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Contents

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From The Editor In Chief

In our aging world, the value of researches conducted by collecting, interpreting and evaluating data in a planned and systematic manner in order to contribute to science on issues that prioritize the elderly, is increasingly coming to the fore.

Based on this idea 7th SCIENTIFIC RESEARCH COURSE IN THE FIELD OF GERIATRICS, was organized by the Turkish Geriatrics Society online on 24-26th Nov, 2022.

The topics that significantly meet the requirements of the attendees both at the research and publication stage were presented by experienced faculty members.

I would like to thank the members of the organizing committee and the valuable trainers who made a significant contribution to the course with their knowledge and experience, and wish that it will be useful for the researchers in terms of their professional development, scientific studies, publications and contributions to public health.

Wishing you a safe, healthy, successful, and prosperous new year!

Prof. Yeşim GÖKÇE KUTSAL, M.D.

RESEARCH

RELATIONSHIP BETWEEN PERCEIVED AGEISM, AUTONOMY, AND SYMPTOMS OF DEPRESSION AND ANXIETY DURING THE COVID-19 CURFEW IN OLD AGE PSYCHIATRIC PATIENTS

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■ Aslı AYTULUN[1]
■ Şahinde Özlem ERDEN AKİ[2]

Abstract

Introduction: Restrictive measures were taken to protect people aged 65 years and older during coronavirus pandemic; however, these measures negatively affected their physical and mental health. Ageist attitudes and age discrimination have also become evident during the pandemic. This study aimed to evaluate the relationship between perceived ageism, sense of autonomy, perceptions of curfews, and anxiety and depression levels in older psychiatric patients who comprised a vulnerable and disadvantaged group during the pandemic.

Materials and Methods: In this cross-sectional study, 171 participants older than 65 years, followed up at Hacettepe University Psychiatry outpatient clinic between December 2019 and February 2020, were interviewed via phone using a survey on sociodemographic characteristics, measures of perceived ageism and autonomy, Generalized Anxiety Disorder Scale, and Geriatric Depression Scale-Short Form.

Results: Of 171 total participants, 57 (34.8%) reported an increase in perceived ageism during the pandemic. Almost one-third of the participants found the curfew decisions for the elderly to be unsuitable. Participants with higher education levels and those who found curfews for the elderly inappropriate showed a greater increase in perceived ageism scores ($p<0.001$). Additionally, perceived ageism scores were significantly correlated with depression and anxiety ($p<0.001$). Anxiety and depression scores were significantly lower among participants who reported more autonomy in their lives ($p<0.05$).

Conclusion: During pandemic, state and health authorities should consider the needs of vulnerable groups, such as older individuals and psychiatric patients, when making plans, and ensure that these groups are minimally affected by the disease, restrictive measures, and ageist attitudes.

Keywords: Ageism; Aged; Pandemics; Depression; Anxiety.

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INTRODUCTION

Ageism is a type of discrimination that is widespread but insidious in every society in the modern world (1). Although identified as the third most common type of discrimination after racism and sexism, it remains largely unnoticed (2). Discrimination can occur with any age group, however, at present times, it is generally targeted towards older people. Older people are considered slower and less efficient, and thus incompatible with the requirements of today's society. Ageist stereotypes and negative attitudes towards older adults are shared by both public and state authorities. Ageist attitudes become more visible in times of crisis; older people are seen as a burden on society because of their vulnerability and need for care, especially when resources are limited (1). During the coronavirus disease (COVID-19) pandemic, many cases of age discrimination have occurred worldwide.

At the beginning of the COVID-19 pandemic, individuals aged older than 65 years constituted most of the death rate reported globally (3). Health and state authorities had taken additional measures to reduce the impact of COVID-19 on older people. However, the measures taken in many countries negatively impacted the lives of older adults by applying strict restrictions for the elderly, including stay-home orders for those aged 65 years and older, quarantines, and restrictions on nursing home visitations (4).

The Turkish government has taken some additional protective measures to prevent the spread of COVID-19. On March 21, 2020, during the initial period of the pandemic, the Ministry of Interior issued a statement that people aged 65 years and older with comorbidities were prohibited from going out on the street (5). On May 10, 2020, people older than 65 years were allowed to go out from 11:00 to 15:00, for four hours daily; in the course of pandemic, these restriction hours were changed according to the number of cases occurring. These direct measures to lower old-age mortality restricted elderly citizens' daily activities and independence. In addition to these measures, disruptions in preventive healthcare and management services, and long-term care services increased the indirect negative effects of the pandemic on the elderly. Although these precautions and prohibitions against elderly individuals were implemented only in Turkey, protective measures aimed at older people have also been implemented in other countries (6,7). Different policies were implemented by every country to protect older people; however, ageism has taken similar forms in all of these. Older persons were deemed expendable due to their lack of contribution to the economy and production. The government of the United Kingdom adopted the herd immunity concept, implying that the weaker population could be sacrificed for the sake of the community, to avert economic catastrophe (7). In Italy, ethical guidelines by the Italian Society of Anesthesia, Analgesia, and Intensive Care (SIAARTI) were released for the allocation of treatment in resource-limited situations, suggesting that an age limit could be set for admission to intensive care units (8). The public, unfortunately, shared the ageist attitudes of policymakers; older people were viewed as a drain on society, and the incidences of name-calling and blaming rose (7).

