0.366(**)
	p	**<0.001**	.469	**<0.001**	**<0.001**	**<0.001**	**<0.001**

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

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

IADL:Instrumental Activities of Daily Living

GDS:Geriatric Depression Scale

health, level of independence, supportive attitudes of family members, and physical appearance provided motivation for exercise. The participants stated that time constraints, aging, poor health, and unsuitable environmental conditions were factors preventing them from participating in exercise. As a result, it was shown that the elderly are interested in maintaining PA, but they have misperceptions about such activity (14). In the elderly group, it was observed that having a fracture experience was a factor preventing exercise; in contrast, the experience of falling did not create a perception of an obstacle to exercise. It is clear that the experience of fracture is much worse for individuals than that of falling. Fracture history was detected as a factor in perceiving as an obstacle to exercise in this study.

Although the physical and psychological benefits of regular PA are known, studies have reported that approximately 30% of the world's population does not engage in PA at the recommended level. This rate reaches 45% over the age of 65 and 75% over the age of 75 (15). In this study, parallel to the literature, 75.4% of the elderly did not exercise (men: 69.7% women: 80.6%), and 55.8% did not walk for exercise. According to Li et al (16)types and locations of physical activity.\nDESIGN: Cross-sectional observation.\nSETTING: Car-dependent urban and rural neighborhoods in Worcester County, Massachusetts, USA.\nPARTICIPANTS: 111 men and 103 women aged 65 years and older.\nMEASUREMENTS: From 2012 to 2014, participants were queried on type, frequency and location of physical activity. Participants wore an accelerometer for 7 consecutive days.\nRESULTS: Compared to women, men had a higher mean daily step count (mean (SD, older men take more daily steps and participate more in physical activities than women do. Moreover, Polard et al (17) found age-related differences in gait in terms of gender in their review study; they determined that women walk more than men at younger ages but that this difference is reversed in older groups. They reported that this situation may be related to the rapid increase in movement restrictions in women (18)and pain is a frequent symptom at older ages. We have investigated the association of different patterns of pain and mobility limitation in a large sample of older adults. A cross-sectional postal survey of all adults aged 50 years and over registered with eight general practices in North Staffordshire, UK, resulted in 18,497 respondents (adjusted response=70.8%. It was also shown that older women had higher levels of morbidity, including musculoskeletal problems, than older men do (19). The differences in the levels of exercise and walking in men and women in this elderly group were similar to those reported in the literature.

In this study, women had higher body mass index (BMI) and lower education levels compared to men. The Geriatric Depression Scale, Benefits of Exercise score, 5 X Sit-to-Stand Test scores were higher in women, whereas the Berg Balance Test scores were higher in men. In a study on the depression status of elderly women, depression was defined by participants as fatigue and weakness. It was also found that depression causes a decrease in PA (20). Studies have shown that PA may reduce the risk of depression in elderly individuals (21). In this study, we can attribute the lower participation of women to exercise to their higher BMI and lower education levels, as well as their perception of more barriers to exercise. The limitations of movement and higher morbidity in women may also explain this situation. We think that the worsening of balance and participation in daily living activities in the female elderly may also be associated with these findings.

The analysis results of high rates of falls (58.3%) and fractures (25.0%) in women compared to the rates of falls (42.4%) and fractures (12.1%) in men might be attributed to the decreased exercise performance of the women. Reduced PA is a risk factor for balance disorders and falls (22). Such findings may also help explain why men have higher balance scores and mobilization times and less depression.



Although the rate of fall and fracture history was 18.8% among all patients in this study, the rate of use of walking aids was 26.8%. Furthermore, the use of walking aids was found to be low compared with the history of falling.

Although the importance of PA is well known, the elderly often believe that they are too old or too weak to exercise. In addition, chronic diseases in older adults restrict participation in PA and exercise. The data on the benefits and barriers of exercise scores in this study are similar to those in the literature. The exercise benefit score in this study was lower in those who exercise and walk. Such factors as self-efficacy, perception of control over one's health, comorbidities, behavioral factors, beliefs, education level, perceived barriers, habits, previous experiences, psychological problems, and environmental factors affect thoughts about the benefits of and barriers to exercise among the elderly.

The main reason for limiting exercise is the lack of time in young adults and poor health in the elderly. The results indicated that the exercise disability score was higher in patients with a history of fracture ($p=0.015$). Indeed, fracture experiences in the elderly may have negatively affected the participants' perception of self-efficacy and control over their health. We surmise that such history may lead them to develop thoughts that prevent them from exercising.

This study, to the best of our knowledge, is a first in evaluating perception of exercise in terms of the benefits of and barriers to exercise regarding the daily life activity and ambulation status in the elderly. Another strengthening concept of the study was including four scales which assess closely related conditions and questioning the fracture history among the old aged population provided the evaluation of multiple factors used to determine more accurate functional status and capacity. The weaknesses included the cross-sectional study design, the samples belonging to a specific region, and some of the measurements based on self-report data. Another limitation was that each question on the scale could not be evaluated separately for all patients; rather the Benefit-Disability Scale was evaluated over total scores. Therefore, the study results might not be extrapolated to other populations.

CONCLUSION

Walking duration and exercise rates are low in the elderly, whereas the risks of falls, fractures, balance problems, and systemic disease are high; In relation to these factors, the perception of benefit regarding exercise was low and the perception of barriers was high. Such factors as chronic diseases, self-efficacy, perception of control over one's health, behavioral factors, beliefs, education level, perceived barriers, habits, previous experiences, psychological problems, and environmental factors affect perceptions of the benefits of and barriers to exercise among elderly people.

Strengthening the positive perception of the benefits of exercise in the elderly and determining the factors that affect the perception of disability are measures with strategic importance in promoting active and healthy aging.

Compliance with Ethical Standards: This study was not funded.

Declaration of Interest: The authors declare no conflict of interests.

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RESEARCH

PROGNOSIS OF GERIATRIC COVID-19 PATIENTS ADMITTED TO INTENSIVE CARE UNIT ACCORDING TO VACCINATION STATUS

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2022.297
2022; 25(3): 377-385

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Received : Jul 13, 2022
Accepted : Sep 16, 2022

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Abstract

Introduction: As of June 27, 2022, the COVID-19 pandemic has caused over 540 million infections and 6.3 million deaths. We aimed to investigate the effect of the vaccine on the clinical course of elderly patients hospitalized in the intensive care unit and to determine the prognosis of the patients according to their vaccination status.

Materials and Methods: The study included 157 patients over the age of 65. Patients were divided into two groups. The first group consisted of patients who were vaccinated with two doses of CoronaVac, and the second group consisted of patients who were not vaccinated. Demographic data of the patients, prehospital clinical frailty scales, Charlson Comorbidity Indexes, APACHE II scores, laboratory values, and patient prognoses were recorded.

Results: Of the 157 patients, 93 (59.2%) were female, and the median age was 76 years (65–99). 96 (61.1%) patients were vaccinated and 61 (38.9%) patients were unvaccinated. Patients were grouped as survivors (n=26) and deceased. We found that APACHE II, prehospital clinical frailty scales, and Charlson Comorbidity Indexes scores were higher in patients who died. There was a significant difference between blood lymphocyte and ferritin levels and survival. The 28-day survival rate was higher and intensive care unit overall survival time were longer in the vaccinated group.

Conclusions: We observed that the vaccinated patients had higher survival times and lower mortality rates than those who were not vaccinated. We think that it is important to vaccinate elderly patients and that additional doses may be needed.

Keywords: COVID-19; Aged; Critical Care; Vaccines.

INTRODUCTION

As of June 27, 2022, the COVID-19 pandemic had caused over 540 million infections and 6.3 million deaths (1). The severity of COVID-19 infection may be limited to mild symptoms but can also result in symptoms that require intensive care unit (ICU) admission. The progression of these symptoms can include hospitalization, respiratory failure, and organ failure, which may lead to serious clinical consequences or death (2). Prehospital data may be important markers of mortality and morbidity in elderly patients admitted to the ICU, and frail elderly may have greater difficulty adapting to various stressful situations such as acute illness and trauma (3,4). COVID-19 is more serious in elderly individuals than in younger individuals, especially those over 60 years of age with increased frailty and underlying chronic diseases. Studies have shown that elderly individuals have a higher risk of death, which increases with age (3,5). Weakening of the immune system caused by aging occurs with increased susceptibility to infectious diseases and cancer, and can also cause autoimmune disorders. These changes in the immune system result in immunosenescence. This effect on immunity generally causes a decrease in vaccine effectiveness in elderly individuals. However, COVID-19 vaccines are necessary to control the pandemic and reduce its life-threatening effects, especially in at-risk individuals (3,6,7).

In the literature, there are limited number of studies examining the clinical course of ICU patients over 65 years of age who were vaccinated with two doses of CoronaVac/Sinovac and those who were not vaccinated. In our study, we examined vaccinated and unvaccinated COVID-19 polymerase chain reaction (PCR)-positive patients, especially elderly individuals admitted to the ICU and at high risk of death. We aimed to investigate the effect of the vaccine on the clinical course of these patients and to determine patient prognosis between the two groups.

MATERIALS AND METHODS

Vaccination of the elderly

With the introduction of CoronaVac/Sinovac vaccines, vaccinations for priority groups in Turkey began on January 13, 2021 for healthcare workers and at-risk age groups. Vaccinations for individuals over the age of 65 started on February 12, 2021 (8).

Study design and data collection

Permission for the study was acquired from the ethics committee of Turgut Ozal University non-interventional clinical research (Decision number: 2021/101). This single-center retrospective study was carried out between January 7, 2021, and November 30, 2021, in the Level 3 COVID-19 ICUs of our hospital. The study included a total of 157 patients over the age of 65, who were classified as elderly according to the World Health Organization (WHO). Patients admitted to the ICU were separated into two groups. The first group consisted of patients who received a double dose of CoronaVac/Sinovac vaccine and had a minimum of 14 days since vaccination, and the second group consisted of patients who were not vaccinated. Patients under 65 years of age, those who received a non- CoronaVac/Sinovac vaccine, those who received a single dose of the CoronaVac/Sinovac vaccine, and those who used immunosuppressive drugs were excluded from the study.

Demographic data of the patients, prehospital clinical frailty scales (CFS), Charlson Comorbidity Indexes (CCI), lengths of stay in the intensive care unit (LOS), times from PCR positivity to ICU admission, comorbidities, APACHE II scores, ICU timing of intubation, laboratory values, and patient prognoses were recorded. The prehospital frailty statuses of the patients were evaluated according to CFS (4). Patients with a CFS score ≥ 5 were defined as frail. CFS scores were calculated based on the patients' medical records and interviews with the



patient and/or relatives. Patients were followed during their stay in the intensive care unit or until their death. Twenty-eight-day mortality was defined as death within 28 days of admission to the intensive care unit. Mortality data of the patients were gathered from the hospital's medical record system.

Statistical analysis

The data obtained from the hospital database were organized and entered into the SPSS 21.0 (Statistical Package for Social Sciences, IBM Corp) program for statistical analysis. The results were evaluated at the 95% confidence interval, with a significance level of $p < 0.05$. The homogeneity and distribution of the variables were evaluated using the Kolmogorov–Smirnov test. Percentage and frequency were used for categorical data. Continuous variables were presented as mean ± standard deviation or median (min–max). We compared the variables between vaccinated and non-vaccinated patients, survivors, and non-survivors. The independent samples t-test was used to analyze the parametric data of two independent groups, and the Mann–Whitney U test was used for non-parametric data. Categorical variables were compared using the chi-square test. Kaplan–Meier analysis was used to determine the patients' overall hospital stay and 28-day survival rates, and the longrank test was used to compare the survival differences between the groups. Cox regression analysis was used to evaluate univariate survival analysis and multivariate survival analysis.

RESULTS

A total of 157 patients were included in the study; of these, 93 (59.2%) were female. The median age of the patients was 76 years (range,65–99 years). Of these patients, 96 (61.1%) were vaccinated and 61 (38.9%) were unvaccinated. The time that had elapsed since the previous dose of CoronaVac ranged from four to eight months. Hypertension (58%), coronary artery disease (52.2%), chronic obstructive pulmonary disease (24.2%), diabetes mellitus (31.2%), and chronic kidney failure (8.3%) were the most common comorbidities. The mean (SD) duration of stay in the ICU was 13.21±9.22 days. Patients were categorized as survivors (n = 26) or deceased (n = 131). We found that age, sex, and LOS had no significant effects on mortality. Only three of the surviving patients were intubated. The ICU intubation timing was not significant in the groups according to vaccination status (p = 0.086).

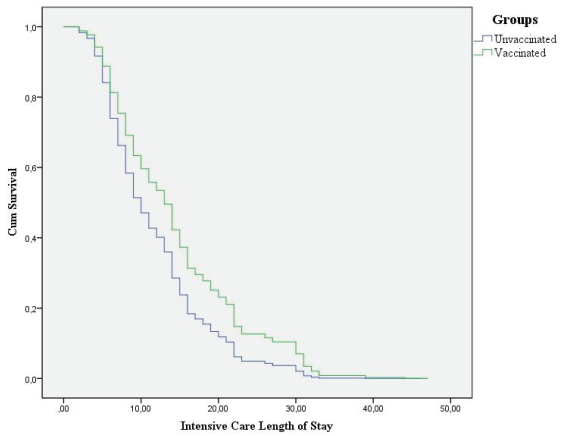
In addition, we found that APACHE II, CFS, and CCI scores were higher in patients who died (p <0.05). Blood lymphocyte levels were lower and ferritin levels were higher in patients who died (p= 0.005 and p = 0.036, respectively). A comparison of the main clinical features and laboratory findings of the two groups is presented in Tables 1 and 2, respectively.

In the analysis based on vaccination status, both groups showed similar characteristics (Tables 1 and 2). We found higher blood lymphocyte and lower ferritin levels in vaccinated patients (95% CI, p = 0.047, p = 0.014, respectively) (Table 2).

In this study, the 28-day mortality and overall mortality in the ICU were 75.2% and 83.4%, respectively (regardless of vaccination status). Multivariate Cox regression analysis was used to identify independent risk factors for mortality. The results of the Cox regression analysis for the effects of vaccination status, CFS score, CCI score, Apache II score, and ICU intubation timing on the survival times of patients are shown in Table 3. Vaccination status (95% CI:0.423–0.874, p = 0.007) and CCI score (95% CI:1.031–1.479, p = 0.022) were significant prognostic factors (Table 3). In addition, the vaccination status and intubation timing of patients in the ICU were significant prognostic factors (p = 0.040 and p <0.001, respectively) (Table 3 and Figure 1).

The overall mortality rate was 86.8% in the unvaccinated group and 81.2% in the vaccinated group.

Figure 1. Vaccination status and intubation timing



No statistical correlation was found between vaccination and mortality (p= 0.355) (Table 1). When the vaccination status of the patients in the ICU was evaluated in terms of 28-day mortality, 83% of the unvaccinated individuals died, while 69.8% of the vaccinated individuals died (95% CI, p =0.05) (Table 3). We used the Kaplan–Meier estimator to analyze the distribution of survival time based on vaccination status: the 28-day and ICU total survival times were statistically significant (according to the log-rank test, p = 0.010 and p = 0.08, respectively) (Figure 2A and 2B).

Table 1. Baseline characteristics of the patients.

		All patients (n = 157)	Survivors (n = 26)	Nonsurvivors (n = 131)	***P* value**	Vaccinated (n = 96)	Unvaccinated (n = 61)	***P* value**
Median age, years (min-max)		76 (65-99)	76(65-86)	76 (65-99)	0.613	76 (65-99)	77 (65-93)	0.494
Sex, n (%)	**Male**	64 (40.8)	10 (38.5)	54 (41.2)	0.794*	41 (42.7%)	23 (37.7%)	0.534*
	Female	93 (59.2)	16 (61.5)	77 (58.8)		55 (57.3%)	38 (62.3%)	
Comorbid disease, n (%)	**Hypertension**	91 (58)	17 (65.4)	74(56.5)	0.401*	56 (58.3%)	35 (57.4%)	0.906*
	COPD	38 (24.2)	4 (15.4)	34 (26)	0.250*	24 (25%)	14 (23%)	0.770*
	DM	49 (31.2)	7 (26.9)	42 (32.1)	0.606*	34 (35.4%)	15 (24.6%)	0.154*
	CRF	13 (8.3)	1 (3.8)	12 (9.2)	0.369*	10 (10.4%)	3 (4.9%)	0.223*
	CAD	82 (52.2)	11 (42.3)	71 (54.2)	0.268*	58 (60.4%)	24 (39.3%)	**0.010***
APACHE-II scores, (Me ± SD)		19.08±5.65	16.38±4.9	19.61±5.65	**0.010**	19.21±5.74	18,8±5.54	0.751
CFS score, (Me ± SD)		4.52 ±1.26	4 ±0.89	4,62 ±1.30	**0.028**	4.48±1.30	4.57±1.21	0.504
CCI, (Me ± SD)		4.83 ±1.43	4.23 ±1.21	4.95 ±1.45	**0.021**	4.95±1.42	4.63±1.44	0.206
CFS Groups, n (%)	**<5**	88 (56.1)	20 (76.9)	68 (51.9)	**0.019**			
	≥5	69 (43.9)	6 (23.1)	63 (48.1)				
ICU Intubation Time. (day), (Me ± SD)		6.53 ±7.51	1.33±0.57	6.65 ±7.55	**0.021**	7.63±8.85	4.90±4.48	0.086
Day of admission to intensive care. (day), (Me ± SD)		5.9 ±4.15	6.30±4.69	5.90 ±4.06	0.820			
Length of stay in the Intensive care unit. (day), (Me ± SD)		13.21 ±9.22	10.46±6.74	13.75±9.56	0.094	14.58±10.1	11.04±7.06	**0.036**
Groups (Vaccinated/ Unvaccinated), n (%/%)		96/61 (61.1/38.9)	18/8 (69.2/30.8)	78/53 (59.5/40.5)	0.355*			

Mann-Whitney U test, *Chi square test, ICU: intensive care unit; CRF: Chronic renal failure; CAD: coronary artery disease; DM: Diabetes mellitus; COPD: Chronic obstructive pulmonary disease;CCI: Charlson Comorbidity Index; APACHE-II: Acute physiology and chronic health evaluation II; CFS: Clinical frailty scale; Me: mean; SD: standard derivation



Table 2. Baseline laboratory findings of the patients.

	All patients (n = 157)	Survivors (n = 26)	Nonsurvivors (n = 131)	**P value**	Vaccinated (n = 96)	Unvaccinated (n = 61)	**P value**
Wbc (10^3/μL)	11.93 ±5.14	11.72 ±5.75	11.97 ±5.04	0.536	11.53±4.84	12.56±5.57	0.216
Lymph (10^3/μL)	0.74 ±0.46	1 ±0.56	0.68 ±0.42	**0.005**	0.81±0.51	0.63±0.36	**0.047**
Urea (mg/dL)	81.7 ±46.9	70 ±40.61	83.97 ±47.97	0.206	83.1±45.8	79.6±49.06	0.340
Crea (mg/dL)	1.36 ±1.12	1.17 ±0.74	1.40 ±1.18	0.374	1.47±1.28	1.19±0.79	**0.041**
AST (U/L)	52.37 ± 85.3	49.03±60.18	53.03±89.62	0.385	59.42±106	41.27±28.2	0.656
ALT (U/L)	43.01±84.9	43.07±51.15	43±90.31	0.944	49.31±106.9	33.09±22.4	0.480
LDH (U/L)	582.81±6.7	501.96±214.21	598.86±341.6	0.153	555.4±337.6	625.8±303.0	0.054
Ferritin	846±605.7	607.72±475.79	893.40±619.03	**0.036**	767.56±602.44	969.6±595.02	**0.014**
Procalcitonin	1.62 ±4.02	2.15±6.48	1.52 ±3.36	0.676	2.07±4.78	0.91±2.23	0.268
D-dimer	3.78±4.63	4.43 ±5.42	3.65 ±4.47	0.630	3.06±3.66	4.91±5.7	0.112
CRP (mg/dL)	9.93±6.7	8.93±6.80	10.13±6.69	0.290	10.87±7.4	8.45±5.06	0.057
Lactate (mmol/L)	2.92±1.91	2.37 ±0.87	3.03±2.04	0.135	2.89±1.75	2.97±2.16	0.860

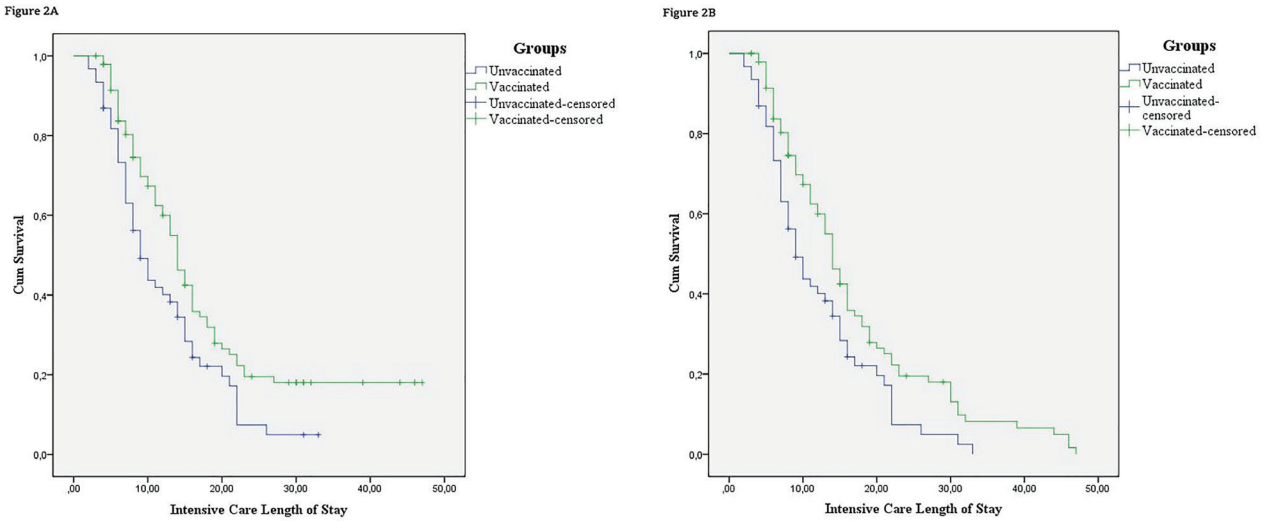
mean (standard deviation); Mann-Whitney U test; CRP: C-reactive protein; AST: aspartate aminotransferase; ALT: alanine aminotransferase; Wbc: white blood cell; Lymph: lymphocytes; Crea: creatinine

Table 3. Multivariate Cox regression analysis of mortality and 28-day mortality analysis

Variables in the Equation	**B**	***P* Values**	**Exp(B)**	**95,0% CI for Exp(B)**	
				Lower Bound	**Upper Bound**
Vaccination status	-0.498	**0.007**	0.608	0.423	0.874
CFS score	-0.144	0.195	0.866	0.696	1.076
Charlson Comorbidity Index	0.211	**0.022**	1.235	1.031	1.479
Apache-II	-0.013	0.431	.987	0.955	1.020
Variables in the Equation					
Vaccination status	-0.376	**0.040**	0.686	0.479	0.983
Intubation Timing	-0.076	**0.000**	0.927	0.900	0.955
28-Day Mortality					
Mortality	**Groups**				**Total**
	Unvaccinated		**Vaccinated**		
Survivors (%)	10 (16.4)		29 (30.2)		39
Nonsurvivors (%)	51 (83.6)		67 (69.8)		118

CCI:Charlson Comorbidity Index; CFS: Clinical Frailty Scale; Apache-II: Acute physiology and chronic health evaluation II; 95% Confidence Interval; *P*=0.05

Figures 2A and 2B. 28-day survival analysis and analysis of overall survival



DISCUSSION

COVID-19 can cause serious disease, especially in frail elderly patients. The ongoing COVID-19 pandemic continues to place a serious burden on the healthcare system, particularly with the increased need for intensive care beds. Therefore, vaccination is particularly important for frail older adults. In our study, the effect of vaccination on individuals aged ≥ 65 years who were hospitalized in the ICU due to COVID-19 was evaluated. The results showed that being fully vaccinated (i.e., having received two doses of CoronaVac >14 days after the previous dose) did not have a significant effect on mortality in this age group based on the total length of ICU stay; however, it was significant on the 28-day mortality. Factors such as fragility, immunosenescence, comorbidities, and time elapsed since the previous vaccine dose are significant in this age group; thus, prolonged life expectancy due to vaccination is important (3,4,9,10). Our study showed a statistically significant difference between vaccinated and unvaccinated individuals in the 28-day survival analysis (p=0.010). In addition, lymphopenia and high CCI scores were associated with increased mortality (P =0.005 and P =0.021, respectively).

Previous studies on CoronaVac have found different efficacy rates in different age groups. In a study on CoronaVac conducted in Turkey that included participants between the ages of 18 and 59 years, vaccination provided 83.5% protection against symptomatic infection compared with placebo (11). A Chilean study reported 65.9% effectiveness for the prevention of COVID-19, 90.3% for the prevention of ICU admission, and 86.3% for the prevention of death (12).

In a study conducted on individuals aged over 75 years in Brazil, 83% of vaccinated individuals received the CoronaVac or Sinovac/Butantan vaccine, whereas 17% received the Oxford-AstraZeneca/Fiocruz vaccine. When unvaccinated elderly individuals were compared with elderly individuals who received two doses, mortality was more than 132 times greater in the unvaccinated group, and the rate of protection against death achieved in vaccinated individuals was 99.2% (13).

In another study, the efficacy of the vaccine against symptomatic COVID-19 at ≥ 14 days after the second dose was 59.0% in those aged 70–74 years (range:43.7%–70.2%), 56.2% in those aged 75–79



years (range:43.0%–66.3%), and 32.7% in those ≥80 years (range:17.0%– 45.5%). The effectiveness of the vaccine to prevent death was 83.9% in those aged 70–74 years (range:59.2%–93.7%), 78.0% in those aged 75–79 years (range:58.8%–88.3%), and 44.0% in individuals aged ≥ 80 years (range:20.3%–60.6%) (14).

In other vaccine types, one study provided early real-world evidence of the efficacy of the Pfizer/BioNTech mRNA and Oxford/AstraZeneca ChAdOx1-S vaccines to prevent hospitalization and death in elderly people in England. The results showed that a single dose of Pfizer/BioNTech vaccine prevented symptomatic disease in adults aged ≥ 70 years and that the vaccines were 60–70% effective, while two doses of the vaccine were approximately 85–90% effective. Those who were vaccinated and had symptoms had a 44% lower risk of hospital admission than unvaccinated individuals (15).

While vaccination efforts are ongoing worldwide, it is important to note that over time. there is a decline in the immunity conferred by two doses of the vaccine, and a third dose is likely necessary (16). A greater number of neutralizing antibodies are obtained with a third vaccination (17). In addition, a study reported that neutralizing antibody titers declined to near or below the lower limit of seropositivity 6 months after the second dose, and the efficacy of vaccination is uncertain, as the threshold of protection of antibody titers against COVID-19 is unknown (10,18).