During these times, all precautions, including those for older adults, were implemented by health or state authorities, but older individuals were not allowed to express their opinions or participate in decision-making processes regarding their lives. The application of these protective measures to older adults without their consultation and without considering the negative impact of these measures can be considered ageist.

The restrictions mentioned above have been put on the agenda to protect the older persons, but non-governmental organizations such as medical professional organizations and elderly rights organizations have pointed out that these restrictions and prohibitions on older individuals negatively affect both their mental and physical health (9). It is known

that the feeling of isolation or loss of social relationships has detrimental effects such as deterioration in immune system functions and sleep disturbance (10), a decrease in cognitive functions, and an increase in depression and other negative emotions (11). The World Health Organization (WHO) reported that measures such as self-isolation and social distancing can cause anxiety, anger, agitation, and withdrawal (12). In a longitudinal study, social disconnection and perception of isolation were associated with anxiety and depression symptoms in older individuals (13).

Among old age individuals, older psychiatric patients are a more vulnerable group than the older persons who do not have any mental health problems (14). Individuals with pre-existing mental health problems constitute a disadvantaged group regarding the discrimination towards them. Old age psychiatric patients, in addition to the burden of aging, are more exposed to prejudiced attitudes related to mental illness, discrimination, and age-related discrimination (15).

Many short comments and expert opinions have been published about the psychological effects and other possible negative consequences of the pandemic and the impact of protective measures and ageist attitudes on the older people in different settings. It is, however, noteworthy that there are relatively few research articles examining psychiatric issues in older people. Many articles discussing COVID-19 mentioned ageism, but few incorporated the perspectives and opinions of the older adults themselves. Furthermore, to the best of our knowledge, no study about ageism has been conducted in elderly patients with psychiatric disorders. This study aimed to contribute to the current literature by evaluating the relationship between perceived ageism and changes in perceived ageism levels, perceptions of curfews, and anxiety and depression levels in elderly psychiatric patients during the COVID-19 pandemic.

METHODS

Participants

All patients aged > 65 years who had applied to Hacettepe University Psychiatry Clinic between December 2019 and February 2020, without a diagnosis of dementia or mild cognitive impairment (MCI), were contacted from October 1 to November 1, 2020, through phone numbers registered in our hospital system. Patients were interviewed using a survey that included questions on sociodemographic measures, diagnoses, treatment, medications received, quality of healthcare during the lockdown; perceptions of the lockdown; and scales on perceived ageism, depression, and anxiety. This study was planned and conducted as part of a large-scale study aimed at evaluating various aspects of older psychiatric patients during the pandemic at the Hacettepe University Department of Psychiatry. Inclusion criteria for the study were aged 65 years and older, Turkish speaking, and voluntary participation in the study. Exclusion criteria were the diagnosis of dementia or MCI, conditions that prevented communication on the phone (loss of hearing and speech problems), and any other neurological disease impairing judgement and communication skills. No fees were paid to participants. The study was approved by the Ministry of Health and the Hacettepe University Ethics Committee. Verbal informed consent was obtained from all the participants.

Scales

Sociodemographic Form

The sociodemographic characteristics of the participants were evaluated with a sociodemographic form including single-item questions evaluating thoughts and perceptions about curfew practices for the elderly and perceptions of physical and psychological well-being. The sense of autonomy and the change in autonomy after the pandemic were evaluated using 1-question survey. Psychiatric

diagnoses of the participants were extracted from electronic hospital records.

Perceived Ageism Measure

Perceived ageism was assessed using a measure of everyday discrimination designed to evaluate interpersonal forms of daily experiences of discrimination (16). In the original form, ten items were used to measure everyday discrimination, and response values for each item consisted of five alternative answers. In our study, we adapted the questions and choices for age discrimination. Six items were used to measure everyday discrimination based on age: being discriminated solely based on age, being treated with less courtesy and respect, being treated as not smart, being insulted or threatened, receiving less benefit from healthcare services, and feeling unimportant and worthless. The answers to these items were constructed as follows: most of the time, sometimes, and never. Decreasing scores on this measure indicated increasing levels of perceived ageism.

We also asked how perceived ageism changed during the pandemic period, and the answers for this item were: decreased, no change, and increased.

Geriatric Depression Scale Short Form (GDS-SF)

The Geriatric Depression Scale Short Form (GDS-SF), consisting of 15 questions developed by Sheikh and Yesavage to evaluate depressive symptoms in older people, was used in this study (17). The validity and reliability study was conducted by Durmaz et al. in Turkish (18). Every question on the scale has a yes-no answer, and the range of the score is 0–15, with higher scores indicating more depressive symptoms. In Turkish study, the cut-off point was determined to be 5 and above.

Generalized Anxiety Disorder Test 7 (GAD-7)

The GAD-7 is a short self-reported test developed by Spitzer et al. (2006) according to Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV TR) criteria and is used to evaluate generalized anxiety disorder (19). It is a 7-item four-point Likert-type scale (0=never, 1=many days, 2=more than half of the days, 3=almost every day) used to evaluate symptoms of anxiety within the last two weeks. The scores obtained vary from 0–21. In the original study, the cut-off scores obtained from the scale were 5, 10, and 15 for mild, moderate, and severe anxiety, respectively. The scale's adaptation to Turkish, validity, and reliability were conducted by Konkan et al. in 2013. In this study, the cutoff point of the scale was determined to be 8 and above (20).

Statistical Analysis

SPSS 22.0 program for Windows (SPSS Inc, Chicago, IL, USA) was used for statistical analysis. Categorical variables were presented as numbers and percentages, and continuous variables, such as age, were presented as means and standard deviations. Relationships between various variables were investigated using the t-test, chi-square analysis, ANOVA, or correlation analysis methods according to the nature of the data. The significance value was set at $p< 0.05$.

RESULTS

Sociodemographic Characteristics

A total of 171 older psychiatric patients were included in this study. The sociodemographic characteristics and distribution of the psychiatric diagnoses of the participants are shown in Table 1.

Findings Related to Depression and Anxiety

Of 171 total participants, 45 (26.5%) had a score of 5 or above on GDS-SF, implying the presence

Table 1. Sociodemographic characteristics of the participants

Gender	n (%)
Women Men	119 (69.6) 52(30.4)
Age, mean ±SD, years	72 ± 5.90
Marital status	n (%)
Married	109 (63.7)
Other	62 (36.3)
Household status	n (%)
Living alone	35 (21.9)
Living with family	132 (78.1)
Education	n (%)
Primary + Middle School	94 (55.7)
High School + University	75 (44.3)
Psychiatric diagnosis	n (%)
Depression	102 (60)
Anxiety Disorders	25 (14.7)
Bipolar Affective Disorder Schizophrenia Other	21 (12.4) 11 (6.5) 4 (2.4)

of depressive symptoms. Those who scored 8 or above on the GAD-7 test are accepted to have generalized anxiety disorder symptoms, and 32 of our participants (18.8%) scored 8 or above on this test. Depression and anxiety scores did not differ according to gender, marital status, or household status (living alone vs. living with family). While depression was more prevalent in the lower-education group than in the higher-education group, there was no difference in anxiety among the different education levels.

During the pandemic, 49 (28.8%) participants reported newly added psychiatric symptoms and increased severity of their psychiatric illness. Both anxiety and depression scores differed significantly at the different autonomy levels. Anxiety scores were significantly lower in participants who reported more autonomy ("I make my decisions always or most of the time" vs "I never make my own decisions"), and depression scores were significantly lower in participants who reported more autonomy in their lives. The results of the depression and anxiety scores are presented in Table 2.

Curfews and Their Effects

Regarding the question, "Can you describe your mood during the curfews?", 28.5% of the participants answered "good," and the remaining participants defined their mood as "anxious, sad, depressed, angry, reluctant-stagnant" and others. Depression and anxiety scores in the group with negative mood states were higher than those in the other group, as expected. A total of 65.1% of the participants reported that the curfew negatively affected their mood; anxiety scores were higher in this group, but there was no difference in the depression scores (Table 2).

A total of 111 participants (69.3%) stated that their physical activity level decreased during the pandemic, but no difference between depression and anxiety scores was found between this group and the group with the same activity level. During the curfew period, 70 (41.7%) stated that their physical health deteriorated due to the restrictions. The total GAD-7 score of the group whose physical health deteriorated was significantly higher than that of the group with no deterioration in physical health, but no difference was found in depression scores (Table 2).

Half of the participants (50.6%) found the curfew decision for people older than 65 years to be appropriate, 15.9% found it appropriate but insufficient, and 30.0% found it unsuitable. Individuals with higher education reported that they did not approve of the restrictions at a significantly higher rate than those with lower education (X^2=21.68, p=0.001). The most common reason for the disapproval of curfew for the elderly was "thinking it as a reflection of discrimination against the elderly" (25.3%), while the least common answer was "I could not meet my

Table 2. The relationship of depression and anxiety scores with sociodemographic characteristics and with variables about curfews