The antibody titers of the vaccinated patients in our study were unknown. However, the time since the previous dose ranged from four to eight months. When we compared vaccinated patients with unvaccinated patients, we found that the mortality rate was higher in the unvaccinated group (83.6%). The 28-day mortality rate of all patients was 75.2%. In a previous study conducted on COVID-19 patients in the ICU, the death rate was 40.8%; however, the median age in this study was 55 years (19); in our study, the median age was 76 years. In addition, in two previous studies on critically ill COVID-19 patients, the mean age was 59.7 years, and the 28-day mortality rate was 61.5% in one study, whereas in the other, the average age was 55 years, 15 of 29 patients died, and the 28-day mortality rate was 51.7% (20,21). We believe that lower vaccine effectiveness with advanced age and comorbidities increases the risk of death.

Previous studies have reported that lymphopenia observed in patients may be associated with disease severity and mortality in critically ill COVID-19 patients (21). Similarly, we found lower lymphocyte levels in patients who did not survive. In addition, when we analyzed the patients according to their vaccination status, unvaccinated patients had lower lymphocyte counts ($p = 0.04$).

Comorbidity and frailty, which are among the factors that play important roles in mortality, may result in an increased mortality rate in elderly patients. The fragility of elderly patients with difficulties adapting to stressful situations, such as acute illness and trauma, can be determined by performing a CFS assessment. A high CFS score (>5) in ICU patients is an important predictor of mortality (4,22). In addition, the Charlson comorbidity index (CCI), which was developed in 1987 and is used to determine the risk of death due to comorbid diseases, has been used as an indicator of long-term survival and prognosis in many studies (23,24). The CCI score may be useful in determining the prognosis of patients hospitalized for COVID-19: a systematic review and meta-analysis found that each one-point increase in the CCI score of patients with COVID-19 increased mortality by 16% (25). In our study, we found that mortality increased with high CFS and CCI scores in all the patients. Multivariate Cox regression analysis performed according to vaccination status revealed a significant relationship between CCI scores and mortality ($p = 0.022$).

LIMITATIONS

This study is limited by some factors. First, it was conducted in a single center and included only patients hospitalized in the ICU. Additionally, only patients vaccinated with a double dose of CoronaVac/Sinovac were included. Next, the antibody titers of the patients at admission were unknown. Finally, patients in critical condition followed up in ICU s have a high mortality rate regardless of their vaccination status.

CONCLUSION

In our study, although the antibody titers in individuals vaccinated with two doses of CoronaVac/Sinovac were not known, vaccination showed prolonged survival in patients and the 28-day mortality rate was lower in vaccinated patients than in those who were not vaccinated. We believe that it is important to vaccinate elderly patients; further, since immunity conferred by vaccination may decline over time, mortality rates decrease with the administration of additional doses.

Financial disclosure

This manuscript did not receive any specific grant from funding agencies in the public, commercial, or not-forprofit sectors.

Conflict of interest

The authors have no conflicts of interest to declare connection with this article.

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RESEARCH

RELATIONSHIP BETWEEN LONELINESS, PHYSICAL ACTIVITY, AND DEPRESSIVE SYMPTOMS AMONG OLDER ADULTS: A CROSS-SECTIONAL STUDY CONDUCTED DURING THE FOURTH WAVE OF THE COVID-19 PANDEMIC IN TURKEY

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2022.298
2022; 25(3): 386-395

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Received : Feb 14, 2022
Accepted : Sep 04, 2022

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Abstract

Introduction: This study aims to examine the prevalence of depressive symptoms, its influencing factors, and the relationship between loneliness, physical activity and depressive symptoms among individuals aged 65 years and above during the COVID-19 pandemic.

Materials and Method: This cross-sectional study was conducted on 1093 older adults in Turkey. A Descriptive Data Form, the Loneliness Scale for the Elderly, the Geriatric Depression Scale-15, and the Physical Activity Scale for the Elderly were used to collect data. In this study, the presence of depressive symptoms was the dependent variable; sociodemographic and individual characteristics, habits, history of chronic illness and COVID-19, perception of loneliness and physical activity level were independent variables.

Results: The prevalence of depressive symptoms among older adults was 66.8%. Depressive symptoms were 3.96 times higher among women, 8.06 times higher in urban areas, 2.56 times higher among those who had equal income and expenses, and 2.78 times higher among older adults who had less income than expenses. Depressive symptoms were further 1.98 times higher among those who had chronic diseases and 25.54 times higher among those diagnosed with COVID-19. Additionally, depressive symptoms increased by 23.24 times among those who did not have a hobby, and 1.53 times for each one-point increase in the level of loneliness. No relationship was found between physical activity levels and depressive symptoms.

Conclusion: The results show that two out of three older adults were depressed. Characteristics such as having had COVID-19, loneliness, and hobbies, were significant influencing factors of depressive symptoms among older adults. There is a need to adopt feasible and protective policies that cater to the needs and control the risk factors of older adults during the pandemic.

Keywords: Depression; Loneliness; Aged; Exercise.

INTRODUCTION

The coronavirus (COVID-19) pandemic has become a significant problem in Turkey as well as globally. The coronavirus pandemic poses a life-threatening risk to the older population with a weak immune system (1). Initially, Turkey enforced lockdown for older adults as one of the measures against the COVID-19 pandemic (1). However, the pandemic is still severe, given the number of infection cases and deaths and continues to affect life (2). The effect of social isolation on older adults is an important issue that needs to be examined multidimensionally. Literature states that 43% of older adults feel lonely (3). This age group, which feels lonely and experiences social isolation during the COVID-19 pandemic, is at risk of mental and physical health (1). Loneliness among older adults is the main risk factor of mental health problems such as depression (4,5).

The mental and physical health of older adults can affect each other. Older adults with health problems such as diabetes and heart diseases are at higher risk of depression (6). Some individuals are at risk of chronic depression. Older adults who experience negative life events are more likely to suffer depression as its source is the complex interaction of social, psychological, and biological factors (1,6). Depression is a common problem among older adults. However, it is not a standard part of aging. Hence, it is important to determine its prevalence among older adults by taking necessary public health measures. Depression, which entails negative consequences such as premature death, increased risk of suicide, and deterioration of the general health status of an individual, can be successfully treated (1,3,6).

Regular physical activity (PA) is important for maintaining overall health later in life. Older adults that engage in regular PA are less likely to experience depression (7). Physical activity has a protective effect against some health problems such as cardiovascular diseases, hypertension, diabetes, depression, and anxiety among older adults (8,9). They are encouraged to exercise regularly at home, especially during the COVID-19 period, owing to its positive effects on the immune system (9,10). Restrictions imposed to protect individuals from COVID-19 and the prolonged pandemic period may affect their mental health and limit their PA practices, hence increasing the risk of more health problems (3). The COVID-19 pandemic may inhibit the control of the comorbidity of physical and mental diseases among older adults.

This study aims to examine the prevalence of depressive symptoms, its influencing factors, and the relationship between loneliness, physical activity and depressive symptoms among individuals aged 65 years and above during the COVID-19 pandemic.

MATERIAL AND METHOD

Study Sample

This cross-sectional study was conducted in Sakarya Province, Turkey, during the fourth wave of the COVID-19 pandemic (September 1-November 26, 2021). According to the Turkish Statistical Institute data, the population of Sakarya Province aged 65 and above totalled 105,605 people in 2020. The proportion of the prevalence of depression among older adults was 40% based on the studies conducted in Turkey (5,11,12). The minimum required sample size was calculated as 1015 on the OpenEpi software based on a 3% margin of error and a confidence level of 95%. The final sample size of the study was calculated as 1116 individuals by adding an extra 10% to the calculated sample size (n=101) in case some individuals refused to participate in the study or were not at home. There are 16 districts in Sakarya province. Sample selection was made in two stages. First, the number of people to be recruited from each district was calculated using the stratified sample method. Since the number of individuals aged 65 and over is not equal in each district, the minimum number of individuals to be

reached was stratified according to the district population. According to the size of the district, the participants were determined by cluster sampling and/or simple random sampling method.

Data Collection

The data were collected through face-to-face interviews conducted by five interviewers after obtaining the necessary permissions. Before data collection, the interviewers were enlightened on the purpose and method of the study, the necessary communication skills while working with older adults, and data collection techniques using a questionnaire. The data for this study were collected during the fourth wave of the COVID-19 pandemic. Until this date, individuals aged 65 and over in Turkey have had two doses of COVID-19 vaccine, and the "lockdown" process has ended, and the "gradual normalization" process has begun. In this study, the interviewers who collected data were trained on the symptoms of COVID-19 and the risk of transmission. Data were collected by allowing the elderly person to sit on a chair in the open area or in front of the door, paying attention to the rules of disease prevention and social distance.

The relevant speech and hearing-impaired individuals that were bedridden, had a history of dementia, or refused to participate in the study were excluded from the study. The data collection tools included a Descriptive Data Form, and the Loneliness Scale for the Elderly, Geriatric Depression Scale-15, and Physical Activity Scale for the Elderly self-assessment scales.

The Descriptive Data Form: This questionnaire included questions on the sociodemographic and individual characteristics, habits, history of chronic illness and COVID-19 and quarantine and the general health perception of individuals aged 65 and above. The form was created by the researchers following a review of the literature.

The Loneliness Scale for the Elderly (LSE): The LSE was developed to evaluate the loneliness level of older individuals and revised by Tilburg and John-Gierveld (13). It comprises 11 items and has a 3-point Likert-type scale. Five items of the scale, which evaluate the social loneliness of older individuals, are positive (0=Yes, 1=Maybe, 2=No); six items, which evaluate emotional loneliness, are negative (2=Yes, 1=Maybe, 0=No). The sum of the two sub-dimensions equals the overall loneliness score. The minimum and maximum scores range between 0 and 22. The Turkish validity study of the scale was conducted by Akgül and Yeşilyaprak, who found Cronbach's alpha value to be 0.85 (14).

The Geriatric Depression Scale-15 (GDS-15): The GDS-15, which comprises 15 questions, was developed to evaluate the depressive symptoms of older adults (15). Participants consider their status in the last week while responding to the 15 'Yes/No' type questions. While evaluating the scale, points are given according to the answers in favour of depressive symptoms. When the total score is calculated, 'No' responses to positive questions and 'Yes' responses to negative questions are assigned 1 point and other responses are assigned 0 points. The recommended cutoff point of ≥5 was used to distinguish the presence of depressive symptoms (16). The Turkish validity and reliability study of GDS-15 was conducted by Durmaz et al., who found Cronbach's alpha value to be 0.92 (16).

The Physical Activity Scale for the Elderly (PASE): The PASE was developed to evaluate the PA level of older individuals. The PASE score is an integration of multiple scores that include leisure, household, and occupational activities. It comprises 12 questions on the frequency and duration of leisure, household, and occupational activities in the last seven days. The scoring of each question is different; the total score is calculated by summing all the activities. The overall PASE score can vary between 0 and 400 (17). Higher total scores indicate higher PA levels. The Turkish validity and reliability study of the scale was conducted by Ayvat et al., who found Cronbach's alpha coefficient to be 0.92 (18).



Ethical Considerations

This study was conducted in accordance with the principles of the World Medical Association Helsinki Declaration. Written permission was obtained from the Non-invasive Research Ethics Committee of the Sakarya University Medical Faculty (date: 01.08.2021, no: 47687).

STATISTICAL ANALYSIS

Descriptive data were presented as mean, standard deviation, number, and percentage values. Kolmogorov-Smirnov tests of normality were used to determine whether the data displayed normal distribution. Non-parametric tests were used to compare the groups for the data with non-normal distribution ($p<0.05$). The relationship between the depressive symptoms level of older adults and loneliness and physical activity level were determined Spearman correlation analysis. Crude and adjusted odds ratios and 95% CIs for determinants of depressive symptoms were calculated using logistic regression analysis. A multiple regression model was created with gender, marital status, place of residence, education, employment status, income, social security, cohabitant, chronic illness, COVID-19 history, presence of COVID-19 positive people, hobby, loneliness level, physical activity level. Statistical analysis was performed on the SPSS 24.0 statistical software package. The statistical significance level was set as $p<0.05$.

RESULTS

A total of 1093 older adults were included in this study (response rate, 97.9%). Of the participants, 684 (62.6%) were female, and the mean age was 71.9±5.9 (min=65, max=95) years. The prevalence of depressive symptoms among older adults was 66.8% (n=730).

The LSE and GDS-15 total scores were found to be moderately and very significantly positively correlated ($p<0.01$). In contrast, the PASE and the GDS-15 total scores were found to be very weakly and significantly negatively correlated ($p<0.05$) (Table 1).

Table 2 shows crude and adjusted odds ratios and 95% CIs for determinants of depressive symptoms among older adults. The presence of depressive symptoms was 3.96 times (CI 95%: 2.03-7.73) more common among women and 8.06 times (CI 95%: 4.41-14.70) more common among those living in urban areas. While it was 2.56 times (CI 95%: 1.43-4.59) more common among those who stated that their income and expenses were equal, it was 2.78 times (CI 95%: 1.33-5.79) more common among those who stated that their income was less than their expenses. The presence of depressive symptoms was 1.98 times (CI 95%: 1.10-3.58) more common among those who had chronic illnesses and 25.54 times (CI 95%: 5.69-114.56) more common among those who were diagnosed with COVID-19. It was 23.24 times (CI 95%: 11.66-46.31) more common among those who did not have any hobbies. It was found that a one-point increase in the LSE total score increased the presence of depressive symptoms by 1.53 times (CI 95%: 1.41-1.66) (Table 2).

DISCUSSION

This study examines the prevalence of the presence of depressive symptoms among individuals aged 65 years and above and the related factors during the fourth wave of the COVID-19 pandemic on a sample representing the province of Sakarya. This study shows that the presence of depressive symptoms is common among older adults. The presence of depressive symptoms was found in approximately 66.8% of older adults who participated in this study. Significant results were found between depressive symptoms and gender, place of residence, income status, presence of chronic diseases, history of COVID-19 diagnosis, presence of a hobby, and perception of loneliness of the participants.

This study further shows that two out of three older adults suffered depressive symptoms. This rate was quite high compared with the result in the

Table 1. The relationship between the depressive symptoms level of older adults and loneliness and physical activity level

n=1093		GDS-15 total score	LSE total score	PASE total score
GDS-15 total score	r	1.000		
	p	-		
LSE total score	r	.610**	1.000	
	p	<0.001	-	
PASE total score	r	-.071*	.144**	1.000
	p	0.019	<0.001	-

** p<0.01, * p<0.05, Spearman correlation analysis

GDS-15: Geriatric Depression Scale-15, LSE: Loneliness Scale for the Elderly, PASE: Physical Activity Scale for the Elderly

Table 2. Factors associated with depressive symptoms assessed by GDS-15 among older adults *

Factors		Bivariate analysis		Logistic regression (Enter) Model		
		cOR	CI 95%	Adj.† OR	CI 95%	p
Gender (n=1093)	Female (n=684)	1.37	1.06-1.77	**3.96**	**2.03-7.73**	**<0.001**
	Male (n=409)	1.00 (ref.)	-	1.00 (ref.)	-	
Age group (n=1093)	65-74 (n=788)	1.00 (ref.)	-	-	-	
	75-84 (n=246)	1.04	0.77-1.42	-	-	
	≥85 (n=59)	1.06	0.60-1.90	-	-	
Marital Status (n=1093)	Single (n=399)	1.59	1.21-2.09†	2.02	0.62-6.55	0.240
	Married (n=694)	1.00 (ref.)	-	1.00 (ref.)	-	
Residence (n=1093)	Urban area (n=775)	3.26	2.48-4.29†	**8.06**	**4.41-14.70**	**<0.001**
	Rural area (n=318)	1.00 (ref.)	-	1.00 (ref.)	-	
Education (n=1093)	≤Low/Moderate (n=687)	1.39	1.01-1.80†	0.52	0.30-1.00	0.053
	≥High school (n=406)	1.00 (ref.)	-	1.00 (ref.)	-	
Working status (n=1093)	Not working (n=312)	3.41	2.46-4.76†	0.71	0.34-1.46	0.358
	Working (n=106)	2.63	1.63-4.36†	0.43	0.16-1.16	0.097
	Retired (n=675)	1.00 (ref.)	-	1.00 (ref.)	-	
Income (n=1093)	Income< expenses (n=272)	1.76	1.25-2.49†	**2.78**	**1.33-5.79**	**0.006**
	Income= expenses (n=536)	2.47	1.82-3.34†	**2.56**	**1.43-4.59**	**0.001**
	Income>expenses (n=285)	1.00 (ref.)	-	1.00 (ref.)	-	



Social security status (n=1093)	No (n=87)	1.53	0.98-2.43	0.63	0.13-3.03	0.566
	Yes (n=1006)	1.00 (ref.)	-	1.00 (ref.)	-	
Living together (n=1093)	Alone (n=267)	1.49	1.10-2.03†	0.41	0.12-1.38	0.151
	Children (n=147)	2.48	1.62-3.83†	1.16	0.29-4.49	0.831
	Spouse and children (n=123)	8.13	4.30-16.72†	0.62	0.23-1.61	0.327
	Spouse (n=556)	1.00 (ref.)	-	1.00 (ref.)	-	
Smoking (n=1093)	Yes (n=145)	1.25	0.85-1.85	-	-	
	No (n=948)	1.00 (ref.)	-	-	-	
Having any chronic disease (n=1093)	Yes (n=788)	1.60	1.21-2.11†	**1.98**	**1.10-3.58**	**0.024**
	No (n=305)	1.00 (ref.)	-	1.00 (ref.)	-	
COVID-19 diagnosis (n=1093)	Yes (n=102)	7.59	3.66-17.97†	**25.54**	**5.69-114.56**	**<0.001**
	No (n=991)	1.00 (ref.)	-	1.00 (ref.)	-	
Quarantine owing to COVID-19 (n=1093)	Yes (n=117)	1.3	0.85-2.01	-	-	
	No (n=976)	1.00 (ref.)	-	-	-	
History of COVID-19 infection in people around (n=1093)	Yes (n=292)	1.44	1.08-1.95†	0.85	0.46-1.57	0.612
	No (n=801)	1.00 (ref.)	-	1.00 (ref.)	-	
Have any hobbies (n=1093)	No (n=638)	19.68	14.2-27.58†	**23.24**	**11.66-46.31**	**<0.001**
	Yes (n=455)	1.00 (ref.)	-	1.00 (ref.)	-	
****LSE total score (n=1093)**		*Every 1-point increment*		**1.53**	**1.41-1.66**	**<0.001**
****PASE total score (n=1093)**		*Every 1-point increment*		1.01	1.00-1.01	0.057

R^2= 0.764; Constant B= -7.791; S.E=0.679; Wald=131.5 ($p < 0.001$)

* Independent variables entered in the Logistic regression model: gender, marital status, place of residence, education, employment status, income, social security, cohabitant, chronic illness, COVID-19 history, presence of COVID-19 positive people, hobby, loneliness level, physical activity level.

†Statistically significant (p<0.01); cOR: Crude Odds Ratio; Adj. OR: Adjusted Odds Ratio CI 95%: confidence interval 95%.

**LSE: Loneliness Scale for the Elderly, PASE: Physical Activity Scale for the Elderly

literature. Studies conducted in Turkey before the pandemic showed that the prevalence of depressive symptoms among older adults ranged from 27% to 53% (5,11,12,19). A study conducted on older adults aged 60 years and above and living in rural areas in Brazil showed that the incidence of depressive symptoms was 8% (20). In another study conducted in China during the COVID-19 pandemic, 37% of older adults were found to suffer the symptoms of depression or anxiety (10). A study conducted on individuals aged 65 years and above during the COVID-19 pandemic in Turkey showed that the prevalence of depressive symptoms was 44% (21). In Spain, this rate was found to be 25% among individuals aged 60 years and above (22). It was determined that the COVID-19 pandemic and the lockdown period increased the presence of depressive symptoms among older adults (21,22).

It is stated that depressed older people are more worried about contracting the virus than the risks of isolation (3). The high prevalence of depressive symptoms in this study may be due to the fact that the study period was in the fourth wave of the COVID-19 pandemic. Studies with a low prevalence of depressive symptoms were conducted in the first wave of the pandemic (21,22). The prolongation of the pandemic may have resulted in an increased prevalence of depressive symptoms in the elderly. Another reason for the differences in prevalence rates may be the use of different scales to evaluate the presence of depressive symptoms. The Geriatric Depression Scale used in this study is administered using a smaller cut-off point (≥ 5).

This study shows that women suffered depressive symptoms more than men. This finding corresponds with the literature. Studies conducted in different countries show that depressive symptoms are more common among women (5,7,11,12,19,20). It is stated that the biological structure and personality, mental characteristics, coping styles, and social and cultural positions in the environment they live in make them more prone to depression (6,20). A study conducted during the pandemic in Turkey showed that the prevalence of depressive symptoms did not change according to gender and that the living conditions brought about by the pandemic influenced depressive symptoms more among both genders (21). During the COVID-19 pandemic in China, women aged 60 years and above were found to suffer the symptoms of anxiety and depression more than men (10). This shows that in addition to other aging-related problems, the COVID-19 pandemic has a more traumatic effect on women.

This study further asserts that the prevalence of depressive symptoms was higher among older adults living in urban areas. The prevalence of depressive symptoms was found to be quite low among those living in rural areas in Brazil (20). It is stated that the place of residence and mental health of an individual during the COVID-19 pandemic are related and that living in urban areas is a predictive factor of depressive symptoms (6). People living in urban areas may have less sleep, worse living conditions and suffer more risk factors of mental health (20). Crowded areas pose a greater risk of the spread and infection of COVID-19, which spreads through droplets. Such viruses can be transmitted more easily in urban areas with a higher human population. Majority of the COVID-19 cases in Turkey are considered to occur in urban areas (2). For this reason, the mental health of older adults living in urban areas is at risk of getting more affected. Since the individual's mental health is affected by the psychosocial environment, environmental and socio-cultural factors should also be taken into account. Due to the lockdown practices during the pandemic, the elderly living in the city could not go out of their homes, while those living in the rural areas were able to go out to the open area more easily. For this reason, as social isolation is more intense in the city, the elderly may have difficulties in meeting their psychosocial needs.

This study shows that depressive symptoms was more common among the older adults who stated that their income was equal to or less than their expenses. Although some studies in the literature show that there is a relationship between economic level and depressive symptoms among older adults (6,7,12), some other related studies contradict this assertion (19,20). A study conducted in Spain stated that the prevalence of depressive symptoms increased among older adults who had incurred economic losses during the COVID-19 pandemic (22). This population is susceptible to economic losses and can suffer increased emotional distress.

A study conducted in Turkey before the pandemic showed that the presence of depressive symptoms was more common among older adults who suffered chronic diseases (12). In Brazil, it was reported that the presence of depressive symptoms was 2.4 times more common among patients who suffered two or more chronic diseases (20). Studies



conducted in Turkey and Korea showed that the presence of depressive symptoms was more common among older adults who had been experiencing constant pain and discomfort (7,19). Consistent with our findings, studies conducted during the COVID-19 pandemic show that depressive symptoms are more common among older adults with chronic diseases (6,21). In old age, an increase in drug consumption and withdrawal from working life in conjunction with chronic diseases may result in less interaction with others, a worse perception of health, and depressive symptoms (20).

In addition to the panic, uncertainty, and the feeling of being out of control during pandemics, the prolongation of the pandemic period may negatively affect the psychology of older adults. This study shows that the presence of depressive symptoms was more common among older adults who had been diagnosed with COVID-19. It is stated that the risk of depression is high among those who take inadequate personal preventive measures to protect themselves from COVID-19 (6). It has been reported that the presence of depressive symptoms in Turkey is more common among older adults who are afraid of contracting COVID-19 (21). Our study data were collected during the fourth wave of the COVID-19 pandemic. The mutation of the virus and the prolongation of the pandemic may have brought about concerns about contracting the disease again among older adults.

According to the loneliness scale used in this study, the level of depressive symptoms increased as the loneliness level increased. Loneliness is common among older adults and can result in an increased prevalence of depression and suicide. It has been suggested that loneliness reduces psychological resilience and impairs social integration, hence increasing isolation (1,4). Social isolation also reduces the anti-viral immune response among the older population (1). Literature shows that there is a positive relationship between depressive symptoms and living alone and an increased feeling of loneliness among older adults (5,21,23,24). A study conducted in Turkey showed that the level of depressive symptoms decreased as the perceived social support level of older individuals increased (12). It is stated that those who receive enough psychological and social support from the family or social environment during the pandemic are less mentally affected by the COVID-19 pandemic (6). Emotional and social support may be important for reducing the feeling of loneliness among older adults during the pandemic.

This study shows that having a hobby was very effective in preventing depressive symptoms among older adults. The presence of depressive symptoms was more common among those who did not have any hobbies. A study conducted during the COVID-19 period showed that older adults managed to overcome the negative emotions they experienced following their regular hobbies, exercise, and daily occupations (3). Spain during the COVID-19 pandemic, the association of low PA with depressive symptoms among in the elderly were revealed (25). Therefore, moderate or vigorous regular physical activity done by older adults may be a protective measure against their psychological health during social isolation (9,24). The results regarding the relationship between PA and depression in some studies in the literature are similar to our findings (20,22). In Korea, regular PA was shown to be directly effective in preventing depressive symptoms among older adults (7). They are encouraged to engage in regular PA owing to its positive effect on maintaining physical health and strengthening the immune system during the COVID-19 pandemic (8,9,10).

This study has some limitations. First, the generalizability of the findings is limited; these findings can only be generalised to the province where the research data were obtained. Approximately two-thirds of the participants of this study were women. The prevalence of depressive symptoms is higher among women. Therefore, this study may have found a higher the prevalence of depressive symp-

toms than it actually is. However, this study is important because it reflects a province in general during the pandemic, given that it was conducted on older adults living in a developed province of Turkey. Another strength of this study was that the overall response rate was high.

In conclusion, the presence of depressive symptoms was determined in two out of three older adults in this study. Psychological characteristics such as a history of COVID-19 and perceived loneliness among older adults who were at risk of contracting the virus were significant influencing factors of depressive symptoms. The presence of depressive symptoms was more common among women, those living in urban areas, those who stated that their income was equal to or less than their expenses, those with a history of a chronic disease, and those who did not have a hobby. During the pandemic period, feasible, and protective policies that cater for the needs and control the risk factors of older adults, who are a vulnerable group, should be adopted. Home care services including a multidisciplinary team can be increased to reduce the feeling of loneliness among older adults and protect their mental health.

Conflict of interest

The authors declare that they have no conflict of interest.