Variable n (%)	GDS (Mean±SD)	*p* Value	GAD-7 (Mean±SD)	*p* Value
Gender[a]				
Women	3.55±3.42	0.65	4.38±4.16	0.951
Men	3.27±3.69		4.43±5.19	
Marital status[a]				
Married	3.37±3.75	0.634	5.01±5.202	0.080
Other	365±2.99		3.31±3.05	
Household status[a]				
Living alone	3.75±3.52	0.637	4.08±4.09	0.654
Living with family	3.42±3.51		4.47±4.60	
Education[a]				
Primary + Middle School	4.14±3.88	0.005*	4.92±5.16	0.720
High School + University	2.64±2.78		3.70±3.35	
Autonomy[b]				
" I make my own decisions"				
Always/most of the time 107 (69.4)	3.02±3.23	0.001*	4.13±4.31	0.020*
Sometimes 37 (24)	3.61±3.39		4.51±4.34	
Rarely or never 10 (6.4)	7.77±4.26		8.2±6.25	
Mood during the curfews[a]				
Good 47 (28.5)	1.68 ± 1.51	0.001*	2.36±2.74	0.001*
Other (negative mood states) 118 (71.5)	4.26 ± 3.83		5.32±4.82	
Effect of curfew on mental health[a]				
Negative 110 (65.1)	3.81 ±3.61	0.093	5.28±4.80	0.001*
No effect 59 (34.9)	2.83 ±3.21		2.84 ±3.33	
Change in physical activity level during curfew[a]				
Decreased 111 (69.3)	3.78±3.47	0.077	4.68±4.56	0.231
Not changed 48 (30.7)	2.70±3.53		3.75±4.33	
Physical health deteriorated during curfew[a]				
Yes 70 (41.7)	3.59±3.34	0.528	5.25±4.46	0.039*
No 98 (58.3)	3.24±3.52		3.76±4.45	

[a] = *Student t test,* [b] = *ANOVA , * p < 0.05*

essential needs" (5.3%). The scores for depression and anxiety were not different among the groups with differing opinions regarding the curfews.

($F_{(2,155)}$ = 0.58, p= 0.560 and $F_{(2,157)}$ = 0.90, p= 0.915, respectively).

Perceived Ageism

Baseline perceived ageism in our sample ranged from 2.4% ("ever threatened or been harassed due to your age?") to 19.4% ("ever felt discriminated solely based on your age?").

A negative correlation between perceived ageism total scores and GDS-SF total scores was found; meaning that as perceived ageism increased, depression scores also increased. Likewise, a negative correlation existed between perceived ageism and the YAD-7 total scores (Table 3).

A total of 57 participants (34.8%) reported an increase in perceived ageism during the pandemic. Age, autonomy, depression, and anxiety scores did not differ significantly between participants who had an increase in perceived ageism and those without. A greater increase in perceived ageism was observed in participants with higher education levels than in those with lower education; participants who found the curfews for the elderly inappropriate had a greater increase in perceived ageism than that in the other groups (Table 4).

DISCUSSION

To the best of our knowledge, this is the first study to examine how the physical and mental health of psychiatric patients aged 65 years and older was affected by curfews implemented for older people during the COVID-19 pandemic, and how perceived ageism affected the psychological state of these patients. Although the restriction measures were implemented to protect the elderly, the risk of negative consequences have been discussed by health professionals, rights defenders, the general public, and the media since the beginning of the pandemic. Although studies examining the effects of ageist attitudes on the elderly have been conducted during the pandemic, the perspectives and opinions of older adults on ageism have not been investigated. Moreover, older psychiatric patients who were more exposed and vulnerable to ageist attitudes have not been studied.

One-fourth of our sample was diagnosed with depression according to the GDS-SF scale, and approximately one-fifth of them were diagnosed with anxiety disorder according to the GAD-7 scale. Individuals with low education levels were found to have a higher rate of depressive symptoms, and individuals in this group were more likely to be affected by restrictions. Although income levels were not assessed in this study, low education levels are expected to be associated with low income, and

Table 3. Correlation analysis of perceived ageism with anxiety and depression scores

	Pearson's correlation analysis			
Variables	***M***	***SD***	***r* Value**	***p* Value**
GAD-7 total score	4.4037	4.47965	-.347*	0.001
GDS total score	3.4717	3.50192	-.308*	0.001

GAD-7: Generalized Anxiety Disorder Scale, GDS-SF: Geriatric Depression Scale-Short Form
M=mean, *SD*= standard deviaton, *r*= correlation coefficient; *p*= significance
*Correlation is significant at the 0.01 level (2-tailed).

Table 4. Change in perceived ageism during pandemic

		Not changed	Increased	*p* Value
n		107	57	-
Age Mean ± SD[a]		72.308±.595	71.175±.740	0.249
Gender[c]	Women	79(68.10%)	37(31.90%)	0.232
	Men	28(58.30%)	20(41.70%)	
Education[c]	Primary +Middle School	71(78.00%)	20(22.00%)	0.001*
	High School +University	35(48.60%)	37(51.40%)	
Thoughts on curfews[b]	"found appropriate"	67 (78.80%)	18 (21.20%)	0.001*
	"appropriate but insufficient"	18 (66.70%)	9(33.3%)	
	"found inappropriate"	21(41.2%)	30(58.80%)	
Autonomy[c]	No change	84(67.70%)	40(32.30%)	0.275
	Decreased	19(57.60%)	14(42.40%)	
GDS-SF Scores[a]		3.60±3.68	3.05±2.90	0.333
GAD-7 Scores[a]		4.29±4.63	4.33±3.71	0.953

GAD-7: Generalized Anxiety Disorder Scale, GDS-SF: Geriatric Depression Scale-Short Form

[a] = *Student t test,* [b] = *ANOVA ,* [c] = chi square test, ** $p < 0.05$*

low-education/low-income people might have limited resources for coping with sudden crises, which could explain the higher rates of depression.

Contrary to our expectations, anxiety and depression rates were not affected by marital status, conditions such as single-family living, or the presence of financial difficulties. The fact that most of the group was composed of individuals living in big cities and relatively similar in terms of socioeconomic and living conditions can explain this situation. By examining groups living in rural areas with different socio-economic and cultural life practices, more precise results can be obtained in this regard.

Most participants in the study reported decreased physical activity level, but depression and anxiety scores did not differ between the groups who reported decreased physical activity and those who did not. Many studies have reported that physical activity is protective in terms of mental health. In a study conducted in Norway during the COVID-19 period, the depression and anxiety levels of adults who were members of a regular activity group were found to be lower than the general population average (21). In the same article, it was also reported that physical activity had no effect on mental health during the pandemic period, which is consistent with our findings. In contrast, in our study, the anxiety scores of those who reported that their physical health was impaired during the pandemic were higher than those who did not report any deterioration in physical health. Physical activity and physical health are related but different concepts. Examining the relationship between physical health and physical activity levels can help us understand the effect of physical activity on mental health.

In our study, baseline perceived ageism was positively correlated with anxiety and depression scores. This finding is in accordance with previous studies reporting that older adults who perceive

ageism are likely to have a negative self-perception of aging and an increase in depressive symptoms (22). Depression and anxiety scores did not differ between participants who had increased perceived ageism during the pandemic and those who did not. This finding was contrary to our hypothesis that increased perceived ageism would be related to increased depression and anxiety scores; however, this might be due to the small sample size or the existence of other factors that might affect depression and anxiety scores during the COVID-19 pandemic, which we did not measure. Another reason for this finding could be the lower prevalence of baseline perceived ageism in our sample than in other populations (23).

Although 65% of our participants reported that the curfews negatively affected their mood, only 30% reported that they did not find these restrictions appropriate. Among the participants with a higher level of education, the rate of disapproval of the restrictions aimed at the older persons was found to be much higher. In addition, the perceived ageism scores increased during the pandemic in the group that disapproved of restrictions. These people may have associated the restrictions targeting the elderly with ageism, since highly educated people are more active and independent in their daily lives, and thus are more affected by the restrictions compared to the lower education group, who might have more family ties and social support in a traditional lifestyle and environment.

During the pandemic, protective measures including "social distancing" and stay-at-home" orders and curfews in some countries were implemented, but those measures caused negative consequences, especially for older adults. Individuals with psychiatric diseases are among the vulnerable groups in society (24), and older psychiatric patients constitute a more vulnerable group with the addition of physical and mental burden due to the advanced age (15). It is important for this group of patients to meet their daily needs, have opportunities for social interaction, and access to healthcare services. Older psychiatric patients could be expected to be affected more by the protective measures taken for the pandemic than the same age population with no psychiatric disorders, considering the possible adverse conditions they have, such as a restricted social environment, greater disease burden, and increased need for healthcare. While ordering restrictions and taking measures to prevent the spread of the epidemic, the needs of vulnerable groups in society should be prioritized. In Turkey, the Psychiatric Association of Turkey has informed the public about the psychological effects of the pandemic and restrictive measures since the first day of the pandemic and has made recommendations for many groups of society, including psychiatric patients. Recommendations have also been published for the most vulnerable groups, including people aged older than 65 years and their relatives (25). In addition to these protective measures and recommendations, state authorities, rights advocacy groups, and the media should also work on measures to decrease ageist attitudes towards older people.

Limitations

This study has some limitations. Due to limited access to outpatient services at the time of the study, all surveys were conducted using phone, and people with hearing loss and difficulties in understanding the questions were excluded from the study; therefore, a vulnerable group that is more likely to be adversely affected by social isolation and ageism was excluded from the study. The lack of pre-COVID-19 period scale scores and longitudinal evaluation may have created a bias since most of the participants had psychiatric diagnoses and were under psychiatric treatment at the time of the study, making it difficult to interpret the scale scores. Different psychiatric diagnoses might affect the coping mechanisms and reactions to the pandemic, however evaluating the effect of these diagnoses would

not be possible in a small sample. Likewise, only generalized anxiety symptoms were evaluated but a diagnostic evaluation was not performed including different anxiety disorders like panic disorder, agoraphobia or health anxiety disorder in this sample.