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RESEARCH

EFFICACY OF NON-INVASIVE CONTINUOUS POSITIVE AIRWAY PRESSURE AND HI-FLOW NASAL CANNULA OXYGEN THERAPY IN GERIATRIC PATIENTS WITH COVID-19 PNEUMONIA ADMITTED TO INTENSIVE CARE UNIT

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2022.299
2022; 25(3): 396-408

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Received : Mar 05, 2022
Accepted : Aug 19, 2022

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Abstract

Background: There is insufficient evidence regarding the effectiveness of non-invasive continuous positive airway pressure and high-flow nasal cannula oxygen therapy to reduce the requirement of invasive mechanical ventilation in geriatric patients with coronavirus disease-2019 pneumonia. This study aimed to compare the efficacy of two oxygenation therapies in geriatric patients with coronavirus disease-2019 pneumonia.

Material and Methods: Data from 141 geriatric patients who underwent continuous positive airway pressure or high-flow nasal cannula oxygen therapies at the intensive care unit of the Anesthesiology and Reanimation Department, Elazıg Fethi Sekin City Hospital, between 1 April 2020 and 1 March 2021 were retrospectively investigated. The primary outcome of interest in our study was to compare patient mortality, patient characteristics and the effectiveness of two accepted respiratory support modalities.

Results: A total of 141 patients, 57 female (40.42%) and 84 male (59.58%), aged 65-99 years met the inclusion criteria. Baseline demographic data and pre-existing comorbidities of geriatric patients with coronavirus disease-2019 pneumonia were recorded. The most common comorbidity was hypertension (69.7%). Of the 65 patients treated with high-flow nasal cannula oxygen, 36 were intubated; 18 of these intubated patients died (27%). Of the 76 patients who were treated with continuous positive airway pressure,28 were intubated;19 of these intubated patients died (25%).

Conclusion: In this retrospective observational study, continuous-positive airway pressure or high-flow nasal cannula oxygen therapy in geriatric patients with coronavirus disease-2019 was associated with a lower risk of invasive mechanical ventilation and no significant difference was found in patient mortality due to either treatment modality.

Key words: Continuous Positive Airway Pressure, Geriatrics, COVID-19.



INTRODUCTION

After the coronavirus disease (COVID-19) was first reported in December 2019 in China, it began to rapidly spread globally. Consequently, the World Health Organization (WHO) announced that the disease had become a pandemic in March 2020. COVID-19 has a broad clinical spectrum and can occur in clinical conditions ranging from asymptomatic cases to cases with severe respiratory failure requiring intensive care. COVID-19 continues to affect millions of individuals worldwide. From the first week to November 7, 2021, a slight upward trend (1% increase) was noted in the number of new weekly cases, with more than 3.1 million new cases reported. The WHO European Region reported an increase in the case and death incidences, while other regions reported declining or stable trends. As of 7 November 2021, over 249 million confirmed cases and over 5 million deaths had been reported (1). The clinical course of COVID-19, a global problem, varies. Although approximately 80% of COVID-19 cases are asymptomatic to mild, approximately 15% of patients show severe symptoms and approximately 5% exhibit a critical course, which frequently includes lung involvement with respiratory failure (2). The patients necessitating hospitalisation for COVID-19 predominantly present with acute hypoxaemic respiratory failure (AHRF)(3). The conventional low-flow oxygen therapy is hold out for patients with mild to moderate disease however patients with severe or critical illness are require more improved support. Endotracheal intubation and mechanical ventilation constitute the highest level of care for patients with AHRF but beds and ventilators in the intensive care unit (ICU) are limited. High-flow oxygen therapy through a nasal cannula (HFNO) or continue positive airway pressure (CPAP) are an important part of the treatment in patients with COVID-19 failing on conventional oxygen therapy in our ICU and has recently been endorsed in the surviving sepsis campaign (SSC) guidelines on COVID-19 (4).

Advanced age, hypertension, diabetes, chronic lung disease, asthma, chronic kidney disease, liver disease, cancer, obesity, and smoking are the risk factors of COVID-19. Age is a well-established risk factor for severe COVID-19 outcomes, with over 90% of deaths in the United Kingdom being reported in people over 60 years of age. Although individuals of all ages are at risk, the risk of severe disease is greater in people aged ≥60 years with chronic medical conditions. Regardless of the chronic condition, the mortality rate is the highest among those aged above 70 years (5).

According to the WHO, people aged 18-65 years are considered young adults, those aged 66–79 years are considered elderly, and those aged ≥80 years are considered very old (1,6). Various risk factors, including old age, male sex, hypertension, diabetes, obesity, chronic pulmonary diseases, and heart, liver, and kidney diseases, play a role in the development of severe COVID-19. Severe hypoxaemic respiratory failure may develop in patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and these patients require respiratory support (7).

COVID-19 patients who develop hypoxaemia despite conventional low-flow oxygen therapy are often treated with HFNO and CPAP therapies, according to international guidelines (4). Non-invasive ventilation (NIV) refers to mechanical ventilatory support using a full-face mask, nasal, oronasal, or helmet (8). CPAP is one of the most commonly used NIV modalities (4,8). The mortality rate of patients who require invasive mechanical ventilation (IMV) due to severe COVID-19 pneumonia is approximately 40%. Thus, non-invasive respiratory treatment modalities, such as HFNO and CPAP, have been widely adopted for patients with hypoxaemic respiratory failure secondary to COVID-19 (6,8).

The use of CPAP for patients with COVID-19 was first suggested based on experience in Italy (9). Similarly, CPAP and HFNO treatments are recommended by Perkins et al. as the basis of non-invasive

respiratory support for COVID-19, and they have reported that they are suitable for use in patients with severe hypoxaemic respiratory failure due to COVID-19 who are not eligible for IMV treatment. HFNO is a non-invasive respiratory support modality that delivers warm, humidified oxygen at a maximum flow rate of 60 L/min and up to 100% of the inspired oxygen fraction (FiO_2) through the nasal cannula (10,11). CPAP treatment aims to increase functional residual capacity (FRC), remedy oxygenation, enhance lung compliance, and delay or avoid intubation (11,12). Endotracheal intubation and mechanical ventilation comprise the highest level of care for patients with AHRF; however, ventilators, healthcare professionals, and beds in the ICUs are limited (4).

Due to the concern about the use of HFNO and CPAP due to viral load in epidemics, we found a limited number of studies in the COVID-19 pandemic, and we aimed to examine the effectiveness of non-invasive methods and contribute to the literature by sharing our experiences, since the need for mechanical ventilators in intensive care units has increased excessively and they are not enough for patients (13).

In this retrospective study, we aimed to examine the effectiveness of oxygen therapy with HFNO and CPAP, length of hospital stay, and mortality rates in geriatric patients diagnosed with COVID-19 who were admitted to the ICU.

MATERIALS AND METHODS

After approval by the Ethics Committee of Elazig Fırat University Faculty of Medicine (number 2021/04-39), data from 141 geriatric patients who underwent CPAP or HFNO therapy in the ICU of the Anaesthesiology and Reanimation Department, Elazıg Fethi Sekin City Hospital, between 1 April 2020 and 1 March 2021 were retrospectively investigated. Data were collected from the hospital electronic record systems and patient charts. Patients' demographic data, including age, gender, preexisting chronic diseases such as hypertension, diabetes mellitus, chronic pulmonary diseases, malignancy, chronic kidney disease, coronary artery disease, cerebral infarction and admission comorbidities were collected. Data analysis was performed for geriatric patients who tested positive for SARS-CoV-2 following the polymerase chain reaction (PCR) test, had typical anamnesis, symptoms, and pulmonary infiltrates on conventional chest radiography or computed tomography scan (CT) and oxygen saturation <92% treated with HFNO or CPAP where CPAP was considered a more advanced modality of respiratory support. All patients included in the study, according to Infectious Disease Society of America (IDSA) and American Thoracic Society (ATS) ICU admission criteria (14), radiological (posterior/anterior) X-ray or CT infiltration > 50%, tachypnea (respiratory rate > 30 breath/min), a ratio of the partial pressure of arterial oxygen (PaO_2) to the fraction of inspired oxygen (FiO_2) (PaO_2/FiO_2) < 300 mm Hg. The clinical data, including admission disease severity scores [Sequential Organ Failure Assessment (SOFA) score and Acute Physiology and Chronic Health Assessment-II (APACHE-II)] and Glasgow Coma Scale (GCS) scores were recorded. APACHE II score and SOFA score were used for predicting ICU mortality and prognosis (15). The patients had partial pressure of arterial carbon dioxide ($PaCO_2$) not higher than 45 mm Hg. The most common types of respiratory failure were patients with COVID-19 in general units, with type 1 and, to a lesser extent, type 2 or a combination. Those with type 1 AHRF were included in the study. The patients were identified as requiring non invasive respiratory support on clinical grounds and supported using a management algorithm based on current SSC and other guidline recommendations (4,16). The patients with geratric COVID-19 pneumonia who had peripheral oxygen saturation (SpO_2) < 92% despite conventional low-flow oxygen therapy of at least 6 L/min for at least 15 minutes received either CPAP or HFNO therapy (Figure 1). All physiological parameters and labora-

Figure 1. Flowchart for the treatment of type 1 respiratory failure

Type1 respiratory failure. Target: All patients without chronic lung disease and COPD patients with PCO_2 < 6.0 kPa: SpO2 92-96%. Patients with COPD and PCO_2 > 6.0 kPa: SpO_2 88-92%	
Oxygen supply	
Mild to moderate COVID-19: Target SpO_2 obtainable with ≤ 5 L O_2/min (FiO_2 0.4), delivered by bi-nasal cannula	
⬆ **Target SpO_2 obtained**	**Target SpO_2 not obtained** ⬇
Severe COVID-19: Target SpO_2 obtainable with 6-15 L O2/min (FiO_2 0.4-0.6). Consider advising ICU-personnel about the patient's condition. Use:	
cCPAP, initially 10-12 cm H_2O, may be increased	
OR	
HFNO with Optiflow™: Initial flow 45 L/min + oxygen to meet SpO_2 requirements.	
OR	
Oxygen by reservoir mask	
⬆ **Target SpO_2 obtained**	**Target SpO_2 not obtained** ⬇
Very severe COVID-19: Target SpO_2 obtainable with > 15 L O_2/min (FiO_2 > 0.6):	
DI:	**DNI:**
Consult ICU consultant: Continue HFNO at higher flow/higher FiO_2 at IMU or ICU	Continue HFNO at higher flow/higher FiO_2 at IMU
OR	**Target SpO_2 not obtained** ⬇
Intubate	NIV, closed system, e.g. 6/16 cm H20. Effect should be evaluated after i.e. 2 hours

DI; Do Intubate, DNI; Do Not Intubate, *CPAP;* continuous positive airway pressure, *COPD;* chronic occlusive pulmonary disease, *FiO_2;* inspiratory oxygen fraction, *PaO_2;* arterial oxygen tension, *ICU;* Intensive Care Unit, *NIV;* non-invasive ventilation, *IMU;* Intermediate Care Unit, *HFNO;* High Flow Nasal Cannula Oxygen. *Adapted from Jeschke KN et al. 2020 (16).*

tory markers of the patients included in the study were analyzed from the records shortly before the initiation of CPAP/HFNO therapy. Laboratory tests including white blood cell counts (WCC), C-reactive protein (CRP), D-Dimer, urea, creatinine and arterial blood gas analysis were also recorded.

The patients receiving <10 L/min standard oxygen therapy on the first day, incomplete results, receiving IMV or bi-level positive pressure (BiPAP) ventilation support, carbon dioxide pressure in venous blood gas (pCO2) > 6 kPa (VBG), a GCS score of 13 points or less, chronic obstructive pulmonary disease stage III-IV and those who decided not to participate were excluded from the study.

The primary outcomes of interest were patient mortality, patient characteristics, length of stay in the ICU, modality of respiratory support, admission, and outcome data. Treatment tolerance was authenticated on a post-hoc basis through a review of patients' adherence to therapies, as documented in their clinical case records.

HFNO treatment strategy

HFNO (Optiflow™ nasal high-flow interface) driven by AIRVO 2 humidification system (Fisher and Paykel Auckland, New Zealand) were used. The initial airflow was set at 45 L/min and adjusted according to patient tolerance. The HFNO was set to a certain humidity of 44 mg H_2O/L, temperature was set to 37 °C, and FiO_2 (between 0.21 and 1.0) was adjusted to maintain an SpO2 of 88-92% (Figure1).

CPAP treatment strategy

The face mask CPAP was started at a flow of 40 L/min and a PEEP of 10 cmH_2O which can be increased to a maximum of 20 cmH_2O at the at the discretion of the physician's. We suspect that the PEEP had normally been used at around 8–10 (−12) cmH_2O (Figure 1). The CPAP machines were Hamilton C3 (Hamilton Medical AG Via Crusch 8, Switzerland) devices.

Patients with facial anomalies and tracheostomy, as well as those who were evaluated by the treating clinician as requiring urgent intubation and invasive ventilation due to severe hypoxia, acidosis and/or respiratory distress, upper airway obstruction, inability to manage airway secretions, or recurrent apneas, were excluded from the study. Patients who were transferred from other hospitals where they were previously treated were excluded.

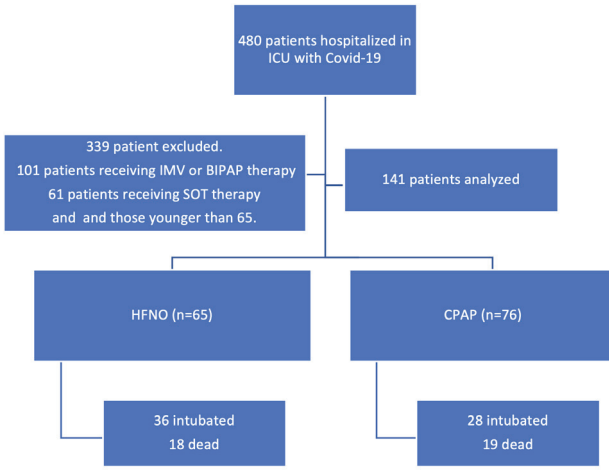
All laboratory markers and physiological parameters included in the study were measured before and after the initiation of CPAP or HFNO treatment. The patients diagnosed with COVID-19 underwent face mask CPAP or HFNO therapy if they had hypoxaemia with an oxygen supply of >10 L/min to maintain SpO_2≥ 92%. The CPAP and HFNO treatments were handled by trained nurses in close collaboration with ICU anaesthesiologists and intensivists. Patients were closely monitored using non-invasive blood pressure (BP) measurements and pulse oximetry during treatment. Contraindications for starting CPAP included pneumothorax, systolic BP < 90 mmHg or diastolic BP < 50 mmHg, nausea/vomiting, or coma. The treatment was stopped if the patient did not tolerate the CPAP mask. The aim of CPAP treatment was to increase FRC, improve oxygenation, increase lung compliance, and conceivably delay or avoid intubation. The intubation rates and mortality rates of the patients who were treated with HFNO or CPAP were recorded (Figure 2).

Statistical Analysis

In the statistical analysis, continuous variables were presented as mean ± standard deviation (SD), and categorical variables were presented as numbers and frequencies (percentages). Continuous variables were expressed as mean ± SD or median with interquartile range (IQR) and were compared between the two groups using the Mann-Whitney U test. All data were exported to SPSS (version 27; IBM, Armonk, NY, USA) for further analysis. Multiple comparisons of continuous variables were per-



Figure 2. Flow chart. *NIV;* Non-invasive Ventilation, *CPAP;* Continuous Positive Airway Pressure, *ICU;* Intensive Care Unit, *HFNO;* High Flow Nasal Canula Oxygen



formed using ANOVA. For the post-hoc analysis, we used a Bonferroni-adjusted *t-test* for multiple comparisons. The significance threshold was set at $P < 0.05$.

Table 1. Basic demographic data and pre-existing comorbidities

Patients (n%)	**141**
Female	57 (40.42)
Male	84 (59.58)
Age (years)	79±14
Body mass index (kg/m²)	27.3±3.7
Hypertension	98 (69.7)
Subsistence of two or overage comorbidities	61 (43.26)
Diabetes mellitus	31 (21.9)
Coronary artery disease	30 (21.27)
Malignancy	29 (20.56)
Asthma	26 (18.43)
COPD	16 (11.34)
Cerebrovascular disease	6 (4.25)
Chronic renal disease	3 (2.41)

Data are presented as % or mean ± SD, unless otherwise defined. COPD: Chronic obstructive pulmonary disease

RESULTS

A total of 141 patients, 57 women (40.42%) and 84 men (59.58%) aged 65-99 years met the inclusion criteria. Basic demographic data and preexisting comorbidities are shown in Table 1. The most common comorbidity detected in geriatric patients with COVID-19 was hypertension (69.7%). In addition, diabetes mellitus (21.9%) was frequently observed in these patients, and its association with hypertension and ischaemic heart disease is common. Prior to starting CPAP or HFNO, all patients had some level of respiratory distress. Of the 65 patients treated with HFNO, 36 were intubated and 18 of the intubated patients died (27%). Of the 76 patients who were treated with CPAP, 28 were intubated and 19 of the intubated patients died (25%) (*Fig 2).*

No significant difference was observed between the mortality rates of both groups ($p > 0.05$) (Table 2). Overall, 47 (72%) patients treated with HFNO and 57 (75%) patients treated with CPAP were discharged from the hospital in good health, without any significant difference ($p > 0.05$) (Table 2). The CPAP group tolerated oxygen therapy better than the HFNO group and had a reduced need for IMV ($p < 0.001$). No significant difference was observed between the mean length of hospital stay in either group ($p > 0.05$). When the laboratory test results of patients in the CPAP and HFNO groups were analysed, creatinine values were found to be higher in the CPAP group ($p = 0.016$). There was no significant difference in the length of (hospital) stay in the ICU between the two groups ($p > 0.05$) (Table 2).

Table 2. Characteristics of the study population and comparison between COVID-19 HFNO therapy and CPAP therapy

	HFNO (n=65)	CPAP (n=76)	P *value*
APACHE II scores	13 (5-17)	12 (6-17)	0.541
SOFA scores	3 (3-6)	3 (3-5)	0.872
GCS scores	15 (14-15)	15 (14-15)	0.962
Observations of the two group patients pre-HFNO/CPAP, mean±SD			
Arterial pH	7.46 (7.41-7.50)	7.43 (7.38-7.47)	0.103
FiO_2	82.7±19.5	81.3±21.5	0.891
PaO_2/FiO_2 ratio	229 (201–276)	227 (214–287)	0.671
Oxygen saturations	88.1±15.0	87.6±18.7	0.651
PaO_2, mmHg	57.3 ± 7.7	51.1 ± 9.3	0.583
Respiratory rate	25.2±6.9	27.4±6.3	0.058
Heart rate	87.6±15.3	91.7±17.7	0.073
Outcomes of the two group patients after HFNO/CPAP treatment, mean±SD			
Arterial pH	7.38 (7.35-7.43)	7.37 (7.36-7.45)	0.987
FiO_2	70.4±15.9	70.0±14.6	0.971
PaO_2/FiO_2 ratio	227 (196–292)	247 (224–304)	0.578
Oxygen saturations	91.6±7.9	93.3±6.8	0.048
PaO_2, mmHg	86.87±9.73	89.11±13.89	0.429
Respiratory rate	24.6±4.7	27.9±6.5	0.143
Heart rate	85.6±14.1	87.9±18.3	0.079
Laboratory results, mean±SD			
WBC $\times 10^9 \cdot L^{-1}$	11.6±5.3	12.6±4.1	0.897
D-Dimer ng mL^{-1}	2398±2154	2476±2259	0.351
C-Reactive protein $mg.L^{-1}$	147±116	163±102	0.161
Lymphocyte count $\times 10^9 \cdot L^{-1}$	1.02±0.63	1.01±0.66	0.635
Creatinine $\mu mol.L^{-1}$	98.1±57.3	109.1±79.7	0.016
Urea $mmol.L^{-1}$	12.1±10.3	13.8±10.7	0.052

Outcomes *n (%)*			
HFNO/CPAP duration days, median range†	3 (1-14)	5 (1-25)	0.062
HFNO/CPAP tolereted	29 (44%)	40 (52%)	0.001
Discharged from hospital	47 (72%)	57 (75%)	0.057
Mean Length of (hospital) stay*(IQR)	10 (4-19)	11,5 (3-23)	0.77
Death	18 (27%)	19 (25%)	0.873

CPAP: continuous positive airway pressure; HFNO: high-flow nasal oxygen; SOFA:Sequential Organ Failure Assessment Score; APACHE-II: Acute Physiology and Chronic Health Assessment-II;GCS: Glasgow Coma Scale; WCC: White blood cell; PaO_2:arterial oxygen tension; FiO_2: inspiratory oxygen fraction.†;n(%) and median range,*IQR:interquartile

DISCUSSION

Ageing, which is characterised by increased mortality and morbidity, is a universal process. Physiological, cellular, and molecular variations also affect the definition of ageing. Ageing affects the gas exchange properties. Arterial oxygenation gradually declines with age, likely secondary to an increase in ventilation/perfusion heterogeneity caused by a decrease in alveolar surface area and premature closure of small airways (4,17). Among the risk factors facilitating the development of pneumonia in elderly individuals are comorbidities, the negative effects of their treatments on the lungs, and changes in physiological parameters, such as the elastic retraction pressure of the lung, respiratory muscle strength, cough reflex with age, and the associated decrease in the defence capacity. In elderly patients, increased colonisation of microorganisms in the throat flora, microaspiration of these microorganisms, and the amount and virulence of the microorganism are factors that facilitate the development of pneumonia (17). In geriatric patients, diabetes, hypertension, chronic lung, kidney, cardiovascular, and cerebrovascular diseases, malignancies, and obesity (body mass index ≥ 40 kg/m²) increase the risk of mortality. In a study conducted in Italy, the data of the first 3200 patients who died due to COVID-19 were examined, and the average age of the expired patients was found to be 78.5 years. Only 481 patients had data on their underlying diseases. Of the 481 individuals, six (1.2%) had an underlying disease, 113 (23.5%) had two diseases, 128 (26.6%) had three diseases, and 234 (48.6%) had four or more diseases. Additional underlying diseases, in order of frequency, were as follows: hypertension (355, 73.8%), diabetes (163, 33.9%), ischaemic heart disease (145, 30.1%), atrial fibrillation (106, 22.0%), chronic kidney failure (97, 20.2%), cancer (94, 19.5%), chronic obstructive pulmonary disease (66, 13.7%), dementia (57, 11.9%), stroke (54, 11.2%), and chronic liver disease (18, 3.7%). The rate of comorbid diseases in patients hospitalised in the ICU is high (72.2%) (18). Similarly, in our study, we observed that the prevalence of hypertension, a comorbid disease, was higher than that of other comorbid diseases.

The patients with COVID-19 pneumonia may develop AHRF. Various indices have been used to define pneumonia. The clinical respiratory symptoms of SARS-CoV-2 infection frequently do not correlated to the severity of lung damage; thence, to correctly stratify COVID-19 patients, it is important to measure the acute lung injury based on well-acknowledged test for acute lung injury such as the partial pressure of arterial oxygen (PaO_2) to fraction of inspired oxygen (FiO_2) ratio (PaO_2/FiO_2). There are studies stating that the PaO_2/FiO_2 ratio can be seriously considered by healthcare professionals due to its accuracy and primitiveness (13,16). In our study, we used this index to detect early progression to

acute respiratory failure in patients who underwent HFNO or CPAP. The HFNO or CPAP therapy is frequently used in hypoxaemic respiratory failure and decreases the need for intubation without affecting the mortality rates (16). Early in the COVID-19 pandemic, these modalities were assumed to be controversial, owing to the lack of quality evidence for their use in the treatment of bacterial pneumonia. CPAP is a non-invasive method for positive airway pressure ventilation (13). In contrast, HFNO is an oxygen supplementation method that provides humidified oxygen at a flow rate of up to 100 L/min and FiO_2 between 21% and 100%. It is assumed that these modalities offer respiratory support by decreasing the work of breathing, providing a low level of positive end-expiratory pressure (PEEP), and improving mucociliary clearance through humidification of oxygen (4,16). First-line options for supporting patients with respiratory failure and hypoxaemia are oxygen with a simple nasal cannula, Venturi masks, and a high-flow nasal cannula. Its heating and humidification properties make HFNO more tolerable. In addition, the soft and loose nasal interface makes it more comfortable to use and does not prevent the patient from speaking and eating. Some indicators are useful in monitoring oxygenation status and predicting outcome in patients with HFNO. If gas exchange worsens and oxygen demand increases despite these treatments, CPAP therapy, NIV, or IMV should be considered. In this study, we observed that the treatment was successful and the need for IMV was reduced by regular monitoring of the PaO_2/FiO_2 ratios of the patients and by increasing the oxygen support with noninvasive methods, HFNO or CPAP instead of considering the presence of hypoxemia according to the clinical situation. We did not find a statistical difference in the need for IMV between the two groups. However, we found that the tolerance to treatment of the patients in the HFNO group was better than in the CPAP group. The overall goal is to provide adequate oxygenation. A target of $SpO_2 \geq 90\%$ or $PaO_2 > 55$ mmHg is recommended (4,10,16).

NIV application in patients with moderate and severe acute respiratory distress syndrome (ARDS) has a failure rate of up to 50% but is associated with a mortality rate of up to 50% in severe ARDS cases (19,20). In several studies, HFNO and CPAP therapies have been limited because of respiratory failure due to COVID-19 pneumonia. Early intubation and IMV are recommended in cases of severe hypoxaemia (PaO2/FiO2 ≤ 200 mm Hg). In our study, early intubation and IMV were used in patients with severe hypoxaemia. We believe that a delay in intubation adversely affects the recovery process in patients with failed NIV, and the risk of transmission to healthcare professionals working in the ICU is higher in cases in which urgent intubation is required (16). $PaO_2/FiO_2 \leq 150$ mmHg indicates hypoxaemic failure and is the threshold value that determines the increased mortality risk (20,21). NIV should be avoided in patients with uncontrolled secretions, risk of aspiration, haemodynamic disorders, multiorgan failure, or impaired mental status (6). The CPAP device consists of an airflow generating unit that is delivered to the airway through a helmet or face mask, and the effects of CPAP have been studied in more than 1100 patients with ARF due to COVID-19 pneumonia (21). The continue CPAP therapy may be considered for a patient with ARF associated with COVID-19 in the following situations. The patients with hypoxic respiratory failure require 6-15 L/min of oxygen (ie, fraction of inspired oxygen (FiO_2, 0.4-0.6) to achieve an acceptable level of oxygen saturation, and clinicians agree that an increase to IMV is an option, but not immediately necessary. An initial pressure of 10–12 cm H_2O may be applied when starting CPAP therapy because, as in other severe ARF cases, the positive end-expiratory pressure must be high (4,16). Generally, CPAP therapy has an almost immediate effect in improving the condition of patients with COVID-19-related ARF; however, intubation and IMV may be required if more oxygen is required**.** We applied CPAP with a face mask to patients who developed respiratory failure due to COVID-19.



Many international guidelines state that healthcare workers using devices that generate bioaerosols have a high risk of contracting the infection and suggest taking care and even contradicting the use of these devices (4,21,22). However, the WHO advocates that health workers can use CPAP, HFNO, or NIV treatment in patients with COVID-19 and respiratory failure, provided they wear appropriate PPE (22,23). In line with the recommendations of the international guidelines at the start of the COVID-19 pandemic, most clinicians prefer standard oxygen therapy or early IMV support for acute respiratory failure caused by COVID-19. They preferred the use of IMV to protect hospital personnel from aerosols formed during treatments, such as CPAP and HFNO. Despite this, the inadequacy of mechanical ventilators in ICUs at some centres and the inadequacy of personnel with sufficient training and experience have forced clinicians to use non-invasive techniques. In our COVID-19 ICUs, we used HFNO and CPAP treatments in accordance with the literature published in the later stages of the epidemic and the recommendations of international guidelines (4,22). We used oxygen support treatments with CPAP or HFNO for patients with COVID-19 after wearing the necessary PPE following the WHO recommendations. In addition, all patient rooms in our ICU had negative pressure and were single rooms. We believe that this significantly reduces bioaerosol exposure among healthcare workers.

A recent study argued for "permissible hypoxemia" and did not impose a target for oxygen saturation, which reduced the number of intubated patients. This was associated with an 83% treatment success rate for CPAP in patients deemed fit for IMV. This suggests that more patients should be treated with non-invasive methods of respiratory support. However, after this report was published, many opposing opinions have been suggested (24).

Geriatric patients have higher mortality rates than the general population. In a study investigating the clinical features of patients with SARS-CoV-2 pneumonia, the mortality rate of patients aged >80 years was 18.8% (25). In this study, the clinical parameters of the 60 geriatric patients were divided into two groups: 65-79 years and >80 years. We included 141 geriatric patients aged ≥65 years who were administered either of two oxygen therapy strategies in the ICU, CPAP or HFNO. The mortality rate was 25% in the CPAP group and 27% in the HFNO group, and no statistical difference was found between these rates ($p > 0.05$).

A multicentre observational study conducted to understand the global impact of severe acute respiratory failure showed no significant difference in the severity of ARDS and ICU and hospital death rates of patients with ARDS treated with NIV or mechanical ventilation. Associated comorbidities and demographic characteristics were examined in both the treatment groups. This study showed that mortality and failure rates in the NIV group were related to the severity of respiratory failure. Compared with HFNO, NIV does not significantly reduce the intubation rate and mortality of COVID-19 patients with ARDS (26). In our study, there was no statistically significant difference between intubation and mortality rates in geriatric patients who developed acute hypoxemic respiratory failure due to COVID-19 pneumonia, who were treated with HFNO or CPAP. We attribute this result to our early application of HFNO or CPAP. In two recent cohort studies, they were able to determine the cut-off value of the PaO_2/FiO_2 ratio as 274 mmHg in patients who developed ARF due to COVID-19 pneumonia (27,28). We also obtained similar findings in our study. In order to achieve successful results in HFNO or CPAP treatment, we believe that the PaO_2/FiO_2 ratio of patients should be followed regularly and correlated with laboratory parameters.

The CPAP and HFNO are appropriate treatment options for patients with hypoxemic respiratory failure due to COVID-19 pneumonia, including those deemed unsuitable for invasive ventilation. With respect to the therapeutic mechanism, HFNO in-

volves low PEEP (3 cmH_2O, on average). Nevertheless, this pressure level is uncontrollable, unstable, and is affected by many factors. In contrast, CPAP can ensure stable and adjustable airway pressure (8,19). In our study, we observed that patients treated with CPAP responded better to treatment and tolerated the treatment better than those treated with HFNO.

Few studies have compared the effectiveness of CPAP and HFNO treatments for acute respiratory failure due to COVID-19 pneumonia. Geriatric patients have several comorbidities, which affect the effectiveness and success of oxygen therapy modalities. This study aimed to contribute to the literature by examining the clinical parameters of geriatric patients with COVID-19.

This study had several limitations. First, only 141 geriatric patients with COVID-19 were included. Although the number of geriatric patients with COVID-19 treated in our ICU was much higher, those treated with IMV, standard oxygen therapy, or BiPAP were excluded from the study. Second, specific information, such as CPAP settings from the ICU data was missing. However, the data on clinical examination, supportive treatment of oxygen, living status, and the duration from ICU admission to death are indisputable. Third, this is a retrospective study. This study was a preliminary assessment of the clinical course and outcomes of geriatric patients with SARS-CoV-2 pneumonia. Further studies are needed to confirm this hypothesis.

CONCLUSION

In this retrospective observational study, the administration of HFNO or CPAP to geriatric patients with COVID-19 was associated with a lower risk of IMV. There was no significant difference in patient mortality according to the treatment modality. However, future multicentre studies with larger sample sizes are needed for more credible evaluation.

Conflicts of Interest

The authors of this article state that they have no conflict of interest.

Funding

No financial support was received from any institution or organization for this research.

Statement of Ethics

The study protocol was approved by the Research Ethics Committee of the Elazıg Fırat University of Medicine Faculty (ethical code 2021/04-39). The study was administrated in agreement with the Declaration of Helsinki.

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RESEARCH

NUTRITIONAL SUPPORT IN GERIATRIC PATIENTS IN INTENSIVE CARE: THE RELATIONSHIPS BETWEEN PREALBUMIN, ALBUMIN AND TOTAL PROTEIN LEVELS AND THE ROUTE OF NUTRITION ADMINISTRATION

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2022.300
2022; 25(3): 409-421

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Abstract

Background: Adequate nutrition for geriatric elderly patients hospitalized in the intensive care unit (ICU) is of great importance.

Objective: This study included critically-ill patients hospitalized in the ICU and aimed to determine the relationships between nutritional status, patient severity and the time-bound changes in various parameters known to be associated with malnutrition.

Methods: The study was conducted by retrospectively examining the files of 112 patients (63 women and 49 men) who received inpatient treatment in the ICU of Bartın State Hospital for at least 21 days.

Results: Apache II score (p=0.001), mortality risk score (p=0.003), intermittent nutrition (p = 0.046), low energy intake on day 7 (p=0.008), total protein level on day 30 (p=0.016), prealbumin level on day 21 (p=0.021), the change in prealbumin level from the 1st to the 21st day (p<0.001), and CRP level on day 30 (p=0.025) were significantly different between the groups. Multivariate analysis performed with these variables revealed that the change in prealbumin level from the 1st to the 21st day was the only parameter to be independently associated with length of stay (p=0.003).

Conclusions: In geriatric elderly patients admitted to the ICU, it was observed that albumin and total protein values did not change significantly during feeding, whereas prealbumin levels increased significantly on the 21st day compared to the 1st day.

Keywords: Nutritionists; Hospitals; Malnutrition; Albumins; Prealbumin.

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Received : Mar 30, 2022
Accepted : Jul 20, 2022

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INTRODUCTION

Malnutrition is a broad term and covers not only protein-energy malnutrition but also deficiencies of other nutrients such as micronutrients (1). Malnutrition can occur when patients are admitted for intensive care as a result of the metabolic response caused by factors such as insufficient nutrition and the severity of the disease (2). Malnutrition is more common in people admitted for intensive care and those with a critical illness. Providing appropriate nutritional support in malnourished patients prevents the increase of complications and purveys clinical, functional, financial benefits, and can increase survival (3).

Old age is usually defined as 65 years of age or older. In geriatric patients with age-related degenerative changes, there is an increase in the frequency of disease as a result of acute and/or chronic disease, restriction, regression, and changes in physical, mental and/or social functions. As age progresses, impaired cognitive function, increased frequency of chronic disease, and postural balance or walking disorders occur, and the frequency of hospitalization increases (4,5).

Protein and energy malnutrition is a common finding in patients admitted to intensive care units (ICU) (40% of patients). In practice, anthropometric measurements, laboratory results, and indirect calorimetry tests help in evaluating nutritional status; however, these measurements are known to be insensitive to short- or mid-term changes in nutrition (4-6). Serum albumin and prealbumin levels are indicated as markers of nutritional status. Low serum albumin and prealbumin levels in ICU patients have been associated with a higher risk of infection and death (7). In addition, low serum albumin and prealbumin levels are also an indicator of inflammation. Care should be taken when assessing a patient's nutritional status based purely on visceral protein markers, as they are non-specific and are affected by changes in homeostasis such as inflammation. The entire clinical context of a patient should be considered when using these values (8). However, levels of C-reactive protein (CRP), which is a non-specific acute phase reactant, is known to be negatively correlated with albumin and prealbumin levels (8,9,10). Assessment of prealbumin levels in combination with CRP levels is more clinical. The main assessment system for determining the risk of nutrition in critical ICU patients is nutritional risk screening-2002 (NRS). NRS is defined as the first step in identifying hospitalized patients who may benefit from the practice of nutrition (10,11). Early enteral and parenteral nutrition positively changes the duration of hospitalization and the clinical picture of patients in the ICU (12-14).

We believe that there is a correlation between the level of CRP values, low serum prealbumin levels, high NRS-2002 values and Apache II values used to determine nutritional status in hospitalized patients.

This study included critically-ill patients hospitalized in the ICU and aimed to determine the relationships between nutritional status (NRS-2002), patient severity (Apache II score) and the time-bound changes in various parameters known to be associated with malnutrition (CRP, serum albumin, prealbumin, total protein level). In addition, we aimed to determine the differences between patients receiving enteral or parenteral nutrition in terms of malnutrition-related parameters and the aforementioned relationships. Finally, we also aimed to identify nutritional parameters associated with the length of ICU stay.

MATERIALS AND METHODS

In this retrospective cohort study, the files of 112 patients hospitalized in the ICU of our hospital between February 2018 and October 2018 were reviewed retrospectively. Patients over 65 years of age who were hospitalized for at least 21 days and were included in a nutrition protocol were included in the study. Data were collected and recorded from



the hospital information system, ICU database, patient files and physician order forms. Study approval was obtained from the Non-Interventional Clinical Research Ethics Committee of Karabuk University (Date: January 3, 2018, Decision no: 1/13).

Total blood protein, albumin, prealbumin and CRP parameters of patients who started treatment in the ICU and received nutritional support were examined on the 1st, 3rd, 7th, 14th, and 21st days. Comparison of prealbumin, albumin, total protein values and CRP levels measured on the 1st and 21st days were performed among patients and longitudinal analyses of the changes were also performed. Values on the 30th and 60th days were also recorded in patients who had a relatively longer stay in the ICU.

Patients' demographic characteristics, admission diagnosis, underlying diseases, duration of hospitalization, Apache II score on admission, mortality, nutrition duration, the route of continuous feeding (enteral, parenteral), the method of feeding administration [nasogastric tube or percutaneous endoscopic gastrostomy (PEG)], and decubitus ulcers were recorded. Target energy and protein values were calculated for each patient (per kilogram weight). The number of calories to be given was determined between 25-30 kcal per kilogram, while obese patients received 18-20 kcal. Target protein was calculated to be 1.2-2 grams per kilogram. Energy and protein requirements were determined on the 1st, 3rd, 7th, and 21st days (and further when ICU stay was longer).

Patients were fed within the first 24-72 hours of their admission to the ICU. Enteral nutrition was used as the initial approach when applicable. Parenteral nutrition was initiated in patients whose gastrointestinal functions or disease course were not suitable for enteral nutrition. Patients receiving parenteral nutrition were switched to enteral nutrition at the earliest possible time when appropriate. Abdominal signs (pain, distension, diarrhea, vomiting, etc.) and residue was closely followed (every 4 hours). Enteral nutrition was discontinued for a short period of time in patients who developed abdominal signs or residue. If necessary, the product was replaced or reductions in the rate of infusion were made. Peripheral parenteral nutrition (PPN) or central parenteral nutrition (CPN) were added to patients who could not attain target levels via enteral administration. Parenteral nutrition was gradually discontinued in patients showing clinically-relevant improvement (determined by the attending physicians).

NRS 2002 values were evaluated separately in each patient. NRS-2002 values, serum albumin, prealbumin, total protein and CRP levels, APACHE II and mortality scores were compared in all patients. Serum albumin, total protein and prealbumin levels were compared in patients who underwent either the enteral or parenteral nutrition program, only. When the patient switched from parenteral nutrition to enteral nutrition, the patient was included in the enteral nutrition group when parenteral nutrition administration was performed for less than 80% of the total calories. The levels of total calories and protein given were recorded at first hospitalization and before the discontinuation of feeding.

Statistical analysis

All analyses were conducted with SPSS v21 (SPSS Inc. Chicago, Illinois, USA). The Kolmogorov-Smirnov test was used to check the normality of distribution in continuous variables. Data were given as mean ± standard deviation or median (25%-75% interquartile values) for continuous variables according to the normality of the distribution, and as frequency (percentage) for categorical variables. Repeated measurements of continuous variables were analyzed by the repeated measures analysis of variance (ANOVA) test for normally distributed variables, and non-normally distributed variables were analyzed by Friedman's analysis of variance. Repeated measurements of categorical variables were made by the Cochran's Q test. Post-hoc pairwise comparisons were done with the Bonferroni correction. In 2-group analyses, comparisons were done with the independent samples t-test for variables

with normal distribution, while the Mann-Whitney U test was used for variables without normal distribution. Linear regression analysis was performed to determine factors associated with the duration of stay in the ICU. $p < 0.05$ values were considered statistically significant results

RESULTS

The study included 112 elderly patients (63 women and 49 men), with a median age of 78 (66.5–84) years. The most common causes of hospitalization were respiratory problems (36.61%), neurological problems (33.93%), and poor overall condition (13.39%). Seventy-six (67.86%) patients had a nasogastric tube and 36 (32.14%) patients had a PEG for enteral nutrition. Eighty-one (72.32%) patients underwent continuous nutrition and 31 (27.68%) patients underwent intermittent nutrition. Forty-four (39.29%) patients had a decubitus ulcer. The average duration of stay in the ICU was 38.5 days (Table 1).

The percentage of parenteral nutrition (only parenteral or with enteral support) on the 1st and 3rd days were significantly higher than that of the 30th day ($p < 0.001$). Total energy intake on the 1st and 3rd days were significantly lower than that of the 30th day ($p < 0.001$). Total protein intake on the 1st and 3rd days were significantly lower than that of the 21st and 30th days ($p < 0.001$).

Energy intake for each kg on the 1st and 3rd days, were significantly lower than that of the 21st and 30th day ($p < 0.001$). Protein intake for each kg on the 1st and 3rd days were significantly lower than that of the 21st and 30th day ($p < 0.001$). Albumin levels on the 3rd days were significantly lower than that of the 30th day ($p = 0.036$). Prealbumin levels on the 1st and 7th day were significantly lower than that of the 21st and 30th day ($p < 0.001$). CRP levels on the 1st day was significantly higher than that of the other days ($p = 0.001$). Blood sugar levels on the 1st day was significantly higher compared to the 21st and 30th day ($p < 0.001$) (Table 2)

Table 1. Summary of patients' characteristics

Age	78 (66.5 - 84)
Gender	
Male	63 (56.25%)
Female	49 (43.75%)
Height	163 (158 - 170)
Weight	63.77 ± 14.49
Body mass index	23.86 ± 5.09
Ideal body weight	58.46 (54.92 - 63.58)
Arm circumference	24.5 (23 - 27)
Basal metabolic rate	1248.97 ± 195.70
ICU indication	
Neurological	38 (33.93%)
Respiratory	41 (36.61%)
Metabolic	1 (0.89%)
Renal	4 (3.57%)
Cardiovascular	7 (6.25%)
Poor general condition	15 (13.39%)
Gastrointestinal	6 (5.36%)
Hematological	0 (0.00%)
Type of ICU	
Level 3	32 (28.57%)
General	55 (49.11%)
Thoracic	24 (21.43%)
Emergency	1 (0.89%)
Energy requirement	
Minimum	1461.51 (1373.02 - 1589.50)
Maximum	1753.82 (1647.62 - 1907.40)
Protein requirement	
Minimum	76.52 ± 17.39
Maximum	127.53 ± 28.98
APACHE II score	18 (14 - 23)
Mortality risk score	29 (21 - 40)
Type of tube	
Nasogastric	76 (67.86%)
PEG	36 (32.14%)
Method of nutrition	
Continuous	81 (72.32%)
Intermittent	31 (27.68%)
Decubitus ulcer	44 (39.29%)
Length of stay in ICU, days	38.5 (28 - 57.5)

Data are given as mean ± standard deviation or median (1st quartile - 3rd quartile) for continuous variables according to the normality of distribution and as frequency (percentage) for categorical variables



Table 2. Summary of nutritional status and laboratory measurements with regard to time

	1st day (n=112)	3rd day (n=112)	7th day (n=112)	21st day (n=112)	30th day (n=94)	p
Parenteral nutrition	41 (36.61%)^{a}	31 (27.68%)^{a}	13 (11.61%)^{b}	8 (7.14%)^{b}	5 (5.26%)^{b}	<0.001
Calorie intake, total	1000 (790-1400)^{a}	1285.5 (1018-1627.6)^{b}	1429 (1200-1782.8)^{c}	1518.5 (1266.5-1773.6)^{c}	1536 (1360-1773.6)^{c}	<0.001
Lower than required	92 (82.14%)^{a}	66 (58.93%)^{b}	55 (49.11%)^{bc}	49 (43.75%)^{bc}	36 (38.71%)^{c}	<0.001
Protein intake, total	40.25 (30-69.65)^{a}	63 (46.75-88.2)^{b}	75.6 (62.6-90.5)^{bc}	77.2 (63.04-90.5)^{c}	81.05 (63.54-100.5)^{c}	<0.001
Lower than required	91 (81.25%)^{a}	67 (59.82%)^{b}	57 (50.89%)^{bc}	55 (49.11%)^{bc}	37 (39.78%)^{c}	<0.001
Calorie intake, for each kg	16.37 (11.76-22.81)^{a}	20.97 (16.76-26.62)^{b}	23.42 (18.23-28.2)^{c}	23.72 (19.32-29.94)^{c}	24.72 (20-29.87)^{c}	<0.001
Protein intake, for each kg	0.69 (0.48-1.1)^{a}	1.01 (0.76-1.38)^{b}	1.19 (0.88-1.52)^{bc}	1.21 (0.96-1.62)^{c}	1.26 (0.99-1.63)^{c}	<0.001
Total protein	5.07 ± 0.98 ^{a}	5.28 ± 0.88 ^{b}	5.46 ± 0.81 ^{c}	5.68 ± 0.90 ^{d}	5.73 ± 0.87 ^{d}	<0.001
Albumin	2.5 (2.1-2.9)^{ab}	2.3 (2.1-2.8)^{a}	2.5 (2.1-2.8)^{ab}	2.45 (2.2-2.8)^{ab}	2.5 (2.2-2.9)^{b}	0.036
Prealbumin	8 (5-11)^{a}	9 (7-12.5)^{ab}	10 (8-13.5)^{bc}	12 (9-14)^{cd}	13 (10-16)^{d}	<0.001
CRP	105 (63-157.5)^{a}	100 (47.1-128)^{b}	82.5 (50.3-121)^{b}	89.5 (53.3-121.5)^{b}	90 (47-110)^{b}	0.001
Glucose	135 (100-182)^{a}	120 (98.5-164.5)^{ab}	116 (95-160)^{ab}	111 (95-155)^{b}	111 (92-157)^{b}	<0.001

Data are given as mean ± standard deviation or median (1st quartile-3rd quartile) for continuous variables according to the normality of distribution and as frequency (percentage) for categorical variables. The same letters denote the lack of statistically significant difference between groups.

Laboratory measurements on days 1, 21 and 30, and the changes in these measurements were analyzed according to the type of nutrition received by the individuals (enteral or parenteral). It was found that the decrease in glucose levels was significantly higher in the parenteral nutrition group compared to the enteral nutrition group (p = 0.005). No significant difference was found between the groups with respect to other laboratory measurements (Table 3).

We additionally analyzed laboratory measurements on the 7th, 21st and 30t^{h} days and the changes in these measurements with respect to protein intake. In the low protein intake group, the prealbumin levels were found to be significantly lower compared to the normal/high intake group (p = 0.043) on the 30th day. No significant difference was found between the groups with respect to other laboratory measurements (Table 4).

Linear regression analysis was performed to determine factors that were independently associated with the length of stay in the ICU. Univariate analysis showed that the Apache II score (p = 0.001), mortality risk score (p = 0.003), intermittent nutrition (p = 0.046), low energy intake on day 7 (p = 0.008), total protein level on day 30 (p = 0.016), prealbumin level on day 21 (p = 0.021), the change in prealbumin level from the 1st to the 21st day (p < 0.001), and CRP level on day 30 (p = 0.025) were significantly different between groups. Multivariate analysis performed with these variables revealed that the change in prealbumin level from the 1st to the 21st day was the only parameter that was independently associated with length of stay (p = 0.003) (Table 5).

According to these results, an increase in prealbumin levels in the first 21 days reduces the duration of stay in the ICU.

Table 3. Summary of laboratory measurements with regard to the type of nutrition on the 1st day

	Type of nutrition on 1st day		
	Only enteral (n=71)	Parenteral (n=41)	p
Total protein			
21st day	5.65 ± 0.88	5.72 ± 0.95	0.685
30th day	5.73 ± 0.85	5.74 ± 0.92	0.979
Change, 1st & 21st day (1)	0.53 ± 0.80	0.73 ± 1.02	0.253
Change, 1st & 30th day (1)	0.57 ± 0.71	0.84 ± 1.17	0.223
Albumin			
21st day	2.5 (2.2-2.9)	2.4 (2.0-2.8)	0.167
30th day	2.6 (2.3-3.0)	2.3 (2.2-2.7)	0.104
Change, 1st & 21st day (1)	0 (-0.2-0.2)	-0.1 (-0.5-0.4)	0.636
Change, 1st & 30th day (1)	0 (-0.2-0.3)	0.1 (-0.5-0.4)	0.962
Prealbumin			
21st day	11 (9-15)	12 (9-14)	0.872
30th day	13 (10-17)	12 (8-16)	0.278
Change, 1st & 21st day (1)	3 (0-6)	4 (1-7)	0.325
Change, 1st & 30th day (1)	4 (1-8)	5 (1-9)	0.546
CRP			
21st day	86 (52-123)	90.3 (54.6-120)	0.830
30th day	88.2 (47-118)	90 (40-110)	0.863
Change, 1st & 21st day (1)	-20 (-55-20)	-24.9 (-70-12)	0.461
Change, 1st & 30th day (1)	-20 (-62-20)	-40 (-95-6)	0.177
Glucose			
21st day	110 (92-151)	111 (100-174)	0.244
30th day	103 (92-155)	116 (100-160)	0.159
Change, 1st & 21st day (1)	0 (-22-0)	-28 (-54-0)	0.005
Change, 1st & 30th day (1)	0 (-29-0)	-16 (-77-0)	0.119

Data are given as mean ± standard deviation or median (1st quartile-3rd quartile) for continuous variables according to the normality of distribution. (1) Negative values represent a decrease in measurements and positive values represent increase in measurements.



Table 4. Summary of laboratory measurements with regard to protein intake on the 7th day

	Protein intake on 7th day		
	Low (n=57)	**Normal & High (n=55)**	**p**
Total protein			
21st day	5.78 ± 0.87	5.57 ± 0.93	0.224
30th day	5.86 ± 0.88	5.61 ± 0.85	0.165
Change, 1st & 21st day (1)	0.62 ± 0.94	0.59 ± 0.84	0.833
Change, 1st & 30th day (1)	0.67 ± 1.04	0.67 ± 0.79	0.994
Albumin			
21st day	2.6 (2.2-2.8)	2.4 (2.1-2.8)	0.334
30th day	2.5 (2.3-2.8)	2.5 (2.1-2.9)	0.480
Change, 1st & 21st day (1)	-0.1 (-0.3-0.2)	0 (-0.3-0.3)	0.427
Change, 1st & 30th day (1)	0 (-0.2-0.2)	0.1 (-0.2-0.4)	0.466
Prealbumin			
21st day	12 (9-14)	11 (9-15)	0.809
30th day	12 (9-15)	15 (10-18)	0.043
Change, 1st & 21st day (1)	4 (1-7)	4 (0-6)	0.304
Change, 1st & 30th day (1)	4 (1-7)	5 (2-9)	0.377
CRP			
21st day	86 (55.8-118)	90 (50-128)	0.802
30th day	90.3 (40.5-104.7)	85.8 (49.3-117)	0.753
Change, 1st & 21st day (1)	-30 (-58.5-19.4)	-11.8 (-60-20)	0.476
Change, 1st & 30th day (1)	-40 (-81-5.9)	-20 (-54-12)	0.212
Glucose			
21st day	116 (95-160)	106 (92-150)	0.278
30th day	121 (95-159)	104 (92-151)	0.239
Change, 1st & 21st day (1)	-13 (-48-0)	0 (-38-0)	0.071
Change, 1st & 30th day (1)	-16 (-59-0)	0 (-34-0)	0.165

Data are given as mean ± standard deviation or median (1st quartile-3rd quartile) for continuous variables according to the normality of distribution. (1) Negative values represent a decrease in measurements and positive values represent an increase in measurements.

Table 5. Significant factors of the length of stay in ICU, linear regression analysis

	Univariate		Multivariate	
	β	p	β	p
Age	-0.153	0.107		
Apache II score	0.302	0.001	0.149	0.437
Mortality risk score	0.274	0.003	0.011	0.957
Type of tube, PEG	0.174	0.066		
Intermittent nutrition	-0.189	0.046	-0.046	0.665
Parenteral nutrition, 1st day	-0.177	0.062		
Low calorie intake, 7th day	-0.250	0.008	0.144	0.170
Low protein intake, 7th day	-0.088	0.354		
Total protein				
21st day	-0.097	0.311		
30th day	-0.248	0.016	-0.165	0.115
Change, 1st & 21st day	0.030	0.754		
Change, 1st & 30th day	-0.185	0.074		
Albumin				
21st day	-0.077	0.421		
30th day	-0.077	0.460		
Change, 1st & 21st day	-0.054	0.574		
Change, 1st & 30th day	-0.054	0.606		
Prealbumin				
21st day	-0.218	0.021	0.216	0.059
30th day	-0.022	0.830		
Change, 1st & 21st day	-0.390	<0.001	-0.310	0.003
Change, 1st & 30th day	-0.179	0.084		
CRP				
21st day	0.062	0.518		



30th day	0.232	0.025	0.135	0.195
Change, 1st & 21st day	0.113	0.234		
Change, 1st & 30th day	0.174	0.093		
Glucose				
21st day	-0.084	0.379		
30th day	-0.122	0.242		
Change, 1st & 21st day	-0.043	0.650		
Change, 1st & 30th day	0.002	0.984		

ß: Standardized Beta coefficient. Adjusted R^2 of the multivariate model = 0.202

DISCUSSION

Early nutritional intervention has beneficial effects in patients with high nutritional risk (11). Early initiation of patients into nutrition therapy within 24-48 hours is recommended by the guidelines for critically ill patients who are unable to provide adequate oral intake (12-15). Regarding the effect of early nutritional nutrition, Tian et al. 's study of 1895 patients showed that the rates of mortality and gastrointestinal intolerance were significantly reduced. Four recent meta-analyses involving up to 25 studies with 3816 patients comparing EN and PN indicated that early onset nutrition has a significant effect on mortality in high-risk groups. According to these studies it also significantly reduces the risk of infectious complications and positively improves the clinical picture of patients (9,16-18). In our ICU, nutritional support begins at an early stage, within the first 24 hours.