The distribution of the people participating in the study by socioeconomic groups is different from the country average; the higher socioeconomic groups are more represented among the participants; therefore, the results cannot be generalized to the entirety of older psychiatric patients. These limitations should be considered when evaluating the results of the present study.

CONCLUSION

The COVID-19 pandemic has seriously affected and continues to affect society in terms of physical and mental health, in both direct (effect of the disease) and indirect (owing to the restrictive measures taken to prevent its spread) ways. During the pandemic, the state and health authorities need to consider the needs of more vulnerable groups, such as older individuals and psychiatric patients, when making plans and implementing preventive strategies, and ensure that these groups are minimally affected by the disease, restrictive measures, and ageist attitudes.

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RESEARCH

NORMATIVE AND PSYCHOMETRIC PROPERTIES OF THE WHOQOL OLDER ADULTS MODULE (WHOQOL-OLD) IN THE NATIONAL REPOSITORY

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Abstract

Introduction: The main objectives of this study were to present population norms and the construct validity of the WHOQOL-OLD using classical and modern (Rasch) psychometric analyses.

Methods: This study was conducted on the pooled data of 29 studies, 16 of which were representative of the population (n=6951). The psychometric properties of the WHOQOL-OLD were evaluated with classical (confirmatory factor analysis and multivariate regression model) and probabilistic test theory (Rasch and DIF) analyses.

Results: The mean age of the Turkish WHOQOL-OLD data pool was 73.2±6.8. The mean overall scale score was 81.27±13.57 and the range of the mean dimension scores was between 12.34 (social participation) and 14.59 (intimacy). The elderly (advanced age) and women are more sensitive to the decrease in quality-of-life (QoL) scores. Both Cronbach's alpha values and item analyses indicated good internal consistency for all dimensions. Exploratory factor analyses (EFA) generated five factors instead of a six-factor original scale structure. "Past, present, and future activities" and "social participation" were combined in a single dimension in the EFA. Confirmatory factor analyses resulted in acceptable goodness of fit indices, such as Confirmation Fit Index (CFI)=0.951 and Root Mean Square Error of Approximation (RMSEA)=0.055. Turkish elders perceive the death and dying dimension as culturally closer to the culture of developing countries than developed Western cultures.

Conclusion:

Turkish older adults' QoL scores were more or less like those of other older adults in developing countries. This study's results confirm that the acceptable psychometric properties of the WHOQOL-OLD-TR with some items (items 9 and 20) need to be worked on further.

Keywords: Aged; Quality of Life; Surveys and Questionnaires; Turkey.

INTRODUCTION

Increasing rates of old age in all societies in recent years have necessitated not only objective indicators but also subjective measures such as quality of life (QoL) in order to manage the health problems and disability of the elderly. Therefore, QoL studies have been fascinating and functional for health professionals dealing with the health conditions and disabilities of the elderly. These studies help to understand and determine whether morbidity and disability in the elderly have an impact on their QoL, in order to determine which treatments are more effective, and increase life satisfaction for older adults.

It is vital that QoL instruments are valid and reliable. Additionally, it is important to ensure invariance between the validity and reliability results among the subgroups in the population. Psychometric analyses of large population samples are required to ensure the validity of the results of commonly used QoL measurement tools in the population. Data representing the population are useful not only for psychometric analysis but also for revealing the community norms of that instrument, and population norm of a QoL instrument is key to interpreting the differences between groups or individuals of different ages or genders living in the society.

The World Health Organization (WHO) developed, the older adult's module (WHOQOL-OLD) of the generic WHOQOL-BREF scale as a tool that evaluates the six elderly-specific dimensions of QoL through a multicenter and multicultural project (1). The WHOQOL-OLD was validated into Turkish on a small-scale study of older adults following the development of the instrument (2). Although various cultural validity studies of the WHOQOL-OLD have been published (3,4), the population norms of the WHOQOL-OLD scale have not yet been published in any country.

The main objectives of this study were to investigate the construct validity of the WHOQOL-OLD using classical psychometric analyses and the Rasch model and to provide normative data for the Turkish WHOQOL-OLD national data pool.

MATERIALS AND METHODS

The authors -who have assisted Turkish researchers about the use and scoring of the WHOQOL-OLD module since 2008 - have obtained permission from researchers using the WHOQOL-OLD data they collected in their studies, to test the reliability and validity of the module in a larger sample and to use the scale in order to generate population norms. In this study, data (n=6951) from 29 researchers who allowed their data to be included in the national WHOQOL-OLD data pool between 2008 and 2022 were used. The studies that contributed to the data pool were evaluated in three different groups: 1) samples that are representative of the community, 2) samples obtained from nursing homes, and 3) clinical studies. Only the data of the studies representing the population of concern were used in the population norm analyses, whereas the entire data pool was used in the psychometric (reliability-validity) analyses.

WHOQOL-OLD

The WHOQOL-OLD module consists of 24 Likert scale items and six dimensions: "sensory abilities" (SAB), "autonomy" (AUT), "past, present, and future activities" (PPF), "social participation" (SOP), "death and dying" (DAD), and "intimacy" (INT). Each of the dimensions has four items, and the score range of possible values for all dimensions is between 4 and 20 (see Table 1). All 24 single items of the WHOQOL-OLD module can be combined to produce a general (overall) score for QoL in older adults. Higher scores represent higher QoL.

Statistical Analyses

Population norms are presented for the mean dimension scores and distribution properties by

age and gender. Psychometric analyses were conducted based on classical psychometric theory and Rasch analyses using both exploratory and confirmatorly approaches. Scale distribution analyses were presented using floor-ceiling effects, skewness, and kurtosis. Item analyses and internal consistency (by Cronbach's alpha value) of each of the dimensions were evaluated to explore any problematic items and the reliability of the structure of each of the six dimensions of the WHOQOL-OLD module. An alpha value ≥ 0.70 indicates acceptable internal consistency of the dimension. Both item-dimension correlation coefficients smaller than 0.35 and alpha values greater than the overall alpha value of the dimension when the item is removed may indicate to a problematic item.

Construct validity was assessed by exploratory factor analysis (EFA), confirmatory factor analysis (CFA), convergent validty and known groups validity analyses. Principal component analyses using the Varimax rotation method were employed in EFA. Kaiser-Meyer Olkin (KMO) values greater than 0.5 confirm the sample size adequacy, and Eigen values greater than 1.0 indicate the factor formation in the EFA. Fit indices such as the Confirmatory Fit Index (CFI), Normed Fit Index (NFI), Root Mean Square Error of Approximation (RMSEA), and chi-square/SD that were generated in CFA were used for the structural properties of the Turkish version compared to the original scale construct. CFI ≥ 0.90 and RMSEA ≤ 0.8 shows acceptable agreement between the original scale structure and the Turkish WHOQOL-OLD scale structure (5). Known groups validity is an approach that shows the difference in scores according to variables whose effects on scale scores are known before. Age, gender, and health condition (ill-well) were used in the known groups validity analyses by Student's t test and Cohen's effect size values.

In item analysis, item difficulty and discrimination of the scale were examined. Items were scored between 0 and 4. The difficulty and discrimination values of the items were calculated in the range of 0–1. When the difficulty value obtained is above 0.5, the response to the item (QoL) increases. In a test in which the correct answer is accompanied by distractors, item discrimination is expected to be in the range of 0.3–0.7. (Strandardized Mean Difference -SMD) (6).

In terms of item difficulty, values close to zero indicate moderate, negative values indicate that they agree with the situation expressed in the relevant item, and positive values indicate that respondents agree with the situation in the related item in a decreasing direction. Infit (weigted mean square [WMS]) and outfit (unweigted mean square [UMS]) values were examined to evaluate scale item fit. Infit shows harmony with the variation of the distribution in the item, while outfit shows the effect of the outlier values. It is desirable that these values be in the range of 0.8 to 1.2 (around 1 value) (6). Another criterion for scale compatibility in Rasch analysis is the person separation index (PSI). The PSI is a measure of how different respondents give different answers from each other. A PSI value above 1.5 refers to a sufficient fit, above 2 is good, and above 3 indicates an excellent fit (7,8). For the item separation index, it is required to be above 1.5 in the analysis at the individual level and above 2.5 in the analysis of the groups (9).

DIF analysis was used in this study to determine the bias of items for gender, age, and educational status. In the DIF analysis, Cochran Mantel Haenszel (CMH) statistics for statistical decision, Effect Size (ES) for delta statistics and sP-DIF classification were made. According to this classification, it was decided whether the items showed DIF feature or not. The CMH procedure tests for statistical significance, and like other hypothesis tests, it is influenced by sample size. Therefore, it is necessary to incorporate practical significance into the identification of DIF in polytomous items such as Likert type items. We used CMH, ES and sP-DIF. Polytomous items have a similar classification scheme, but it only involves a

consideration of practical significance. The rules follow the recommendations for the sP-DIF statistic by dividing the Strandardized Mean Difference (SMD) by the item score range. This change to the SMD limits it to values between 0 and 1. Refer to this new value of the SMD as sP-DIF. According to Dorans et al., the rules are as follows: AA" items have an sP-DIF value strictly less than 0.05; "BB" items are neither "AA" nor "CC" items; "CC" items have an sP-DIF statistic that is 0.10 or larger (10).

SPSS v. 23 was used in conventinal statistics and Exploratory Factor Analyses, JASP (Version 0.16.3 in CFA and Jmetrik for Polytomus Rasch Analysis 4.1.1. version (11) was used. Maximum type 1 error is accepted as 0.05 in all hypothesis testing analyses.