Although the negative effects of malnutrition on ICU inpatients have been known for a long time, the issue of screening tests or approaches that can be used to determine malnutrition is still controversial. The European Association for Enteral and Parenteral nutrition (ESPEN) recommends the NRS 2002 screening test to determine the risk of malnutrition in hospitalized adult patients (11). But the effectiveness of this screening test in assessing malnutrition in intensive care patients is still unknown. There is currently no specific algorithm, screening test, or specific marker that enables the assessment of malnutrition in patients admitted to the ICU. Nutritional risk is only evaluated with the NRS-2002 and it has not been effective in reducing undesirable clinical results (16,19). In a study conducted on critical patients in an ICU in Thailand, the effects of nutrition on sepsis and mortality were evaluated and having an NRS-2002 risk score of ≥3 was found to be associated with death and septic shock (12,19). In this study, the NRS-2002 score was used as a screening test and an NRS-2002 risk score of >3 was identified in 99.4% of the patients. NRS 2002 >3 means the presence of malnutrition in patients and the need for urgent nutritional support therapy. The reasons for such a high rate of malnutrition may be that patients were elderly and had at least one underlying chronic disease.

For the last 20-30 years, the importance and necessity of enteral nutrition have been advocated. It is recommended that early nutrition is started in intensive care patients if possible (within the first 24 hours), unless there is a contraindication. Many studies have found that early enteral nutrition reduces hospitalization time in intensive care patients, duration of stay on mechanical ventilators, infec-

tious or other complications (such as organ failure), or mortality. Early enteral nutrition has advantages over parenteral nutrition, and has been demonstrated to shorten patients' recovery times (20,21). In this study, the effects of enteral and parenteral nutrition on biochemical data and anthropometric measurements in intensive care patients were examined. In intensive care patients followed for 21 days who received enteral and parenteral nutrition, the daily calorie and protein intake in the enteral-fed patients reduced their energy requirements.

It remains unclear what the optimal protein energy goals should be and exactly when they should be achieved (22,23). In a recent meta-analysis discussing the importance of early nutrition therapy the authors state that excess protein and energy intake may be associated with increased mortality in patients at risk of malnutrition (24,25). The number of macronutrients for critically ill patients should be carefully tailored to each individual patient. The optimal amount of energy, what the goals should be and when they should be achieved should be determined, especially in the acute phase of the critical illness, and not just calorie sufficiency should be targeted (22). A multicenter study conducted in Europe found that nutritional support started at an average of 46.5 hours (8.2-149.1 hours) in ICUs participating in the study, and the target calorie and protein levels were fully delivered in only 2.5% of patients (24). In a study of 201 ICUs from 26 countries, Heylan et al., found that enteral nutrition was initiated at an average of 38.8 ± 39.6 hours. Patients in this study were found to have received 61.2% of their calorie requirements and only 57.6% of their protein requirement. It was found that 80% of the calories needed to be reached within the first week were reached in only 26% of patients. The authors emphasized that European ICUs are better relative to other regions at achieving target calories and protein levels (19,20). In this study, only 50% of the targeted calories and only 36% of the targeted protein were given on the third day of nutritional support. The target calorie was reached only in 31.4% of patients, and the target protein was reached only in 33.3% of patients. Energy consumption per kilogram increased gradually from the first day to the second day. The decrease in daily glucose levels in the parenteral nutrition group was significantly higher than in the enteral nutrition group when analyzed according to dietary pattern.

Prealbumin acts as a protein transporter that binds thyroxine and retinol and its plasma half-life is 21 days. Changes in nutrient intake are observed within 1 week. In the presence of metabolic stress, a faster change is observed (24). Compared to albumin, prealbumin shows nutritional changes in a shorter time. Evaluating prealbumin levels together with CRP levels may result in better clinical guidance (25). A previous study showed a negative correlation between serum albumin levels and CRP, white blood cell count and neutrophil-to-lymphocyte ratio in critically-ill ICU patients (23). Serum albumin is a negative acute phase reactant; therefore, CRP, white blood count and neutrophil-to-lymphocyte ratio decrease while albumin increases if the critical ICU patient begins to recover (21). In this study, it was observed that albumin and total protein values did not change statistically during nutrition, while prealbumin levels were significantly higher on the 13th day compared to the first day. Daily prealbumin levels were significantly lower in the group receiving low protein. According to these results, an increase in prealbumin levels within the first 21 days may reduce the length of stay in the ICU. CRP levels were found to be relatively high at first hospitalization in patients undergoing both enteral and parenteral nutrition in this study. The CRP levels on the 21st day were found to be significantly lower compared to day one and day seven. The long-term "enteral or parenteral" issue is debated and emotionally debated as it happens. Two large multicenter randomized controlled trials (RCTs) showed no fatal differences in the treatment of early nutrition, while



they were found to benefit the clinical picture of patients (24,25).

In this study, early nutritional evaluation was performed, the degree of risk was determined via NRS-2002 values, and early nutritional support was started in all patients. No statistically significant difference was found between different feeding methods in terms of hospitalization or NRS-2002 values. But statistically significant differences in baseline and pre-discharge NRS-2002 values (the latter was higher) were found. This suggested that even if the calculated caloric and protein needs of patients were determined and nutrition was started promptly, nutritional support was still not fully achieved in critically-ill ICU patients. This finding may also put into question the utility of the NRS-2002 system as a reliable method of monitoring the nutritional status of ICU patients; however, this particular conclusion requires further studies on the subject.

Limitations of the study

Our study was retrospectively planned which carries all related limitations, and it is clear that patients are not diagnostically homogeneous. Because of the exclusion criteria, only patients over 65 and those who received clinical nutrition therapy were included in the study, resulting in a small number of patients. The fact that this was a single-center and retrospective study may have reduced the strength of the study and the availability of some data. Finally, this study was conducted under the supervision of a dietitian. It should not be overlooked that the nutritional support received by each patient was not decided directly by a dietitian, but by a group of individuals, including the attending physician. Therefore, nutrition calculations and administration of feeding were based on patient-, dietitian- and physician-related decisions; thus, applying the same criteria and approach to these decisions may not have been possible. In the future, we recommend prospective, observational studies in which diagnostically homogeneous ICU patients are included.

CONCLUSIONS

The prealbumin, albumin and total protein levels of geriatric intensive care patients were evaluated and the effect of reducing the development of malnutrition in geriatric patients by assessing early nutritional therapy (enteral compared to parenteral nutrition) is highlighted. Albumin and total protein values did not change statistically during nutrition, while prealbumin levels were significantly higher on the 13th day when compared with the first day. Planning nutrition by evaluating values such as prealbumin, albumin, total protein at an early stage facilitates the nutritional treatment of patients. Independent of which nutrition method is used, prealbumin should be followed primarily, because changes in prealbumin levels can indicate ICU stay and prognosis of elderly patients. Further studies are needed to evaluate the effects of nutritional support therapy on malnutrition in the elderly. We recommend that new systems be developed to monitor the nutritional status of patients during their stay in the ICU.

Acknowledgment

This study was completed without any financial support.

Authors' Contribution

PG: Conceptualization, Methodology, Writing-review & editing, Visualization. All authors have read and approved the final version of the manuscript; **HDG:** Conceptualization, Data curation, Project administration, original draft, Writing-review & editing.

Conflicts of Interest

The authors declare no conflicts of interest in this study.

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RESEARCH

A BIBLIOMETRIC AND ALTMETRIC ANALYSIS OF ALZHEIMER'S DISEASE: TOP 100 ARTICLES

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2022.301
2022; 25(3): 422-431

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Abstract

Introduction: Alzheimer's disease is the most common cause of dementia in elderly people, and aging is the most important risk factor. Our aim is to provide bibliometric and altmetric approaches to Alzheimer's disease for better evaluation.

Materials and Method: The word 'Alzheimer' was searched from the Web of Science database and Altmetric.com website to create, respectively, the Top 100 citation and altmetric lists. The articles were analyzed and compared according to study type, topic of study, publication year, citation number, journal quartile in category, impact factor, and altmetric attention score.

Results: The median citation number of Top 100 cited articles was 2,043 (range: 1,411-3,212) and median altmetric attention score was 22 (range: 0-566). The median altmetric attention score of T100 altmetric articles was 771 (range: 550-3,378) and median citation number was 43 (range: 0-1,917). There was a significant correlation between citation number and altmetric attention score in citation list ($p < 0.001$, $r = 0.438$). In the citation list, most common study type, topic of study, and publication year were 'original scientific paper,' 'pathophysiology, genetic,' and '1993,' while in the altmetric list, it was 'original scientific paper,' 'etiology, risk factors,' and '2017 and 2018,' respectively.

Conclusion: While academia tries to better understand disease mechanisms to find new treatment options, social media is more curious about how to be protected from a particular disease. Combining altmetric analysis with bibliometric analysis could be useful to develop convenient policies on the awareness of the society about Alzheimer's disease.

Keywords: Alzheimer Disease; Geriatrics; Dementia.

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Received : Apr 28, 2022
Accepted : Aug 04, 2022

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INTRODUCTION

Alzheimer's disease (AD) is the most common cause of dementia in elderly. The most important risk factor for AD is aging. There are 5.3 million Alzheimer's patients in the United States and only 200 thousand of them are younger than 65 years (1,2). Due to the aging of the world's population, AD has become the second most costing disease after cancer. According to 'amyloid-cascade hypothesis", accumulation of beta-amyloid plaques outside neurons, and tau tangles inside neurons activate immune system cells in the brain (3). This chronic inflammation causes cell loss, so atrophy or shrinkage of the brain occurs. Currently, there are many clinical trials for prevention and treatment of this fatal disease (4,5).

Today, despite some debates and criticisms, the strength of an article is generally defined by the impact factor of the journal in which it was published and the number of citations the article received after publication (6). Researchers frequently benefit from bibliometric analysis to identify the most valuable publications in their field. For this reason, bibliometric analysis (citation analysis) gains importance. Today, academic research is also shared, interpreted and disseminated on social media. In 2011, the concept of 'Altmetric Attention Score' (AAS) had emerged after Altmetric Explorer (Altmetric, London, UK) began to analyze social media data. The AAS gives an opinion on how often articles are discussed and disseminated on social media. Nowadays, publishers are also interested in altmetric and they have started to give AAS in addition to the citation number on their site (7).

This study aims to provide a bibliometric and altmetric perspective on Alzhiemer's diesase, and evaluate the relationship between the Top100 (T100) citation list and the T100 altmetric list with respect to the number of citations, AAS, IF, study type, article subject and journals.

METHODS

This study does not require approval from an ethics committee because it performs a bibliometric analysis/citation analysis of the existing published classical studies. The author declares that the research has been conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects".

Data collection and inclusion criteria

We searched on January 1, 2021 for the keyword "Alzheimer" in articles published between 1975-2021 years, from the Thomson Reuters Web of Science (WoS) all databases (Philadelphia, Pennsylvania, USA). The WoS database lists all articles with "Alzheimer" in any of the title, abstract, keywords and keywords plus. Two researchers independently read the articles, removed the articles not related to "Alzheimer" and unanimously created the T100 citation list by finding the first one hundred articles. As former articles were likely to have more citations than newer articles, we used the average number of citations per year (ACpY) values derived from WoS to eliminate time as a factor. With the consensus of the two researchers, the T100 citation list categorised according to the study type, the subject of the study, the first author, the year of publication, the number of citations, the Q rank and IF values of the journal they were published in. In addition, the keywords and institutions of the T100 citation list were given in the form of network visualization map.

The keyword ‚Alzheimer' was scanned on the Altmetric.com website (Altmetric, London, UK) on the same day with scanning of WoS, January 1, 2021 and the T100 altmetric list was created by excluding the publications unrelated to AD by the researchers independently. AAS is calculated automatically by using an algorithm, based on the weighted amount of all the attention on a research. Altmetric score is presented in the middle of the donut. Each color in the donut indicates a source (e.g. red for News, blue for Twitter), and the area of each color is proportion-

al to contribution of the relevant source to AAS (8). The highest coefficient in calculating AAS belongs to News, and this coefficient also varies according to where the news is published. Blogs, policy documents, patent, Wikipedia, Twitter, Facebook, Sina Weibo, Syllabi, Google+, LinkedIn, Reddit, Youtube and Pinterest are other highest contributors after News. Mendeley readers, Dimensions citation counts and CiteULike bookmarks do not contribute to the score (9). In addition to all these, on the same date, the AAS of the articles in the T100 citation list were controlled from 'altmetric.com' website and the number of citations of the articles in T100 altmetric list were obtained from WoS.

Statistical analysis

Numerical variables were defined as median (minimum-maximum). Since the data are not normally distributed, Mann-Whitney U was used for two groups; and The Kruskal-Wallis test was used to compare three or more groups. Spearman correlation analysis was used to evaluate the correlation between AAS, ACpY and citation in the T100 citation list; between AAS and citation in the T100 altmetric list. Analyzes were performed by using IBM SPSS-20 (Statistical Package for Social Sciences, Chicago, Illinois, USA).

RESULTS

When we searched for the word ,' Alzheimer ,' in the Web of Science, 212.254 articles were found. The median of the citation number of the Top 100 cited article was 2,043 (range: 1,411-23,212), while the median of the altmetric score was 22 (range: 0-566). The article titled ,Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of the Department of Health and Human Services Task Force on Alzheimer's Disease', written by McKhann et al in 1984 in the journal of ,Neurology' had the highest citation and ACpY (n = 23,212; n = 610 respectively) (10). And also the article, ,The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease, written by McKhann et al. and published in 'Alzheimer's & Dementia in 2011, had the second highest AcpY (n = 560) and was the 6th article in T100 citation list (n=6161) (11). When Spearman correlation analysis was used to define the correlation between citation number and altmetric score of the T100 citation articles, a significant positive correlation was found ($p < 0.001$, $r = 0.438$). There were also a significant positive correlation between AcpY with citation and AAS ($p < 0.001$, $r = 0.659$; $p < 0.001$, $r = 0.627$, respectively).

When the word 'Alzheimer' was scanned on the 'altmetric.com' website, 62.453 research outputs were obtained. While the median of the citation count of the Top 100 articles with highest altmetric scores was 43 (range: 0-1.917), the median for the altmetric score was 771 (range: 550-3.378). The article titled 'Porphyromonas gingivalis in Alzheimer's disease brains: Evidence for disease causation and treatment with small-molecule inhibitors' published in 'Science Advances' in 2019 had the highest altmetric score (n = 3.378) (5). The article 'Meta-analysis of 74,046 individuals identifies 11 new susceptibility loci for Alzheimer's disease', also included in the Top 100 citation list, had the highest number of citations in the Top 100 articles with highest altmetric scores (n = 1917) (12). This article was the only article being in both the T100 citation and altmetric lists. According to Spearman correlation analysis, there was no correlation between citation number and AAS of T100 altmetric articles ($p = 0.839$, $r = -0.021$).

When the keywords of the articles in the T100 citation list were evaluated, most commonly used keywords were AD, acute phase protein and chemokine, respectively. Network visualization cluster map for keyword analysis in the field of AD for the top 100 cited articles was given in Figure 1. The most contributing institutions to T100 citation list were

Harvard University, Brigham and Women's Hospital and Duke University, respectively. The correlation and clusters of contributing institutions in the field of AD for the top 100 cited articles were given in Figure 2. The first three countries of the authors with the most articles in the T100 citation list were the United States of America, the United Kingdom, and Canada, respectively.

The first three journals with the highest number of articles in the T100 citation list were Nature (n = 15, IF 42.7), Science (n = 10, IF 41.8) and Neurology (n = 9, IF 8.7), respectively. First three journals with the highest number of articles in the T100 altmetric list were Nature (n = 15, IF 42.7), Alzheimer's & Dementia (n = 9, IF 17.1) and Journal of Alzheimer's Disease (n = 8, IF 3.9), respectively. The median of the time passed since the publication of the article were 24 (range: 5-40) years in the T100 citation list and 4 (range: 1-15) years in the T100 altmetric list. The year with the highest number of published articles in the T100 citation list was 1993 with seven articles. The years with the highest number of pub-

Figure 1. Network visualization map for keyword analysis

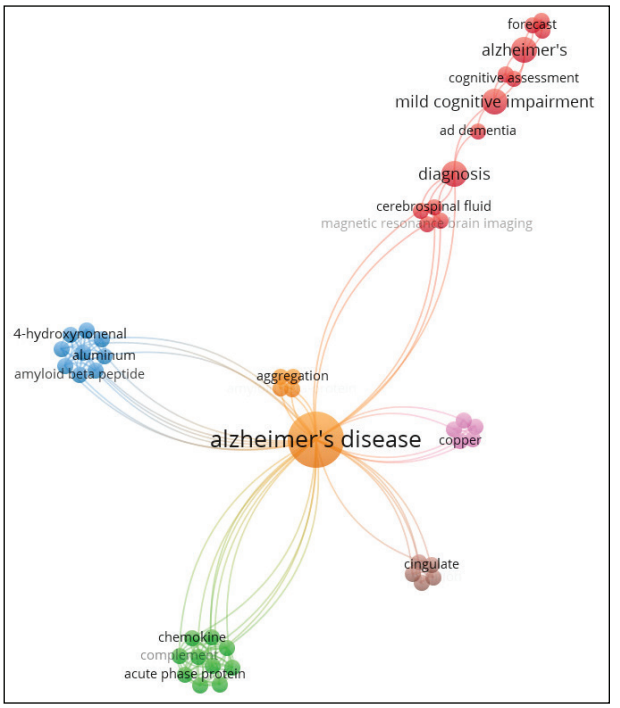
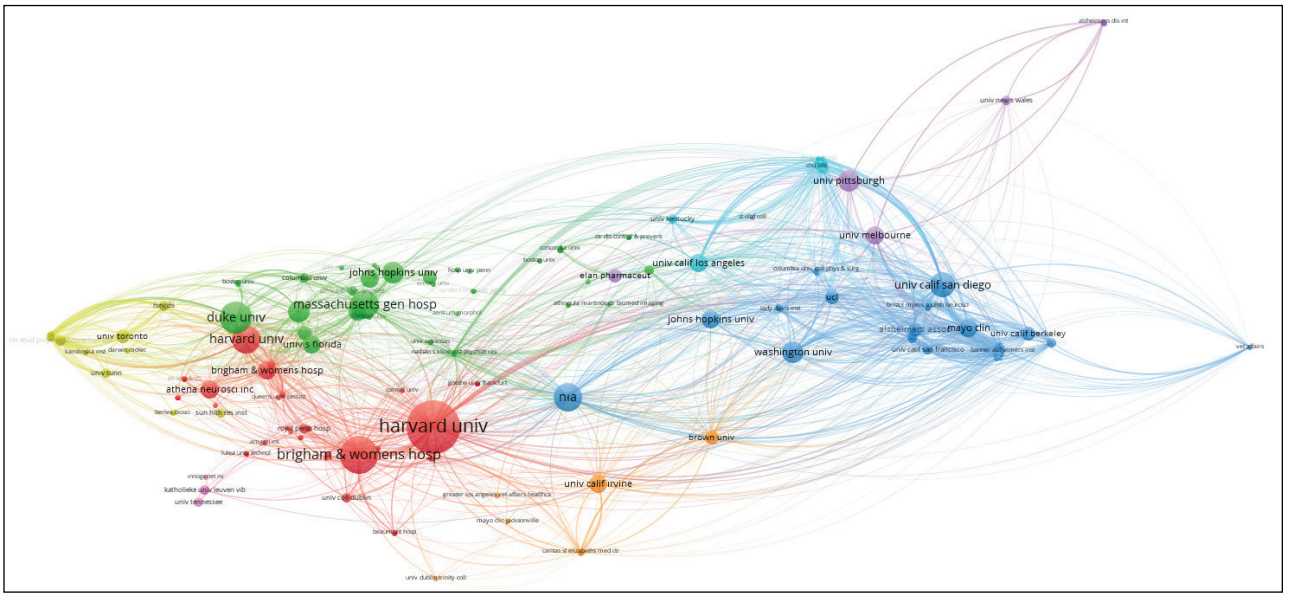


Figure 2. The clusters of contributing institutions



lished articles on the T100 altmetric list were 2017 and 2018, each with twenty articles.

When we evaluated the study types in the T100 citation list, the first two lines were original scientific paper (n = 57) and review (n = 21). Similar to citation list, the most common study type was original scientific paper (n = 56) and animal study (n = 21) was the second in the T100 altmetric list. The lists according to the study types, including AAS and citation numbers, were given in Table 1.

According to the subject, we categorized the articles as 'Etiology, risk factors', 'Treatment, prevention', 'Definition, diagnosis', 'Pathogenesis, physiology, genetic', 'Epidemiology, health policy', and others. The lists according to the topics of the articles, including AAS and citation numbers, were

Table 1. Study types top 100 altmetric and citation list

Type	Number of articles	Citations, median (minumum-maximum)	*p* value	AAS, median (minumum-maximum)	*p* value
Top 100 citaiton list	**100**	**2043 (1411-23212)**		**22 (0-566)**	
Original scientific paper	57	1879 (1413-9546)		19 (0-448)	
Review	21	2186 (1426-9629)	0.453	26 (0-240)	0.177
Others	22	2609 (1411-23212)		55 (0-566)	
Animal Study	10	2238 (1467-3354)		29 (0-90)	
Guidelines and advisory documents	9	2896 (1466-23212)		66 (3-136)	
Systematic reviews and meta-analyses	2	2252 (1917-2587)		333 (101-566)	
Case report	1	1411		0	
Top 100 altmetric list	**100**	**43 (0-1917)**		**771 (550-3378)**	
Original scientific paper	56	35 (0-1095)		795 (550-3012)	
Animal Study	21	116 (11-518)		693 (559-3378)	
Review	13	13 (0-1245)	**0.041**	772 (663-2054)	0.386
Others	10	31 (1-1917)		846 (566-2851)	
Systematic reviews and meta-analyses	6	31 (1-1917)		846 (566-1407)	
Case report	2	29 (4-55)		1713 (575-2851)	
Editorial	1	7		611	
Guidelines and advisorydocuments	1	54		928	

Abbreviations: AAS, Altmetric Attention Score

given in Table 2. The most frequent topics were 'Pathogenesis, physiology, genetic' (n = 54) and 'Definition, diagnosis' (n = 18) in the T100 citation list. In the T100 altmetric list, the first two most common topics were "Etiology, risk factors" (n = 32) and "Treatment, prevention" (n = 28).

When the subaltmetric analysis of the 10 articles with the highest AAS was done according to the source, Twitter was the most contributing social networking service with an average number of 1882 tweets. The article with the highest AAS and number of tweets belonged to Dominy SS et al (5). Twitter was followed by news outlets with an average of 141 and Facebook posts with an average of 31. Detailed analysis was given in Table 3.

Table 2. Topics of the top 100 citation and altmetric list

	Number of articles	Citations, median (minumum-maximum)	*p* value	AAS, median (minumum-maximum)	*p* value
Top 100 citation list	**100**	**2043 (1411-23212)**		**22 (0-566)**	
Pathogenesis, physiology, genetic	54	1838 (1461-9629)		19(0-566)	
Definition, diagnosis	18	3008 (1466-23212)		31 (0-121)	
Treatment, prevention	6	1768 (1470-3354)	**0.002**	31 (0-74)	0.300
Etiology, risk factors	6	1720 (1546-6401)		108 (1-448)	
Epidemiology, health policy	5	1986 (1588-3521)		49 (0-101)	
Others	11	3401 (1708-7929)		20 (0-248)	
Top 100 altmetric list	**100**	**43 (0-1917)**		**771 (550-3378)**	
Etiology, risk factors	32	39 (0-1001)		868 (550-2851)	
Treatment, prevention	28	94 (1-906)		885 (569-3378)	
Definition, diagnosis	14	30 (3-498)	0.707	893 (551-1860)	
Pathogenesis, physiology, genetic	9	60 (11-584)		648 (559-763)	**0.008**
Epidemiology,health policy	7	51 (3-195)		653 (557-809)	
Others	10	20 (7-1917)		673 (556-928)	

Abbreviations: AAS, Altmetric Attention Score

Table 3. Sub-altmetric distribution of altmetric score for top 10 articles

Rank	Title	Altmetric Score	News Outlets	Blogs	Policy sources	Twiters	Facebook Pages	Wikipedia page	Google+ users	Redditors	Weibo users	Patents
1	Porphyromonas gingivalis in Alzheimer's disease brains: Evidence for disease causation and treatment with small-molecule inhibitors		134	28	0	6247	43	3	18	7	0	0
2	The antibody aducanumab reduces Aß plaques in Alzheimer's disease		253	29	0	1194	61	2	19	2	0	6
3	Resistance to autosomal dominant Alzheimer's disease in an APOE3 Christchurch homozygote: a case report		262	11	0	3013	12	2	0	0	0	0
4	Multiscale Analysis of Independent Alzheimer's Cohorts Finds Disruption of Molecular, Genetic, and Clinical Networks by Human Herpesvirus		217	27	0	771	37	1	0	3	0	0
5	In Alzheimer Research, Glucose Metabolism Moves to Center Stage		1	0	0	3063	49	0	0	3	0	0
6	Discriminative Accuracy of Plasma Phospho-tau217 for Alzheimer Disease vs Other Neurodegenerative Disorders		147	7	0	1143	5	1	3	0	0	0
7	Aluminium in human brain tissue from donors without neurodegenerative disease: A comparison with Alzheimer's disease, multiple sclerosis and autism		1	0	0	2121	13	0	0	3	0	0
8	Sauna bathing is inversely associated with dementia and Alzheimer's disease in middle-aged Finnish men		135	14	0	522	69	1	2	3	0	0
9	Evidence-based prevention of Alzheimer's disease: systematic review and meta-analysis of 243 observational prospective studies and 153 randomised controlled trials		113	3	0	681	8	0	0	1	0	0
10	Alzheimer's disease drug-development pipeline: few candidates, frequent failures		152	21	3	67	11	2	3	1	1	3



DISCUSSION

Although there are a few bibliometric studies about AD in the literature, we could not find any altmetric studies. Dong et al. demonstrated the study trends of AD in the world and in China with their bibliometric study (13). Pozo et al. divided 40 years of research in AD into four decades and evaluated the trends by decades (14). We believe that this is the first bibliometric and altmetric study of the top 100 most-mentioned articles on AD. In addition, to the best of our knowledge, this is the first study paying attention to the correlation between citation numbers and AAS in both the T100 altmetric and citation lists.

While there was a correlation between citation with AAS and citation with average citation per year in the T100 citation list, there was no correlation between citation and AAS in the T100 altmetric list. The reason for the correlation in the T100 citation list but not in the T100 altmetric list may be that the articles in the T100 citation list had enough time for citation and AAS to accumulate. Again, the fact that the journal with the most articles in T100 citation and altmetric lists was Nature , suggests that the citation numbers and AAS can be correlated in the T100 altmetric list after enough time. Similar to our study, the most-cited 300 articles in 15 journals with the highest IF in the field of urology were evaluated and a correlation was found between the AAS and the number of citations (15). Again, in a study with 140 most-cited articles from 14 journals with the highest IF in the field of pediatric surgery, a correlation was found between AAS and number of citations (16).

The most attractive topics in the T100 citation list as well as the first two most-cited articles were 'pathogenesis, physiology, genetic' and 'definition, diagnosis'. The most-cited article written by McKhann et al. focused on the clinical diagnosis of AD (10). The second most-cited article was about the amyloid hypothesis in AD (17). When we evaluated the T100 altmetric list, we found the most interesting topics to be 'etiology, risk factors' and 'treatment, prevention', as in the first three articles with the highest AAS. The article with the highest AAS score was an experimental study that indicates porphyromonas gingivalis, which is the cause of chronic periodontitis in the brain in AD, and its neurotoxic effect can be reduced with gingipain inhibitors (12). The second article in the list was a clinical experiment showing that aducanumab reduces beta-amyloid plaques in AD (4). The article in the third place in the list was aimed at the discovery of risk-reducing genes in AD (18). As can be seen, social media users are more interested in 'etiology, risk factors' and 'treatment, prevention', which is different from the interests of academia. Academia cares more about the pathogenesis, genetics, and diagnosis of AD to understand the disease mechanism and thus find new treatment options. Social media users are more curious about what AD does, what should be done to be protected, and what the new treatments are; thus social media users want information that could be useful to them in their daily life.

According to the subaltmetric analysis of 10 articles with the highest AAS, the highest interaction averages were in Twitter and news outlets, respectively, but news outlets had more impact on AAS. The reason is that when calculating AAS, the highest multiplier in mainstream social media is in news outlets, while the multiplier of Twitter is in the 12th place (9).

Limitation

The number of citations of both T100 citation and T100 altmetric lists were searched from the WoS database; as a result, articles not included in the WoS database could not be taken into account. Another limitation is that self-citation was not excluded while defining the number of citations.

CONCLUSION

This study gave us a bibliometric and altmetric overview, along with the evaluation of Alzheimer's

literature. The most attractive topics in the T100 citation list were 'pathogenesis, physiology, genetic' and 'definition, diagnosis' and the same for the T100 altmetric list were 'etiology, risk factors' and 'treatment, prevention'. This showed us that the interests of academia and social media users are different. Based on our study, we think that it will be beneficial to evaluate articles using both altmetric and bibliometric analyses because AAS can give us an idea about what society wants to know. Through such analyses, it is possible for scientists not only to formulate relevant policies on the awareness of the society about AD but also develop appropriate policies for the diagnosis, prevention, and treatment of this fatal disease.

Acknowledgments: The author is very grateful to Veysel Suzan for his contribution on composing the T100 altmetric and citation lists as the second researcher.

Conflict of Interest: No conflict of interest has been declared by the author.

Financial Disclosure: The author declares this study to have received no financial support.

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RESEARCH

IS THE WHIPPLE PROCEDURE SAFE AND FEASIBLE IN ELDERLY PATIENTS?

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2022.302
2022; 25(3): 432-440

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Received : Apr 26, 2022
Accepted : Aug 19, 2022

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Abstract

Introduction: The world population is getting older due to increasing life expectancy. Deciding to perform surgery for pancreatic cancer in elderly patients has been difficult due to high comorbidities and limited survival. This study aimed to compare the results of the Whipple procedure performed in elderly patients with non-elderly patients to demonstrate the safety and feasibility of the Whipple procedure.

Materials and Methods: Patients underwent the Whipple procedure for pancreatic adenocarcinoma between January 2010 and December 2019 were retrospectively analyzed. Patients were classified into two groups as, Group I (<65 years) and Group II (≥65 years), and compared.

Results: 178 patients were included, with 97 (54.5%) in group I and 81 (45.5%) in group II. The mean age of the patients was 63.48±12.95 years, while 65.2% were male and 34.8% were female. Gender distribution, preoperative hyperbilirubinemia, The American Society of Anesthesiologists score, and endoscopic retrograde cholangiopancreatography status were found to be statistically similar between the groups. Group II had more comorbid disease (p=0.002), longer hospital stay duration (p<0.001), and more intensive care unit admission (p=0.001). There was no statistical difference between the groups regarding postoperative complications, pancreatic cancer stage, and R0 resection rate. There was no difference between the groups regarding survival (p=0.11).

Conclusion: The Whipple procedure is an operation with a high complication rate regardless of age. The most adverse factor affecting survival is the aggressive nature of the disease rather than older age. Therefore, the Whipple procedure is safe and feasible in elderly patients.

Keywords: Aged; Pancreatic Neoplasms; Survival; Pancreaticoduodenectomy.



INTRODUCTION

The world population is aging due to increasing life expectancy. Thus, the number of elderly cancer patients has increased worldwide (1). As a result, healthcare systems have seen the beginnings of the "silver tsunami" with the increasing proportion of the population defined as geriatric (2). However, old age is not considered a contraindication for surgical treatment, and many studies have supported that older patients should undergo surgical treatment as the younger patients should (3,4).

The Whipple procedure (WP), also known as pancreaticoduodenectomy, is the most common curative resection performed for pancreatic adenocarcinoma confined to the head of the pancreas, including ampullary cancers. In this procedure, the head of the pancreas, the first and second portions of the duodenum, distal stomach, proximal jejunum, a portion of the common bile duct, the gallbladder, and the surrounding lymph nodes are removed. The reconstruction for gastrointestinal continuity includes connecting the jejunum to the remaining pancreatic duct with pancreaticojejunostomy, the bile duct with hepaticojejunostomy, and the stomach with gastrojejunostomy. WP complication rate is high and is a highly invasive operation. Despite improvements in surgical techniques, chemotherapy, and follow-up methodology, pancreatic tumors remain a fatal disease, with a five-year survival rate of less than 10% (1). The majority of patients present with locally advanced or metastatic disease, and less than 20% of patients are fit for resection at the time of diagnosis (5). Ampullary tumors are rarer than pancreatic tumors. The one-year survival rate and three-year survival rate are 60.5% and 27.7% (6). Surgical resection is still considered the only potentially curative treatment.

In this study, we aimed to compare elderly patients who underwent WP for pancreatic adenocarcinoma with nonelderly patients and investigate the factors affecting morbidity and mortality in patients in the postoperative period and the effects of age on prognosis and survival.

METHODS

Study Design

Data of patients who underwent PD for pancreatic adenocarcinoma in our clinic between January 2010 and December 2019 were retrospectively analyzed by reviewing the hospital database system. Combined visceral resection with PD or total pancreatectomy patients were excluded from the study. Additionally, patients who had missing data files were excluded from the study. Demographic characteristics, pancreatic cancer stage, comorbid diseases, The American Society of Anesthesiologists (ASA) score, endoscopic retrograde cholangiopancreatography (ERCP) status, operation time, intensive care unit (ICU) admission status, length of hospital stay, postoperative complications, perioperative mortality rates, and survival were recorded. Data from 178 patients were included. Patients were analyzed in two groups according to their age: group I (<65 years) and group II (≥65 years).

Surgical intervention and risks were explained to all patients, and informed consent was obtained before surgery.

Statistical analyses

In the analysis of the data, the mean and standard deviation, the minimum and maximum values of the features, frequency, and percentage values were used when defining the categorical variables while performing the statistics of the continuous data on the scales. Student's t-test was used to compare the means of two independent groups. Chi-square test statistics were used to evaluate the relationship between categorical variables. To evaluate the relationship between age and clinical outcomes, logistic regression analysis was performed using backward and enter methods with statistically

significant variables. The results were accepted as a 95% confidence interval, and the statistical error margin was 0.05. The cumulative survival rate was calculated using Kaplan-Meier survival analysis, and the difference between groups was evaluated using the log-rank test. The statistical significance level of the data was taken as $p<0.05$. In evaluating the data, www.e-picos.com New York software and the MedCalc statistical package program were used.

RESULTS

A total of 178 patients were included in the study, with 97 (54.5%) in group I and 81 (45.5%) in group II. The mean age of the patients was 63.48±12.95 years, while 65.2% were male and 34.8% were female.

The demographic and clinical characteristics of the patients are summarized in Table 1. Gender distribution, preoperative hyperbilirubinemia, and ERCP status were found to be statistically similar between the groups. In total, 64.9% and 85.2% of the patients in group I and group II, respectively, had comorbid disease (p=0.002). ASA score was found to be similar in statistical evaluation (p=0.15). Hospital stay duration was found statistically longer in group II with 13.09±1.61 days, while it was 11.67±1.92 days in group I (p<0.001).

Thirty-three (34.0%) patients in group I were admitted to the postoperative ICU, while 47 (58.0%) patients were in group II. There was a statistical difference in ICU admission between the groups (p=0.001). The reason for ICU admission in group 1 was preoperative high-risk stratification due to comorbidities with major surgery, The reasons for ICU admission in group 1 were preoperative high-risk stratification due to multiple comorbidities with major surgery in 17 patients, hemorrhage to cause hypotension in 6 patients, cardiac causes in 5 patients, respiratory insufficiency in 3 patients and other reasons in 2 patients. The reasons for ICU admission in group 2 were preoperative high-risk stratification due to multiple comorbidities with major surgery in 22 patients, cardiac causes in 9 patients, hemorrhage to cause hypotension in 8 patients, respiratory insufficiency in 4 patients, and other reasons in 4 patients. While blood transfusion was given to 25 (25.8%) patients in group I, 33 (40.7%) patients in group II received a blood transfusion. There was a statistical difference in blood transfusion between the groups (p=0.03). There were 4 (4.1%) biliary fistule and 27 (27.8%) pancreatic fistule in group 1 while there were 2 (2.5%) biliary fistule and 19 (23.5%) pancreatic fistule in group 2. There was no statistical difference between the groups' postoperative complications, biliary fistula, and pancreatic fistula without grade classification. However, when pancreatic fistula grade classification was considered, there was a statistically significant difference between the groups (p=0.03). Grade a pancreatic fistula developed in 26 patients and grade b pancreatic fistula in 1 patient in group 1, grade a fistula developed in 13 patients in group 2, and grade b fistula in 6 patients. There was no statistical difference between the groups' pancreatic cancer staging according to The American Joint Committee on Cancer (AJCC) 8th classification and R0 resection rate.

The relationship between age and clinical outcomes with multivariate analyses is summarised in Table 2. With a 95% confidence interval, preoperative blood transfusion and postoperative ICU admission were found to be related to the age of patients (OR 10.28, 95% CI 5.11-20.67 p<0.05; OR 2.68, 95% CI 1.48-4.93 p<0.05 respectively). Conversely, multivariate analysis found that postoperative blood transfusion, complications, pancreatic fistula, and biliary fistula were unrelated to age with a 95% confidence interval.

The geriatric age patient group was re-evaluated by dividing them into subgroups in decades to examine in more detail. There were 47 patients in age between 65-74, 24 patients in age between 75-84, and 10 patients over 85 years. There were no statistical differences between these groups at hos-

Table 1. Demographic and Clinical characteristics according to age groups

	All (n=178)	Group I (n=97)	Group II (n=81)	p-value
	x±SD	**x**±SD	**x**±SD	
Age	63.48±12.95	53.85±5.49	75.01±8.42	**<0.001**
Gender	**n (%)**	**n (%)**	**n (%)**	
Male	116 (65.2)	62 (62.9)	54 (66.7)	0.71
Female	62 (34.8)	35 (36.1)	27 (33.3)	
Comorbid Disease	132 (74.2)	63 (64.9)	69 (85.2)	**0.002**
Preop Hiperbilurubinemia	97 (54.5)	51 (52.6)	46 (56.8)	0.57
ERCP	116 (65.2)	60 (61.9)	56 (69.1)	0.31
Preop Anemia	90 (50.6)	26 (26.8)	64 (79.0)	**<0.001**
ASA Score				
I	20 (11.2)	14 (14.4)	6 (7.4)	0.15
II	58 (32.6)	46 (47.4)	33(40.7)	
III	69 (38.8)	35 (36.1)	37 (45.7)	
IV	31 (17.4)	2 (2.1)	5 (6.2)	
Hospital Stay (days)	12.33±1.91	11.67±1.92	13.09±1.61	**<0.001**
ICU Admission	80 (44.9)	33 (34)	47 (58)	**0.001**
Blood Transfusion	58 (32.6)	25 (25.8)	33 (40.7)	**0.03**
Postop Complication	91 (51.1)	47 (48.5)	44 (54.3)	0.44
Biliary Fistule	6 (3.4)	4 (4.1)	2 (2.5)	0.54
Pancreatic Fistule	46 (25.8)	27 (27.8)	19 (23.5)	0.51
Pancreatic Fistule Grade				
Grade A	40 (86.9)	26 (96.3)	13 (64.4)	**0.03**
Grade B	6 (13.1)	1 (3.7)	6 (35.6)	
Grade C	-	-	-	
Pancreatic Cancer Stage (AJCC 8th)				
Stage I	53 (29.8)	30 (30.9)	23 (28.4)	0.58
Stage II	64 (36)	37 (38.2)	27 (33.3)	
Stage III	61 (34.2)	30 (30.9)	31 (38.3)	
Stage IV	-	-	-	
R0 Resection	144(80.9)	80(82.4)	64(79.0)	0.56

ERCP: endoscopic retrograde cholangiopancreatography, ASA: The American Society of Anesthesiologists score, ICU: intensive care unit, AJCC: The American Joint Committee on Cancer.

Table 2. The relationship between multivariant analysis of group 2 (age(≥65 years) compared to group 1(age<65 years), age, and clinical outcomes

	OR (Odds ratio)	95% CI (Confidence interval)	p-value
Preop blood transfusion	10.28	5.11 – 20.67	**<0.05**
Postop ICU admission	2.68	1.48 – 4.93	**<0.05**
Postop blood transfusion	1.98	1.00 – 1.94	>0.05
Postop complication	1.27	0.70 – 2.29	>0.05
Pancreatic fistula	0.99	0.50 – 1.98	>0.05
Biliary Fistula	0.59	0.11 – 3.29	>0.05

ICU: intensive care unit

Table 3. Subgroup analyses of patients over 65 years

Age	65-74 (n=47)	75-84 (n=24)	>85 (n=10)	p-value
	x±SD	**x**±SD	**x**±SD	
Hospital Stay (days)	12.84±2.05	13.56±2.73	14.11±2.32	0.19
ICU Admission	**n (%)**	**n (%)**	**n (%)**	
Blood Transfusion	26 (55.3)	15 (62.5)	6 (60)	0.84
Postop Complication	16 (34)	11 (45.8)	6 (60)	0.26
Biliary Fistule	28 (59.6)	11 (45.8)	5 (50)	0.52
Pancreatic Fistule	12 (25.5)	5 (20.8)	2 (20)	0.87
Pancreatic Fistule Grade	1 (2.1)	1 (4.2)	-	0.76
Grade A				
Grade B	9 (75)	4 (80)	1 (50)	0.71
Grade C	3 (25)	1 (20)	1 (50)	
Pancreatic Cancer Stage (AJCC 8th)	-	-	-	
Stage I				
Stage II	10 (21.3)	8 (33.3)	5 (50)	0.39
Stage III	17 (36.2)	7 (29.2)	3 (30)	
Stage IV	20 (42.6)	9 (37.5)	2 (20)	

ICU: intensive care unit, AJCC: The American Joint Committee on Cancer



pital stay, ICU admission, blood transfusion, postop complication, biliary fistule, pancreatic fistule, and Pancreatic Cancer Stage. Statistical analyses between the groups were summarized in Table 3.

The mean survival was 14.71 months in group I and 13.17 months in group II (Table 4). In addition, there was no statistical difference between the survival of the groups (p=0.11). In the survival analysis performed by dividing geriatric patients into subgroups, the mean survival was 14.71 months in patients under 65 years of age, 13.55 months in patients aged 65-74 years, 11.48 months in patients aged 75-84 years, and 11.51 months in patients over 85 years of age. There was no statistical difference between the survival of the groups (p=0.23).

DISCUSSION

Pancreatic cancer is the 14th most common cancer with 495,773 (2.6% of all new cancer cases) new cases and the 7th leading cause of cancer-related death with 466,003 (4.2% of all cancer-related deaths) patients in 2020 (7). Pancreatic cancer arises from the exocrine or endocrine systems of the pancreas. The most common form of pancreatic cancer is ductal adenocarcinoma. More than half of patients diagnosed with pancreatic cancer are diagnosed at an advanced age. (8). Surgical resection is the only way to offer a potential cure. Once advanced age was a relative contraindication for surgery and chemotherapy, the usage areas of these applications are gradually expanding. The increasing elderly population reveals the need to recognize the specific risks associated with surgery being applied to elderly patients. Unfortunately, there is no consensus on the age limit in the definition of the elderly individuals worldwide. Traditionally, the United Nations has used measures and indicators of population ageing primarily or entirely based on people's chronological age, defining older persons as those aged 60 or 65 years or over (9). This provides a simple, clear, and easily reproducible way to measure and monitor various indicators of population aging. Therefore, in designing our study, we accepted the age threshold as 65.

The preoperative hyperbilirubinemia status and the need for ERCP were similar between the groups in the setting of preoperative assessment of the groups. In addition, the distribution of pancreatic cancer staging according to the AJCC 8th classification and ASA Score was comparable between the two groups. Gastinger et al. found a perioperative

Table 4. Survival Analyses of the Groups

	Mean (Months)	%95 CI (Confidence interval)	p-value
Overall	14.10	12.96 – 15.04	
Group 1 (<65 years)	14.71	13.28 – 16.13	0.11
Group 2 (>65 years)	13.17	11.64 – 14.69	
	Mean (Months)	**%95 CI (Confidence interval)**	**p-value**
<65	14.71	13.28 – 16.13	0.23
65-74	13.55	11.84 – 15.23	
75-84	11.48	8.49 – 14.47	
>85	11.51	9.41 – 13.59	

mortality of 2.1% in patients with an ASA score of 1 or 2 who underwent pancreatic surgery and 5.4% in patients with an ASA score of 3 or 4 (10). Moreover, all malignant and benign pancreatic surgeries were included in this multicenter study, which included 2003 patients. The similar ASA score distribution in our study is because patients with high ASA scores rejected surgery due to high mortality expectations.

PD morbidities range from 41% to 62% in the reported literature (11-13). In this study, postoperative complications were found 54.3% of the elderly and 48.5% of nonelderly patients. Despite the presence of more comorbid diseases in the elderly group, the postoperative complication rate was statistically similar to that in the non-elderly group. Biliary fistula and pancreatic fistula are complications specific to PD. Reported literature reveals that age does not affect their development (8,14). In this study, complications specific to PD were found to be similar between the groups, consistent with the published literature. The International Study Group of Pancreatic Fistula (ISGPS) developed a definition and grading of postoperative pancreatic fistula in 2005 and redefined their grading in 2016 (15). In our study, there was no statistical difference in the presence of a pancreatic fistula. However, in the evaluation of the grading in the subgroup analysis in terms of pancreatic fistula, it was observed that the grade of the pancreatic fistula was higher in the elderly. This may be because leaks from the more fragile pancreatic tissue with advanced age take longer, or tissue healing due to advanced age is prolonged. Nevertheless, binary logistic regression analysis showed that postoperative complications and pancreatic and biliary fistula were not correlated with age.

Cameron et al. reported that patients' hospital stay at Johns Hopkins Medical Center decreased from 21 days to 10 days over decades (16). In our study, the median hospital stay was significantly longer in the elderly (13.09±1.61 days) than in the nonelderly (11.67±1.92 days), which may be due to the higher admission rate to the ICU in the elderly group. The ICU admission delayed early mobilization, resulting in a prolonged hospital stay. In the reported literature, elderly patients were far more likely to be discharged to a rehabilitation facility than home (11,17). In our study, most elderly patients were discharged to home rather than a facility on the contrary.

Anemia is common in geriatric patients, and its prevalence increases with age after 65 years of age (18). In our study, preoperative anemia was seen at a higher rate in the elderly group, thus leading to more postoperative blood transfusions in the elderly group. Abitagaoglu et al. found ICU admission rates to be higher with aging (19). Consistent with the published literature, in our study, binary logistic regression analysis showed that preoperative blood transfusion and postoperative ICU admission were significantly associated with older age.

In survival comparison, some studies have found lower survival rates for PD performed for pancreatic cancer in the elderly than in the nonelderly (11,20). Conversely, the literature finds comparable survival between the elderly and the nonelderly (4,21). In our study, the overall survival was similar between the elderly and nonelderly groups, which was related to the fact that pancreatic cancer is a highly morbid disease regardless of age (Figure 1). Even when geriatric patients were divided into subgroups, no statistically significant difference was observed in terms of survival (Figure 2).

Our study has several limitations. Firstly, it was a retrospective study with a single center design leads to a small number of patients. Retrospective design leads to the inability to use a scoring system other than ASA in the preoperative evaluation due to missing data. Possible selection bias that may occur in retrospective studies and the incompleteness of the data may reveal possible relationships rather than causal relationships. Therefore, multicenter prospective studies are needed to reveal the causal relationships. Despite these limitations, our study will contribute to the known literature. There are a

Figure 1. Kaplan Meier Survival Curve of the groups.

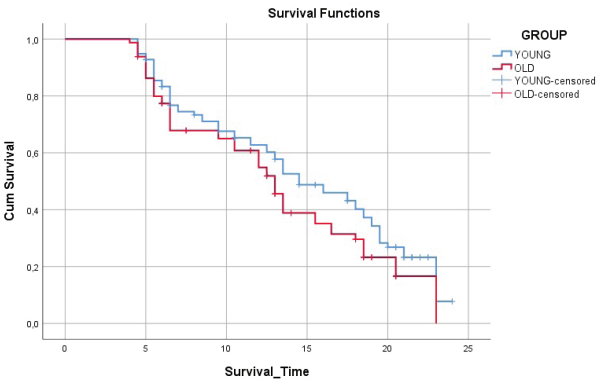
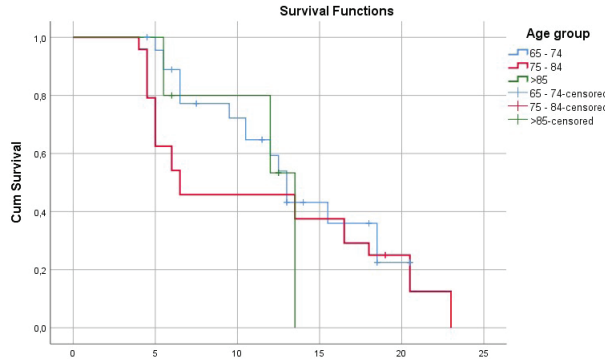


Figure 2. Kaplan Meier Survival Curve of under 65 age patients and subgroup geriatric patients.



limited number of studies examining the relationship between pancreaticoduodenectomy and age in the current literature, and also this study differs from them by re-examining geriatric age groups with subgroups according to decades.

CONCLUSION

PD is an operation with a high complication rate regardless of age, and the most adverse factor affecting survival is the aggressive nature of the disease rather than older age. Therefore, PD for pancreatic adenocarcinoma is a safe and feasible treatment in elderly patients, and surgeons should apply the same procedures and strive to achieve the same goal as younger patients.

Conflict of Interest

The authors declare that they have no conflict of interest.

Ethical approval

This article does not contain any studies with human participants performed by the author. However, ethical approval was obtained from the Mersin University Clinical Research Ethics Committee for this study with the date 05/02/2020 and the number 2020/100.

Funding

The authors received no financial support for this article's research, authorship, and/or publication.

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RESEARCH

TOTAL KNEE ARTHROPLASTY: UNILATERAL, SIMULTANEOUS BILATERAL OR STAGED BILATERAL IN ADVANCED AGE?

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2022.303
2022; 25(3): 441-451

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Abstract

Introduction: Most people with arthritic knees often present with symmetrical joint involvement, a condition often requiring surgery for both knees. There are, however, some disagreements concerning whether or not total knee arthroplasty should be performed simultaneously or in stages. This study aimed to evaluate the length of hospital stay, the need for erythrocyte suspension transfusion, the need for intensive care, and the mortality rates of the patients who underwent unilateral, simultaneous bilateral, and staged bilateral total knee arthroplasty.

Materials and Methods: This retrospective study included 1,129 patients, who were divided into three groups based on whether they underwent unilateral, simultaneous bilateral, or staged bilateral total knee arthroplasty, and they were evaluated in terms of hospital stay, erythrocyte suspension transfusion needs, intensive care needs, and mortality rates.

Results: Of all the patients, 85.5% were women, with the mean age of 67.58±7.23 years; and 75.6% of them underwent unilateral, 19.9% underwent simultaneous bilateral, 4.5% had staged bilateral total knee arthroplasty, 8.8% required ICU care, and 5 patients died.

The need for erythrocyte suspension transfusion and length of hospital stay were highest in those who underwent staged bilateral knee arthroplasty surgery, while it was lowest in those who underwent simultaneous bilateral total knee arthroplasty surgery (all $p<0.001$). There was no statistically significant difference in terms of the need for intensive care need, length of stay in intensive care unit and mortality rates between patients who underwent unilateral, simultaneous bilateral, and staged bilateral total knee arthroplasty.

Conclusion: Simultaneous bilateral total knee arthroplasty may be preferred in younger patients with bilateral knee osteoarthritis but without risky comorbidities, just as we practiced in our clinic.

Keywords: Osteoarthritis, Knee; Arthroplasty, Replacement, Knee; Mortality.

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Received : Feb 12, 2022
Accepted : Sep 04, 2022

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INTRODUCTION

Osteoarthritis is defined as a number of changes including damage, abnormal bone formation, reactive changes in the synovial membrane, and pathological synovial fluid produced in the knee joint cartilage (1). Knee osteoarthritis (gonarthrosis) is an important public health concern, the frequency of which is increasing day by day with the aging population as well as the rising prevalence of obesity worldwide and in Turkey.

The prevalence of patients who underwent total knee arthroplasty (TKA) with a diagnosis of gonarthrosis in 2010 among the entire population of the USA was 1.52%, and the prevalence was found to be higher in women than in men. The same study reported that the ratio of those who underwent TKA at the age of 80 to the entire population reached 10.38% (2). Ceyhan et al. reported that a total of 283,400 and 9,900 primary and revision knee arthroplasty, respectively, were performed due to the diagnosis of gonarthrosis between 2010 and 2014 in Turkey, that 67% of those who underwent primary knee arthroplasty were women, and that TKA was mostly performed in patients between the ages of 60 and 69 (3).

In this context, advanced age, female sex, ethnicity, genetic characteristics, congenital/developmental conditions, and diet are considered as systemic risk factors for knee osteoarthritis, whereas obesity, injury/surgery history, occupation, physical activity, mechanical factors, and knee laxity are known as local risk factors (4).

Choosing cartilage treatment methods in patients with gonarthrosis depends on the degree of the disease, patient's reactions to pain, and deterioration in daily activities due to the disease, age, and general condition of patients (5). TKA should be performed in those with end-stage degenerative and inflammatory arthritis who do not respond to conservative treatment (6). Being the most frequently preferred surgical method in patients with advanced knee osteoarthritis, TKA is a cost-effective option that increases the quality of life of patients by reducing pain and improving knee joint functions (7-9).

Most patients with arthritic knees present with symmetrical joint involvement. Therefore, surgery is often required for both knees (10). Nevertheless, there are some disagreements regarding whether TKA should be performed simultaneously or in stages. According to some researchers, simultaneous bilateral TKA has proven to be relatively safer than the staged bilateral TKA (9), and that single-session bilateral TKA may be appropriate for compatible patients aged <70 years, who have no comorbidities (10); moreover, bilateral TKA may be more beneficial than two-stage surgery due to its advantages such as shorter hospital stay, shorter duration of anaesthesia in total, total duration of physical therapy, fewer days with pain after surgery, and lower medical costs (11,12).

Based on the hypothesis that the advantages of simultaneous bilateral TKA will outweigh its disadvantages as long as it is performed on the right patient, this study aimed to evaluate the length of hospital stay, need for erythrocyte suspension (ES) transfusion, need for intensive care, and mortality rates in patients who underwent unilateral, simultaneous bilateral and staged bilateral knee replacement surgeries. In addition, the impacts of concomitant anaemia and advanced age on hospitalization in the intensive care unit (ICU) and mortality were also investigated separately in patients who underwent unilateral, simultaneous bilateral and staged bilateral TKA.

MATERIALS AND METHODS

Study design, participants and technique

The population of this retrospective study consisted of 1,218 patients who underwent TKA for gonar-



throsis at the Orthopedics Clinic at Antalya Ataturk Public Hospital, between 1 January, 2018 and 31 December, 2019. This study included 1,129 patients after excluding those who underwent revision knee arthroplasty, and those whose medical records could not be reached. The patients who underwent a TKA surgery on the contralateral knee within 1 year were also excluded from the scope of the study, as they could be considered as having undergone a staged bilateral TKA. Only TKA operations performed on different days, usually 1 week apart, during the same hospital stay were considered as a staged bilateral TKA.

The patients were divided into three groups based on whether they underwent unilateral, simultaneous bilateral, or staged bilateral TKA, and were evaluated in terms of hospital stay, ES transfusion needs, intensive care needs, and mortality rates. They were further divided into groups based on whether they were anaemic or non-anaemic, and according to age (≤70 years or >70) in order to determine the effect of anaemia and age on the process.

All patients within the scope of the study had grade 3 and 4 osteoarthritis according to the Kellgren and Lawrence system, and did not respond to conservative treatment. They were evaluated by an orthopaedic surgeon and an anaesthesia team preoperatively, and relevant preoperative workup and optimization was performed. The patients were also examined by cardiology, endocrinology, pulmonology or other relevant specialists according to their comorbidity status. All patients were provided with standard preoperative, intra-operative and post-operative care, including antibiotics, deep vein thrombosis (DVT) prophylaxis, rehabilitative physiotherapy and routine monitoring of their vitals and respective comorbidities. They were discharged following the restoration of a stable hemodynamic status with independent, pain free mobilization, after which a follow-up was planned by the relevant orthopaedic surgeon who performed the surgery.

Regardless of whether it is unilateral, simultaneous bilateral or staged bilateral TKA surgery, the surgical technique does not differ in our clinic. In this connection, the points to be considered by an anaesthesiologist in the selection of anaesthesia include cardiac comorbidities such as hypertension, psychiatric problems such as panic attacks that may increase the sympathetic activity of the patient during the operation, anatomical disorders in the region if spinal anaesthesia is to be applied, or previous medical history in that region, rather than the type of operation to be performed being unilateral, simultaneous bilateral or staged bilateral.

Currently, tranexamic acid is used as a standard in our clinic to reduce bleeding during unilateral, simultaneous bilateral or staged bilateral TKA surgery. It was, however, not used in all cases as a standard during the study period. Since the amount of bleeding could be higher, the use of tranexamic acid was relatively more common in cases that underwent simultaneous bilateral TKA than in those with unilateral TKA or staged bilateral TKA during the given study period.

Ethical approval

Prior to the study, ethical approval was obtained from the Clinical Research Ethics Committee of University of Health Sciences, Antalya Training and Research Hospital. The study was conducted in accordance with the principles of Declaration of Helsinki.

Data collection and laboratory measurements

Demographic and clinical data of the patients and their surgical results were obtained from electronic patient files, medical records, and operation notes, including sex, age, follow-up duration, and number of blood transfusion units, complications and mortality status.

Statistical analysis

G*Power 3.1.9 program was used to calculate the sample size in the study. The findings of another study conducted by Memtsoudis et al. were used to determine the sample size. In the study, the rate of procedure-related complications was reported as 12.2% in bilaterally operated patients and 8.5% in unilaterally operated ones (13). For an 80% statistical power and 0.05 margin of error, the minimum number of samples to be included in the study was determined as 1,061 patients.

In the present study, continuous data are presented as mean ± standard deviation (SD) or median (IQR: 25-75. percentile). Categorical variables are presented as frequencies (n) and percentages (%), and analysed using Pearson's chi-square and Fisher's exact tests. Normality assumptions were controlled using the Shapiro-Wilk test. The Student's t-test and Mann-Whitney U test were used for the comparison of numerical data between the two groups, as appropriate. One-way ANOVA was used for the comparison of parametric variables among groups, and Tukey's HSD test was performed as a post-hoc test for significant results. The Kruskal-Wallis test was carried out to compare non-parametric variables among the groups, and the Bonferroni-Dunn test was performed as a post-hoc test for significant results. Univariate and multivariate logistic regression analyses were used to establish the predictor variables that were significantly related to the length of ICU stay. Odds ratios (OR) with corresponding 95% confidence intervals (95% CIs) were reported. Statistical analysis was performed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA). A two-sided p-value of < 0.05 was considered statistically significant.

RESULTS

This study included a total of 1,129 patients, 85.5% of whom were women, with a mean age of 67.58±7.23 years. Three most common comorbidities were hypertension (38.5%), diabetes mellitus (13%), and cardiovascular disease (9.3%), whereas anaemia was detected in 50.8%. Of all the patients, 75.6% underwent unilateral, 19.9% simultaneous bilateral and 4.5% staged bilateral TKA. In the study, 99 patients (8.8%) required ICU care, while 5 patients died (4 patients died in the hospital and 1 patient died within 1 month after discharge).

When the patients were divided into three groups, according to whether they underwent unilateral, simultaneous bilateral, or staged bilateral TKA, it was determined that the need for ES transfusion and the length of hospital stay were highest in those who underwent staged bilateral, but the lowest in those who underwent simultaneous bilateral TKA (all p<0,001). However, no statistically significant difference was found between the groups in terms of type of anaesthesia (general anaesthesia or spinal anaesthesia), intensive care need, ICU length of stay, and mortality rates (Table 1).

There was no statistically significant difference between patients with and without anaemia in terms of the type of anaesthesia, length of hospital stay, need for intensive care, ICU length of stay, and mortality rates, except for the need of ES transfusion, which increased significantly in anaemic patients, set as p=0.011 (Table 2).

In addition to comorbidities (p<0.001), the incidence of anaemia (p<0.001), need for intensive care (p=0.006), and mortality rate (p=0.014) were significantly higher in patients aged ≥70 years (Table 3).

No statistically significant difference was found in terms of the need for intensive care admission and mortality rates between patients with and without anaemia who underwent unilateral TKA, simultaneous bilateral TKA and staged bilateral TKA (Table 4).

Similarly, no statistical significance was observed in terms of need for ICU hospitalisation and mortality rates between patients younger than 70 and those aged ≥70, who underwent unilateral TKA, simultaneous bilateral TKA and staged bilateral TKA (Table 5).



Table 1. Comparison of demographic and clinical characteristics of patients who underwent unilateral, simultaneous bilateral and staged bilateral TKA

Variables	Unilateral (n=853)	Simultaneous bilateral (n=225)	Staged bilateral (n=51)	p values
Age (years)	67.65±7.58	66.88±5.79	69.52±6.7	0.056
Female	67.52±7.4[a,b]	66.50±5.83[a]	69.74±6.93[b]	**0.025**
Male	68.47±8.61	69.06±5.1	68.83±6.1	0.923
Gender				
Female	735(86.2)	191(84.9)	38(76)	0.135
Male	118(13.8)	34(15.1)	12(24)	
Comorbidity	397(46.5)[a]	118(52.4)[a,b]	32(64)[b]	**0.023**
HT	304(35.6)[a]	105(46.7)[b]	26(52)[b]	**0.001**
DM	122(14.3)[a]	15(6.7)[b]	10(20)[a]	**0.003**
CVD	72(8.4)	27(12)	6(12)	0.210
CKD	48(5.6)	11(4.9)	2(4)	0.822
CPD	51(6)	8(3.6)	0(0)	0.082
Anaemia	447(52.4)	103(45.8)	24(48)	0.192
ES transfusion unit	3(3-3)[a] Mean Rank=561.41	3(2-3)[b] Mean Rank=500.37	6(3-8)[c] Mean Rank=905.80	**<0.001**
Type of anaesthesia				
General anaesthesia	228(26.7)	75(33.3)	10(20)	0.066
Spinal anaesthesia	625(73.3)	150(66.7)	40(80)	
Length of hospital stay	6(5-7)[a] Mean Rank=565.51	6(5-7)[b] Mean Rank=476.93	13(8-15)[c] Mean Rank=941.34	**<0.001**
ICU hospitalization	69(8.1)	24(10.7)	6(12)	0.340
ICU length of stay	1(1-1)	1(1-1)	1(1-1)	0.253
Mortality	4(0.5)	1(0.4)	0(0)	0.999

Results are presented as mean ± SD, median (IQR) or n (%). One-way ANOVA, Kruskal-Wallis test, Pearson chi-square test, Fisher's Exact test.

TKA: Total knee arthroplasty, HT: Hypertension, DM: Diabetes mellitus, CVD: Cardiovascular disease, CKD: Chronic kidney disease, CPD: Chronic pulmonary disease, ICU: Intensive care unit.

Table 2. Comparison of demographic and clinical characteristics of patients with and without anaemia

Variables	Patients without anaemia (n=555)	Patients with anaemia (n=574)	p values
Age (years)	66.73±7.08	68.4±7.28	**<0.001**
Female	66.6±6.77	68.16±7.35	**0.001**
Male	67.46±8.55	69.92±6.71	**0.041**
Gender			
Female	468(84.3)	497(86.6)	0.281
Male	87(15.7)	77(13.4)	
Comorbidity	253(45.6)	295(51.4)	0.051
HT	201(36.2)	234(40.8)	0.116
DM	63(11.4)	84(14.6)	0.101
CVD	47(8.5)	58(10.1)	0.344
CKD	27(4.9)	35(6.1)	0.363
CPD	23(4.1)	36(6.3)	0.108
HGB level	13.37±1.05	10.8±0.8	**<0.001**
ES transfusion unit	3(3-3) Mean rank: 544.69	3(3-3) Mean rank: 584.64	**0.011**
Type of anaesthesia			
General anaesthesia	146(26.3)	168(29.3)	0.267
Spinal anaesthesia	409(73.7)	406(70.7)	
Length of hospital stay	6(5-7)	7(5-7)	0.121
ICU hospitalization	44(7.9)	55(9.6)	0.326
ICU length of stay	1(1-1)	1(1-1)	0.838
Mortality	2(0.4)	3(0.5)	0.999

Results are presented as mean ± SD, median (IQR) or n (%). Student's t-test, Mann-Whitney U test, Pearson chi-square test, Fisher's Exact test.

TKA: Total knee arthroplasty, HT: Hypertension, DM: Diabetes mellitus, CVD: Cardiovascular disease, CKD: Chronic kidney disease, CPD: Chronic pulmonary disease, ICU: Intensive care unit.



Table 3. Comparison of demographic and clinical characteristics of patients by age groups

Variables	<70 years (n=649)	≥70 years (n=480)	p values
Gender			
Female	575(88.6)	390(81.3)	**0.001**
Male	74(11.4)	90(18.8)	
Comorbidity	218(33.6)	330(68.8)	**<0.001**
HT	154(23.7)	281(58.5)	**<0.001**
DM	78(12)	69(14.4)	**0.245**
CVD	17(2.6)	88(18.3)	**<0.001**
CKD	7(1.1)	55(11.5)	**<0.001**
CPD	17(2.6)	42(8.8)	**<0.001**
Anaemia	300(46.2)	274(57.1)	**<0.001**
ES transfusion unit	3(3-3)	3(3-3)	0.716
Type of anaesthesia			
General anaesthesia	180(27.7)	134(27.9)	0.946
Spinal anaesthesia	469(72.3)	346(72.1)	
Length of hospital stay	6(5-7)	6(5-7)	0.375
ICU hospitalization	44(6.8)	55(11.5)	**0.006**
ICU length of stay	1(1-1) Mean rank: 52.61	1(1-1) Mean rank: 47.91	**0.049**
Mortality	0(0)	5(1)	**0.014**

Results are presented as mean ± SD, median (IQR) or n (%).Student's t-test, Mann-Whitney U test, Pearson chi-square test, Fisher's Exact test.

TKA: Total knee arthroplasty, HT: Hypertension, DM: Diabetes mellitus, CVD: Cardiovascular disease, CKD: Chronic kidney disease, CPD: Chronic pulmonary disease, ICU: Intensive care unit.

DISCUSSION

This study revealed that the need for ES transfusion and the length of hospital stay were highest in patients who underwent staged bilateral TKA and lowest in those who underwent simultaneous bilateral TKA. However, no significant differences were found between the groups in terms of intensive care needs, ICU length of stay, and mortality rates. Although the need for intensive care and mortality rates increased significantly in patients aged ≥70 years, performing unilateral, bilateral or staged TKA did not appear to have caused an additional increased risk when compared in terms of age groups.

Table 4. ICU hospitalization and mortality rates according to the presence of preoperative anaemia

Variables	Patients without anaemia (n=555)	Patients with anaemia (n=574)
ICU hospitalization		
Unilateral	29(7.1)	40(8.9)
Simultaneous bilateral	11(9)	13(12.6)
Staged bilateral	4(15.4)	2(8.3)
p values	0.284	0.510
Mortality		
Unilateral	1(0.2)	3(0.7)
Simultaneous bilateral	1(0.8)	0(0)
Staged bilateral	0(0)	0(0)
p values	0.463	0.999

Results are presented as n (%).Pearson chi-square test, Fisher's Exact test.

Table 5. ICU hospitalization and mortality rates according to the age

Variables	<70 years (n=649)	≥70 years (n=480)
ICU hospitalization		
Unilateral	30(6.2)	39(10.7)
Simultaneous bilateral	10(7.4)	14(15.6)
Staged bilateral	4(15.4)	2(8.3)
p values	0.181	0.377
Mortality		
Unilateral	-	4(1.1)
Simultaneous bilateral	-	1(1.1)
Staged bilateral	-	0(0)
p values	-	0.999

Results are presented as n (%).Pearson chi-square test, Fisher's Exact test.

A review of the relevant literature on bilateral TKA revealed that administering anaesthesia as a single session, shorter duration of surgery, and reduced use of painkillers, lower costs, excellent clinical results, as well as patient satisfaction could be considered as the advantages of this procedure (14). Considering the similar advantages, simultaneous bilateral TKA was performed in selected cases in our clinic. However, in accordance with the opinions of anaesthesiology and reanimation specialists, unilateral or staged bilateral TKA is mostly preferred for patients of advanced age and those having serious comorbidities or doubts about their haemodynamic stability.

Despite the availability of various studies in the literature evaluating the results of unilateral - bilateral (simultaneous + staged) or simultaneous bilateral - staged bilateral TKA, the number of studies evaluating the results of unilateral - staged bilateral - simultaneous bilateral TKA are limited. For example, a study conducted in Pakistan that included 658 patients reported no statistically significant differences regarding mortality and major complications between patients who underwent unilateral and those that underwent bilateral TKA. The same study further reported that 3 patients who had undergone bilateral TKA developed DVT complications. The study also suggested that bilateral TKA may be preferred in selected patients with bilateral knee osteoarthritis in terms of its additional benefits such as lower surgery costs, faster recovery, less absenteeism, single anaesthesia exposure, single hospital admission, and lesser follow-up necessity (15). In our study, no statistically significant difference was found in terms of major complications, such as severe haemodynamic disorders, DVT, and pulmonary embolism, which may cause mortality and ICU hospitalisations between patients who underwent unilateral, simultaneous bilateral, and staged bilateral TKA. Undoubtedly, the most important factor in obtaining this result in our clinic was based on the fact that simultaneous bilateral TKA was performed



in younger patients, in those without serious comorbidities, and in those who were more haemodynamically stable. Since the amount of bleeding could have been higher, the use of tranexamic acid was relatively more common in cases that underwent simultaneous bilateral TKA than in cases with unilateral TKA or staged bilateral TKA. This situation may have prevented increased mortality and ICU hospitalizations associated with postoperative hemodynamic disorders that patients who underwent simultaneous bilateral TKA could have developed.

However, in another study evaluating the results of simultaneous bilateral and staged bilateral TKA, Liu et al. analysed the data obtained from ten studies involving 92,782 patients and reported that the prevalence of mortality in patients who underwent simultaneous bilateral TKA increased significantly when compared with those who underwent staged bilateral TKA. The meta-analysis also indicated that the risk of deep infection and respiratory complications was lower in patients who underwent simultaneous bilateral TKA than in those who underwent staged bilateral TKA, though pulmonary embolism and DVT were observed more frequently. No statistical significance was observed in terms of revision, superficial infection, arthrofibrosis, cardiac complications, neurological complications, or urinary complications (16). In another similar study, Yoon et al. compared TKA performed bilaterally in a single session and in two separate sessions, emphasising the probability of a significant increase in systemic complications in patients aged ≥70 who underwent bilateral TKA in a single session compared to that performed in stages. The same study noted that simultaneous bilateral TKA in elderly or high-risk patients may increase the rate of systemic complications, and it should, therefore, be performed with caution, particularly in this group (17). In our study, we investigated the effect of advanced age on the need for ICU admission and mortality, especially in patients who underwent unilateral, staged bilateral, and simultaneous bilateral TKA. Regardless of how significantly the need for intensive care and mortality rates increased in patients aged ≥70, we found that performing unilateral, bilateral or staged bilateral TKA did not result in an additional risk in terms of an increased need for ICU hospitalisation or mortality.

Similar to our study, Bohm et al. examined the results of unilateral, staged bilateral, and simultaneous bilateral TKA cases in a study conducted with approximately 240,000 patients, and reported that those who underwent simultaneous bilateral TKA were younger and had with fewer comorbidities than those who underwent unilateral TKA and staged bilateral TKA. The same study further indicated that patients undergoing simultaneous bilateral TKA had a shorter hospital stay, but generally more blood transfusion was needed than the case in other groups. It was also reported that there was no statistically significant difference regarding in-hospital mortality between patients who underwent simultaneous bilateral and unilateral TKA, while those who underwent staged bilateral TKA had the lowest in-hospital mortality rate (18). Similarly, the present study found that the mean age of those who underwent simultaneous bilateral TKA was lower, although not statistically significant, and that comorbidities, especially DM, were also significantly less common in general than those who underwent staged bilateral TKA. In our study, the need for ES transfusion and the length of hospital stay were highest in those who underwent staged bilateral TKA and lowest in those who underwent simultaneous bilateral TKA. No statistically significant differences were found between the groups in terms of intensive care need, length of ICU stay, and mortality.

In the literature, there are studies conducted with fewer patient groups comparing unilateral and bilateral TKA in terms of pain levels and functional improvement. In one of those studies, Alghadir et al. reported a significant decrease in pain intensity and considerable improvement in functional capac-

ity observed on postoperative day 30, after total knee replacement (TKR) surgery in both groups. Nonetheless, no significant difference was noted between simultaneous bilateral and unilateral TKR in terms of alleviating the intensity of pain and of improving functional capacity on postoperative day 30 (19). In a similar study, Yıldız et al. compared the results of unilateral unicompartmental and bilateral unicompartmental knee arthroplasty by evaluating the results of the patients, whose clinical results were also examined in terms of the Oxford Knee Score and the International Knee Documentation Committee. They concluded that one-stage simultaneous bilateral Oxford medial unicompartmental knee arthroplasty was a safe and effective method with acceptable complication rates compared to those of unilateral surgery (20). Our study examined the reliability of simultaneous bilateral TKA; however, the lack of various scores evaluating the effectiveness of such surgery could be considered a limitation. In addition, the fact that the patients included in the study were operated by different orthopaedic surgeons and were followed up by different anaesthesia teams can also be considered as a limitation of the study, as this may have affected the results. The strength of our study rests on the evaluation of patients' mortality and morbidity when exposed to bilateral simultaneous TKA within a large patient population of >1000 people.

Contrary to some studies in the literature, it is undeniable that the mortality rates of patients who underwent simultaneous bilateral TKA in our study were lower because elderly patients with comorbidities, who underwent the procedure in our hospital, were mostly closely observed in the ICU on the first postoperative day.

CONCLUSION

In conclusion, the results of our study showed no statistically significant difference in terms of the need for intensive care admission, length of stay in the ICU, and mortality rates between patients who underwent unilateral TKA, simultaneous bilateral TKA, and staged bilateral TKA.

Most patients with arthritic knees have bilateral knee involvement. Just in the same way we implemented in our clinic, simultaneous bilateral TKA may be preferred over staged bilateral TKA in patients under 70 years of age with bilateral gonarthrosis, but without any significant comorbidities, considering that the former can be performed with a single administration of anaesthesia, and provides shorter surgical time, reduced painkiller use, shorter hospital stay, and lesser need of ES transfusion, in addition to the fact that it increases neither the rate and length of ICU hospitalisation, nor mortality. Finally, the attitude of an anaesthesiology and reanimation specialist in the postoperative follow-up and management of risky patients is as important as the choice of protocol by a surgeon for each patient.

Acknowledgments

The author would like to thank Başak OĞUZ YOLCULAR for her contribution to the statistical editing of the article.

Funding

No financial support was received from any institution or organization for this work.

Competing interest

The authors declare that they have no conflict of interest.

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RESEARCH

EVALUATION OF FACTORS AFFECTING MORTALITY IN GERIATRIC HIP FRACTURE SURGERY: A RETROSPECTIVE STUDY

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2022.304
2022; 25(3): 452-464

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Abstract

Introduction: The primary aim of this study is to evaluate the effect of anesthesia methods on in-hospital, 30-day, and six-month mortality following geriatric hip fracture surgery. The secondary aim is to evaluate the effect of preoperative comorbidities on mortality.

Method: This retrospective study included patients aged ≥75 years who had undergone femoral neck fracture surgery.

Results: The data of 135 patients were analyzed. The postoperative stay in the intensive care unit of patients who were given general anesthesia ($p < 0.05$) was significantly longer. In the comparisons made according to survival, the exitus cases were found to have higher rates of renal disease and dementia. The variables found to be significantly different in the paired comparisons and determined to be a risk factor as a result of logistic regression analysis were applied with an receiver operating characteristic analysis, as a result of which a cutoff value of 6 in the modified Charlson comorbidity index score was found to be statistically significant area under curve = 0.727, $p < 0.001$, 95% CI: 0.644–0.800). The cutoff value for preoperative hemoglobin was determined to be 11.4 (Area under curve = 0.643, $p = 0.005$, 95% confidence interval: 0.556–0.723).

Conclusions: Ensuring the preoperative waiting time does not exceed 48 hours, optimizing the medical and hemodynamic status with a multidisciplinary approach, and determining the anesthesia method according to the clinical characteristics of each patient may contribute to reducing mortality rates.

Keywords: Hip Fractures; Geriatrics; Anesthesia; Mortality.

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Received : Jul 27, 2022
Accepted : Sep 20, 2022

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INTRODUCTION

As the population of the elderly grows worldwide, the incidence of surgical interventions for elderly individuals has also increased, the most common of which has been reported to be orthopedic operations. Hip fractures occur in approximately 1.6 million people per year worldwide, and it is estimated that this number could reach 6 million by 2050 (1). Despite efforts made to improve perioperative care, complications and mortality rates following geriatric hip fracture surgery continue to be a problem throughout the world. It is thought that hip fractures due to osteoporosis and osteopenia may increase in more elderly patients due to longer and more active lives. (2).

Patients with hip fractures generally constitute a population of people of advanced ages with multiple comorbidities and a high fragility index; therefore, these are the patients with the highest morbidity and mortality incidence in the orthopedic operating theatre. Previous studies have reported a one-year mortality rate after hip fractures between 14% and 37% (3). Factors, such as advanced age, gender, and multiple comorbidities, have an effect on mortality that cannot be changed, whereas preoperative waiting time, fluid electrolyte imbalance, nutritional status, a high serum creatinine level, and a low hemoglobin level are modifiable factors. The anesthesia method applied to patients undergoing operations is also among the modifiable factors that can have an effect on mortality. Many studies in the literature have investigated the effect of anesthesia methods on postoperative complications and mortality in this patient group, but to date, no anesthesia method has been shown to be superior to others (4).

In this study, the effect of the anesthesia type on mortality was investigated in patients aged ≥75 years, who were operated on to treat their hip fractures. The primary aim of this study is to evaluate the effect of the anesthesia selected for these advanced-age patients on in-hospital, 30-day, and six-month mortality. The secondary aim of this study is to evaluate the effect of other factors on mortality.

METHOD

Study design

The Ethics Committee of Ankara City Hospital granted approval for this study. The electronics record system of the hospital was retrospectively examined for the information of patients aged ≥75 years, who presented at the Emergency Department and were admitted for surgery because of a femoral neck fracture between February 2019 and May 2021. The identified patients were contacted by telephone so that their postoperative health status could be recorded. Patients were excluded from the study if they had a femur fracture in the middle or distal section, pathological fracture, bilateral femur fracture, or concomitant multiple trauma, or if they were admitted for further surgery for revision or a recurrent fracture.

All patients were evaluated with respect to their age, gender, comorbidities, American Society of Anesthesiologists (ASA) score, operation type, anesthesia type, preoperative modified Charlson comorbidity index (mCCI) score, preoperative hemoglobin level, preoperative waiting time (days between the point of hospital admission and surgery), postoperative stay in the Intensive Care Unit (ICU), postoperative length of stay in the hospital, postoperative complications, in-hospital mortality, and mortality of discharged patients in the first 30 days and first six months.

Statistical Analyses

The data obtained for the study were analyzed statistically using SPSS vn. 25.0 (IBM Corpn., Armonk, NY, USA) and MedCalc 15.8 (MedCalc Software Bvba, Ostend, Belgium) statistical programs. InIn addition to the descriptive statistical methods for data evaluation (stated as the number, percentage, mean, standard deviation, median, and minimum–maximum values), the Chi-square test

was conducted to compare the qualitative data. The conformity of the data to normal distribution was assessed with the Kolmogorov–Smirnov test, skewness and kurtosis, and visual graphic methods (histogram, Q-Q plot, stem-and-leaf plots. the evaluation of the quantitative data showing normal distribution, an independent samples t-test was conducted. To determine the differentiation ability of the variables, the receiver operating characteristic (ROC) curve analysis was performed, and to determine the risk ratio, binary logistic regression analysis was performed. In the survival analyses, the Kaplan-Meier, logrank, Breslow, and Tarone-Ware tests were performed. A value of $p < 0.05$ was accepted as statistically significant.

Power Analysis

The power analysis was performed using the G*Power 3.1.9.7 (Franz Faul, Universität Kiel, Germany) software and, based on the mCCI score, determined a power of 98% with $n_1 = 95$, $n_2 = 40$, $\alpha = 0.05$, and effect size (d) = 0.8.

RESULTS

From the hospital records system, a total of 151 patients were identified who were aged ≥75 years and were admitted to the hospital for surgery because of a femoral neck fracture between February 2019 and May 2021. A total of 16 patients were excluded from the study: three cases with femoral shaft fracture, five with distal femur fracture, one with revision surgery, three with multiple trauma, two with incomplete hospital data, and finally, two cases with unknown survival status after discharge (as they could not be contacted). Thus, the data of 135 patients were analyzed, comprising 65.2% females and 34.8% males with a mean age of 85.0 ± 5.6 years. The ASA scores were determined to be I–II in 24.4% of the patients and III–IV in 75.6% (Table 1).

In the comparisons made according to the anesthesia type, the postoperative length of stay in the ICU was found to be statistically significantly longer in the patient group who were administered general anesthesia ($p < 0.05$). No statistically significant difference was determined between the anesthesia types with respect to any other variables.

In the comparisons made according to their survival, the exitus cases were found to have higher rates of renal disease and dementia (specifically, Alzheimer's disease), higher ASA and mCCI scores, a lower preoperative hemoglobin value, higher rates of postoperative complications, and a longer postoperative stay in the ICU ($p < 0.05$) (Table 2).

The results of the correlation analysis showed a correlation between survival–mortality and the following:

- mCCI value; r = 0.364
- Postoperative length of stay in the ICU; r = 0.333
- Preoperative hemoglobin level; r = –0.226
- Renal disease; r = 0.364
- Dementia (Alzheimer's disease); r = 0.249
- ASA score; r = 0.256
- Postoperative complications; r = 0.286

All these correlations were determined to be statistically significant ($p < 0.05$).

The variables for which a difference was found in the paired comparisons between survival and mortality—renal disease, dementia (Alzheimer's disease), ASA score, mCCI score, preoperative hemoglobin value, postoperative complications, and postoperative stay in the ICU—were included in the regression model using the backward stepwise method. Further, the model was terminated in the fifth step. The dependent variable (survival–mortality) explained approximately 32% of this model (Nagelkerke $R^2 = 0.317$). According to this model, there was a statistically significant correlation between the survival–mortality status and mCCI and the preoperative hemoglobin level ($p < 0.05$). The exitus status was approximately 3.5-fold higher in

patients with dementia (Alzheimer's disease) compared to those without, approximately 1.7-fold higher in patients with a higher mCCI value, and approximately 1.4-fold higher in those with a low preoperative hemoglobin value (Table 3).

ROC analyzes of risk factors provided logistic regression analysis :

- The cutoff value for the mCCI value was found to be 6 (Area under curve = 0.727, $p < 0.001$, 95% confidence interval (CI): 0.644–0.800).
- The cutoff value for the preoperative hemoglobin level was found to be 11.4 (Area under curve = 0.643, $p = 0.005$, 95% CI: 0.556–0.723) (Figure 1).

In the comparisons made according to mortality, a statistically significant difference was determined in gender, renal disease, mCCI, and length of stay in the ICU, according to the mortality status ($p < 0.05$). Post-hoc tests were applied to determine from which group or groups the difference originated. Exitus within the first six months was determined at a higher rate in females, while in-hospital exitus was higher in males, and the rate of renal disease was lower in patients who were exitus within the postoperative first 30 days. The mCCI value was higher in patients who were exitus in the hospital than in those who were exitus within the postoperative first 30 days. The postoperative length of stay in the ICU was higher in patients who were exitus in the hospital (Table 4).

DISCUSSION

The results of this study showed that regional anesthesia was applied at a high rate (83.7%) to patients aged ≥75 years, who were operated on for hip fracture, but no significant relationship was observed between the anesthesia method and their mortality. Postoperative mortality was determined to be significantly increased in patients with preoperative kidney dysfunction or failure and in patients diagnosed with dementia. The study results also showed that a high preoperative mCCI score and low hemoglobin value were risk factors for mortality. In patients with a postoperative outcome of mortality, there was a significant increase in the postoperative length of stay in the ICU and the frequency of complications.

In a prospective, single-center study by Huette et al., no relationship was found between the anesthesia type and mortality in a one-year follow-up

Figure 1. ROC Analysis

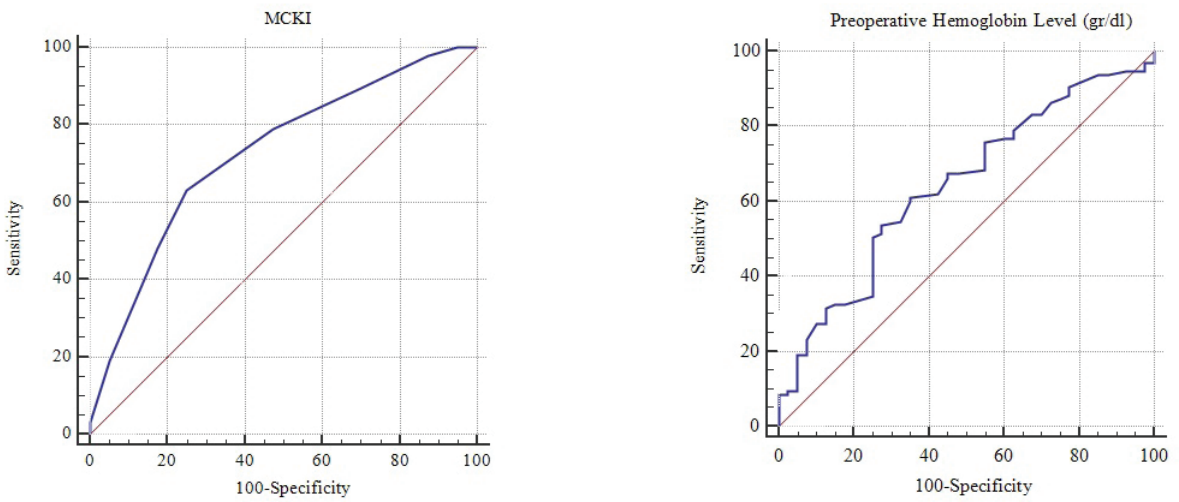


Table 1. Demographic Data of the Patients (mean±SD, min-max; n, %)

		n mean ± SD	% Median (Min-Max)
Gender *	female	88	65.2
	male	47	34.8
Age (years)**		85.0 ± 5.6	85.0 (75.0 – 99.0)
ASA*	I-II	33	24.4
	III-IV	102	75.6

*: n / %, **: Mean ± Standard Deviation / Median (Min-Max)

Table 2. Comparisons according to survival

		Survival		P
		Survived (n=95)	Exitus (n=40)	
Gender	Female	64 (67.4%)	24 (60.0%)	0.533 [a]
	Male	31 (32.6%)	16 (40.0%)	
Age (years)		84.3 ± 5.3	86.4 ± 6.2	0.053 [b]
Comorbidities	Absent	14 (14.7%)	1 (2.5%)	**0.040** [a]
	Present	81 (85.3%)	39 (97.5%)	
	HT	*56 (58.9%)*	*28 (70.0%)*	*0.310* [a]
	DM	*28 (29.5%)*	*11 (27.5%)*	*0.982* [a]
	CAD-CHF	*28 (29.5%)*	*18 (45.0%)*	*0.124* [a]
	Arrhythmia	*14 (14.7%)*	*5 (12.5%)*	*0.944* [a]
	COPD	*22 (23.2%)*	*10 (25.0%)*	*0.993* [a]
	Renal disease	*9 (9.5%)*	*13 (32.5%)*	***0.002*** [a]
	Malignancy	*6 (6.3%)*	*3 (7.5%)*	*0.724* [a]
	Dementia-Alzheimer	*16 (16.8%)*	*16 (40.0%)*	***0.008*** [a]
	CVE	*10 (10.5%)*	*8 (20.0%)*	*0.230* [a]
	Parkinson	*6 (6.3%)*	*2 (5.0%)*	*1.000* [a]
Operation type	Arthroplasty	53 (55.8%)	26 (65.0%)	0.423 [a]
	Screw- plate	42 (44.2%)	14 (35.0%)	



ASA	I-II	30 (31.6%)	3 (7.5%)	**0.006** [a]
	III-IV	65 (68.4%)	37 (92.5%)	
Anesthesia type	Regional	81 (85.3%)	32 (80.0%)	0.616 [a]
	General	14 (14.7%)	8 (20.0%)	
mCCI		6.0 ± 1.7	7.6 ± 1.9	**0.000** [b]
	≤4	*18 (18.9%)*	*2 (5.0%)*	**0.001** [a]
	5-7	*57 (60.0%)*	*17 (42.5%)*	
	≥8	*20 (21.1%)*	*21 (52.5%)*	
Preoperative Waiting Time (days)		2.6 ± 1.9	2.8 ± 1.8	0.536 [b]
	1 day	*31 (32.6%)*	*7 (17.5%)*	0.203 [a]
	2 days	*27 (28.4%)*	*14 (35.0%)*	
	≥3 days	*37 (38.9%)*	*19 (47.5%)*	
Postoperative stay in ICU (days)		0.7 ± 2.5	3.4 ± 6.9	**0.021** [b]
Postoperative stay in hospital (days)		5.3 ± 5.9	6.3 ± 6.8	0.377 [b]
Preoperative Hemoglobin level (gr/dl)		11.6 ± 1.9	10.7 ± 1.6	**0.011** [b]
	Normal	*50 (52.6%)*	*10 (25.0%)*	**0.006** [a]
	Anemic	*45 (47.4%)*	*30 (75.0%)*	
Postoperative complications	Absent	71 (74.7%)	18 (45.0%)	**0.002** [a]
	Present	24 (25.3%)	22 (55.0%)	
	Pulmonary Complications	*4 (16.7%)*	*3 (13.6%)*	--
	Cardiac Complications	*4 (16.7%)*	*1 (4.5%)*	
	Renal Complications	*9 (37.5%)*	*13 (59.1%)*	
	Neurological Complications	*2 (8.3%)*	*0 (0.0%)*	
	Infectious Complications	*0 (0.0%)*	*2 (9.1%)*	
	Delirium	*5 (20.8%)*	*3 (13.6%)*	

a: Chi-Square Test (n (%)), b: Independent Samples t Test (Mean ± SD), ICU: Intensive care unıt. mCCI: (modified Charlson Comorbidity Index). ASA (American Society of Anesthesiologists). HT: Hypertension, DM: Diabetes Mellitus, COPD: Chronic Obstructive Pulmonary Disease, CAD, CHF: coronary artery disease/ congestive heart failure, CVE: cerebrovascular event.

Table 3. Evaluations with Logistic Regression Analysis

Risk Factor	B	Odds	95% CI	Wald	P*
Dementia-Alzheimer	1.255	3.507	1.40 – 8.78	7.181	**0.007**
mCCI	0.509	1.664	1.30 – 2.14	15.934	**0.000**
Preoperative Hemoglobin level (gr/dl)	-0.317	1.372	1.08 – 1.75	6.543	**0.011**
Constant	-1.163				

*: Binary Logistic Regression Test, Nagelkerke R^2 = 0,317, Hosmer and Lemeshow Test = 0,631, Variable(s) removed on: Step 2: Comorbidities Step 3: Renal Disease, Step 4: ASA, Step 5: Postoperative stay in ICU

Table 4. Comparisons according to Mortality

		Mortality			P
		In-hospital Exitus (n=15)	Exitus within 30 days of postoperative discharge (n=11)	Exitus within 30 days-6 months of postoperative discharge (n=14)	
Gender	Female	6 (40.0%)	6 (54.5%)	12 (85.7%)	**0.039** [a]
	Male	9 (60.0%)	5 (45.5%)	2 (14.3%)	
Age (years)		86.5 ± 6.2	85.7 ± 6.6	86.8 ± 6.3	0.913 [b]
Comorbidities	Absent	0 (0.0%)	1 (9.1%)	0 (0.0%)	0.259 [a]
	Present	15 (100.0%)	10 (90.9%)	14 (100.0%)	
	HT	*11 (73.3%)*	*6 (54.5%)*	*11 (78.6%)*	*0.402* [a]
	DM	*5 (33.3%)*	*3 (27.3%)*	*3 (21.4%)*	*0.773* [a]
	CAD-CHF	*7 (46.7%)*	*5 (45.5%)*	*6 (42.9%)*	*0.978* [a]
	Arrhythmia	*3 (20.0%)*	*0 (0.0%)*	*2 (14.3%)*	*0.304* [a]
	COPD	*4 (26.7%)*	*2 (18.2%)*	*4 (28.6%)*	*0.823* [a]
	Renal disease	*7 (46.7%)*	*0 (0.0%)*	*6 (42.9%)*	***0.025*** [a]
	Malignancy	*3 (20.0%)*	*0 (0.0%)*	*0 (0.0%)*	*0.067* [a]
	Dementia-Alzheimer	*7 (46.7%)*	*4 (36.4%)*	*5 (35.7%)*	*0.800* [a]
	CVE	*3 (20.0%)*	*1 (9.1%)*	*4 (28.6%)*	*0.482* [a]
	Parkinson	*1 (6.7%)*	*0 (0.0%)*	*1 (7.1%)*	*0.670* [a]



Operation type	Artroplasty	12 (80.0%)	7 (63.6%)	7 (50.0%)	0.237 [a]
	Screw-plate	3 (20.0%)	4 (36.4%)	7 (50.0%)	
ASA	I-II	0 (0.0%)	2 (18.25)	1 (7.1%)	0.220 [a]
	III-IV	15 (100.0%)	9 (81.8%)	13 (92.9%)	
Anesthesia Type	Regional	11 (73.3%)	8 (72.7%)	13 (92.9%)	0.328 [a]
	General	4 (26.7%)	3 (27.3%)	1 (7.1%)	
mCCI		8.5 ± 1.7	6.4 ± 1.8	7.6 ± 1.8	**0.018** [b]
	≤4	*0 (0.0%)*	*1 (9.1%)*	*1 (7.1%)*	--
	5-7	*4 (26.7%)*	*7 (63.6%)*	*6 (42.9%)*	
	≥8	*11 (73.3%)*	*3 (27.3%)*	*7 (50.0%)*	
Preoperative Waiting time (days)		2.7 ± 1.8	2.8 ± 1.2	3.0 ± 2.3	0.888 [b]
	1 day	*4 (26.7%)*	*1 (9.1%)*	*2 (14.3%)*	0.740 [a]
	2 days	*4 (26.7%)*	*4 (36.4%)*	*6 (42.9%)*	
	≥3 days	*7 (46.7%)*	*6 (54.5%)*	*6 (42.9%)*	
Postoperative stay in ICU (days)		7.2 ± 10.1	1.2 ± 2.0	1.1 ± 2.2	**0.025** [b]
Postoperative stay in hospital (days)		8.1 ± 9.8	5.5 ± 4.8	5.0 ± 3.1	0.427 [b]
Preoperative Hemoglobin level (gr/dl)		10.8 ± 1.6	10.4 ± 1.9	10.8 ± 1.6	0.743 [b]
	Normal	*2 (13.3%)*	*3 (27.3%)*	*5 (35.7%)*	0.372 [a]
	Anemic	*13 (86.7%)*	*8 (72.7%)*	*9 (64.3%)*	
Postoperative Complications	Absent	5 (33.3%)	5 (45.5%)	8 (57.1%)	0.436
	Present	10 (66.7%)	6 (54.5%)	6 (42.9%)	
	Renal	*6 (60.0%)*	*4 (66.7%)*	*3 (50.0%)*	--
	Pulmonary	*2 (20.0%)*	*1 (16.7%)*	*0 (0.0%)*	
	Delirium	*0 (0.0%)*	*0 (0.0%)*	*3 (50.0%)*	
	Infectious	*2 (20.0%)*	*0 (0.0%)*	*0 (0.0%)*	
	Cardiac	*0 (0.0%)*	*1 (16.7%)*	*0 (0.0%)*	

a: Chi-Square Test (n (%)), b: Independent Samples t Test (Mean ± SD), mCCI: (modified Charlson Comorbidity Index). ASA (American Society of Anesthesiologists). HT: Hypertension, DM: Diabetes Mellitus, COPD: Chronic Obstructive Pulmonary Disease, CAD, CHF: coronary artery disease/ congestive heart failure, CVE: cerebrovascular event

period of 309 patients operated on for hip fracture (5). Waesberghe et al. reviewed 23 studies in a meta-analysis and reported that the anesthesia type did not affect 30-day mortality but significantly decreased in-hospital mortality and the length of stay in hospital (6). O'Donnell et al. conducted a meta-analysis of the data collected from 15 large observational studies and reported no difference between the two anesthesia techniques with respect to 30-day mortality (7). In contrast, some studies have predicted that neuraxial anesthesia could prolong survival compared to general anesthesia. Ahn et al. compared national data on patients who had undergone hip surgery and found that regional anesthesia provided a better outcome than general anesthesia with respect to 30-day mortality in elderly patients (8). In a comprehensive cohort study in Canada, there was reported to be an increase in 30-day survival by 20–25% of hospitals with the use of neuraxial anesthesia in hip fracture operations (9). Peterson et al. compared regional anesthesia with general anesthesia in a population-based cohort study of patients aged >70 years and reported an 18% decrease in 30-day mortality with regional anesthesia (10). In a retrospective study by Desai et al., the in-hospital mortality rate was found to be higher in patients administered general anesthesia and in those transferred from regional anesthesia to general anesthesia. However, after the discharge of these cases from the hospital, no significant difference was determined between the two anesthesia types with respect to mortality rates. Previous research has concluded that both anesthesia methods can be used in these patients. However, the most important point is that the method selected is appropriate to the clinical characteristics of the patient, and it is recommended that this should be administered carefully by experienced anesthetists.

It has been reported that when general anesthesia is selected, rapid fluctuations in intraoperative arterial pressure can be prevented by administering titred anesthetic agents at low doses. When spinal anesthesia is selected, intraoperative hypotension has been seen less with a reduced volume (<10mg) of intrathecal 0.5% hyperbaric bupivacaine. Previous studies have shown that the application of the fascia iliaca nerve block and the femoral nerve block together under ultrasonography guidance reduced anesthetic doses in patients administered with general anesthesia. It has also been reported that positioning during spinal anesthesia application facilitates and allows the use of low-dose local anesthetics.

Previous studies have shown that age is closely related to mortality in hip fracture surgery. In a retrospective study, Endo et al. showed that the strongest factors increasing in-hospital mortality after hip fracture surgery were age, gender, congestive heart failure, kidney failure, and fluid electrolyte imbalance, and of these, advanced age (especially >85 years), congestive heart failure, weight loss, and fluid electrolyte imbalance were reported to be stronger markers of mortality than other risk factors (11). It is the aim of the current study to create a more homogenous population by including geriatric patients aged ≥75 years. The mean age at which hip fractures were seen in this age range was determined to be 84–85 years in this study. The in-hospital mortality rate in the current study was found to be 37.5%, and this high rate was thought to be on account of the study including patients of advanced age.

Chronic renal disease has been reported to be a risk factor for fragility fractures. Moreover, in elderly patients presenting at the hospital with hip fractures, frequently seen findings have been reported to be severe fluid deficiency and associated fluid electrolyte imbalance and elevated urea–creatinine, even without any underlying kidney disease. In patients who are not treated preoperatively, this can result in acute renal failure. Among the current study's patients identified in the hospital's computerized system as having acute or chronic renal failure or renal dysfunction, regardless of their preoperative



blood biochemistry tests, the in-hospital mortality rate was observed to be significantly increased. In a case-control study conducted by Chiang et al. to determine the risk of in-hospital mortality after hip fracture surgery, the data of 841 patients were compared, and there was determined to be a significant correlation between renal dysfunction and in-hospital mortality (12).

Systematic planning of the postoperative care of patients with hip fractures should be started preoperatively. It has been recommended that by rapidly transferring elderly patients presenting with hip fractures to a separate ICU, treatment can be provided promptly by a primary care team, including an ICU specialist, a thoracic disease specialist, and a cardiologist (13).

Patients with dementia are generally less active and have poor self-care capabilities, which can increase postoperative complications, such as surgical site infections, urinary tract infections, and respiratory complications (14). In a recent meta-analysis of 18 studies, one-year mortality was found to be 39% in patients with dementia (15). In the current study, no significant correlation was observed between dementia and in-hospital and 30-day mortality, but the rate of dementia in patients with the outcome of mortality in the total postoperative six-month period was high (40.0%). In the current study, a diagnosis of dementia (Alzheimer's disease) was present in 23.7% of the patients. In the logistic regression evaluation, mortality was determined to be approximately 3.5-fold more in patients with a preoperative diagnosis of dementia (Alzheimer's disease) compared to those without (ß: 1.255, Odds: 3.507, 95% CI: 1.40–8.78, Wald: 7.181, p: 0.007). Patients aged >70 years presenting at the hospital with hip fractures were evaluated in a population-based cohort study by Peterson et al., and the postoperative 30-day mortality among them was determined to have a 1.5-fold increase in patients with a diagnosis of dementia compared to those without (HR = 1.50 [95% CI 1.31–1.72]) (16).

The most serious form of hip fractures, which could potentially diminish patients' quality of life and lead to being a great cost burden to society, are osteoporotic fractures. Generally, the Charlson comorbidity index (CCI) is related to increased mortality among patients with fragility fractures. Osteoporosis has been determined at a more advanced level in elderly patients with a higher CCI, but the time to surgery and the length of stay in the hospital have not been found to be significantly longer (17). The age-adjusted mCCI has been used to predict mortality in hip-fracture patients and has also been strongly associated with fragility. Studies have reported that mCCI of ≥6 in an elderly patient with a femur fracture is associated with a high complication risk and mortality rate (18). These patients have poor bone quality, and it is well known that they often have osteoporosis. Furthermore, osteoporotic fractures are fragility fractures, which occur as a result of low-energy mechanical forces or forces at a level lower than that which would create a normal fracture. With logistic regression modeling in the current study, the mCCI calculated preoperatively was found to be a risk factor for mortality at a moderate level, and patients with a high mCCI value were determined to be exitus at a rate approximately 1.7-fold higher than those with lower mCCI values. In the ROC analysis, the cutoff value for mCCI values was found to be 6 (Area under curve= 0.727, $p < 0.001$, 95% CI: 0.644–0.800). Wang et al. conducted a similar study and found a positive correlation between complications and an mCCI value of ≥6 with staged logistic regression modeling (OR: 4.27, $p = 0.02$) (19).

One of the findings in the current study is that a significant correlation was determined between a low preoperative hemoglobin level and mortality. The preoperative hemoglobin level was found to be a risk factor as a result of logistic regression analysis, and in the ROC analysis, the cutoff value was determined to be 11.4 (Area under curve = 0.643, $p = 0.005$, 95% CI: 0.556–0.723). In a retrospective study

by Nia et al. of geriatric patients operated on for proximal hip fracture, anemia (Hgb <12) was determined to be an independent risk factor for mortality (20). Yombi et al. also found significantly higher rates of short-, medium-, and long-term mortality after hip fracture surgery in patients with a preoperative hemoglobin level of <12 (21). Some factors, such as age, gender, fracture type, hereditary predisposition, and comorbidities, which affect mortality in patients with hip fracture, cannot be changed, while there are also modifiable factors, such as physical health, nutritional status, high serum creatinine level, and low hemoglobin level. Although the hemoglobin level is a potentially modifiable factor, there remains uncertainty about the benefit of blood transfusion in patients with preoperative anemia, which is associated with increasing blood transfusions, healthcare costs, morbidity, and mortality. In patients hospitalized because of hip fracture, it has been reported that by increasing the erythrocyte production and oxygen carrying capacity, the optimization of anemia with preoperative erythropoietin (EPO) and intravenous iron treatment reduces transfusion rates and complications associated with transfusions. In a recent systematic meta-analysis that reviewed 12 clinical studies, it was seen that preoperative intravenous iron treatment in patients undergoing orthopedic surgery reduced the rate of perioperative blood transfusion by 31%, shortened the length of stay in the hospital by 1.6 days, and reduced the postoperative infection rate by 33%, but it had no effect on mortality (22).

The waiting time for surgery of the patients in the current study who presented with hip fracture was seen to be similar in both patients who survived and who were exitus. In a multicenter, prospective analysis by Orosz et al., there was found to be no significant effect of waiting time on mortality, but the presence of comorbidities were determined to increase mortality (23). Leer-Salvesen et al. determined that a preoperative delay of more than 48 hours significantly increased early mortality in an observational study of geriatric patients operated on for hip fractures. It has been emphasized that the preoperative waiting time should not exceed 48 hours to optimize medical and hemodynamic statuses (24). Klestil et al. analyzed 28 prospective studies in a meta-analysis and reported that there was a 20% lower risk of one-year mortality in patients operated on within 48 hours (25). In the current study, the waiting times for surviving and exitus patients were calculated as 2.6 and 2.8 days, respectively, with no significant difference determined between the groups. In both groups, the waiting time exceeded 48 hours.

Age is one of the most important factors affecting mortality in patients operated on for hip fractures. The aim was to standardize the age factor in this study by only including patients aged ≥75 years. In this respect, this study is the first to be conducted on advanced-age hip-fracture patients. However, this condition meant that the study was completed with a low number of patients, which can be considered a limitation of the study. There is a need for further multi-center, similar studies with greater numbers of patients. Another limitation of the study is that, as the data were retrospectively collected from the computer database, it was not possible to evaluate the preoperative level of fragility of the patients and the intraoperative hemodynamic status, which can play a role in mortality.

In conclusion, preoperative classification with a routine determination of a risk score can be of guidance for the clinicians of patients of advanced age undergoing surgery to treat hip fracture. The modifiable factors include not exceeding the preoperative waiting time of 48 hours, optimizing the medical and hemodynamic status with a multidisciplinary approach and selecting the anesthesia method according to the clinical characteristics of each patient. Care given to these factors could contribute to reducing mortality rates.



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Turkish Journal of Geriatrics

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