RESULTS

This research was conducted on the WHOQOL-OLD national data repository (pool), which consisted of the data of 29 different studies conducted between 2008–2021 (*see Supp. Table 1*). Sixteen of these studies were population-based studies (n=5156). In this paper, the normative findings of the WHOQOL-OLD module were created by analyzing the data from population-based studies, while the validity and reliability results were produced over the entire data pool (n=6951).

All data of the WHOQOL-OLD revealed that the mean age of the data pool was 73.2±6.8; 51.2 % was female; 27.0% had no school diploma and 39.2% were primary school graduates; 56.8% were retired; 91.8% had social security and 75.7% were ill (*see Supp. Table 2*).

Standardized scores for the six dimensions of the WHOQOL-OLD by age group and gender are presented in Table 1. The mean WHOQOL-OLD overall score was 81.27±13.57, and the range of the mean dimension scores were between 12.34 (social participation) and 14.59 (intimacy). The range of the mean overall WHOQOL-OLD scores was between 10.86 (social participation) and 14.59 (intimacy) in women and 10.87 (social participation) and 15.21 (death and dying) in men. The mean overall scale score range was between 77.89 (age group 80-84) and 79.91 (age group 70-74) in women and 79.44 (age 90+) and 83.20 (age group 70-74) in men. As age increases, women are more sensitive than men to decreasing QoL scores.

Psychometric analyses of the WHOQOL-OLD national data pool consist of distribution characteristics, item analyses, reliability, and validity analyses. The distribution properties, item analyses, and the internal consistency of the dimensions are presented in Table 2. Floor and ceiling effects were within acceptable limits for all dimensions except for the death and dying dimension, which had a borderline ceiling effect (16.1%), if we consider the upper acceptable limit as 15.0% for ceiling effect. On the other hand, skewness, and kurtosis values were all within acceptable limits for all the dimensions.

Alpha values of the WHOQOL-OLD dimensions were all over 0.70, indicating good internal consistency. Items 9, 14, 20, and 21, which have limited contribution to internal consistency (those items whose alpha value calculated by their removal was higher than the total alpha value of the dimension they belong to), were all associated with a correlation coefficient higher than 0.35 with the dimension score to which they belong. Construct validity of the WHQOL-OLD-TR was evaluated by factorial validity, convergent validity, and known groups validity analyses.

Exploratory factor analyses generated five factors instead of a six-factor original scale structure. Past, present, and future activities and social participation dimensions were united under the same dimension. The remaining items were all distributed under their original dimensions (*see Supp. Table 3*).

The Fit Indices of the five factor structure that emerged in the exploratory factor analyses are as follows: CFI=0.94, NFI=0.94, RMSEA=0.062, on the other hand, the CFA of the original six-dimension structure showed acceptable goodness of fit indi-

Table 1. Standardized scores for the six domains of the WHOQOL-OLD Turkish data pool. by age groups and gender (n=5156)*

		WOMEN						MEN						Overall sample
Domain	Age groups	65-69 n:1123	70-74 n:613	75-79 n:479	80-84 n:245	85-89 n:114	>90 n:44	65-69 n:918	70-74 n:591	75-79 n:447	80-84 n:312	85-89 n:118	>90 n:32	n:5156
Sensory Abilities	Mean score	13.46	13.43	13.53	12.93	13.03	13.14	13.63	13.79	13.73	13.61	13.25	13.19	13.56
	SD	2.80	2.77	2.78	2.90	2.70	2.90	3.00	2.85	2.80	2.97	3.01	2.44	2.85
	Floor (%)	0.4	0.3	0.2	0.4	1.8	4.5	0.4	0.5	0.2	0.6	0.8	3.1	0.3
	Ceiling (%)	0.2	0.2	0.4	1.2	1.8	4.5	0.7	1.0	0.4	0.6	0.8	6.3	0.4
	Skewness	-0.535	-0.324	-0.114	-0.074	-0.183	0.020	-600	-0.543	-0.392	-0.353	-0.249	-0.232	-0.431
	Kurtosis	0.102	-0.420	-0.806	-0.409	-0.925	-1.134	-0.061	-0.035	-0.436	-0.530	-0.846	-0.984	-0.264
Autonomy	Mean score	13.36	13.21	13.00	12.83	12.60	12.48	14.23	14.07	13.70	13.34	13.64	13.44	13.58
	SD	3.16	3.31	3.29	3.37	3.29	3.79	2.86	3.11	3.05	3.06	3.14	3.38	3.18
	Floor (%)	0.4	0.7	0.4	1.2	1.8	4.5	0.1	0.3	0.2	0.3	1.7	3.1	0.3
	Ceiling (%)	1.5	2.1	1.3	2.9	2.6	4.5	2.7	4.4	3.4	1.9	4.2	6.3	2.7
	Skewness	-0.089	-0.125	-0.148	0.076	0.135	0.200	-0.084	-0.230	-0.095	0.029	0.137	0.233	-0.129
	Kurtosis	-0.275	-0.346	-0.434	-0.518	-0.271	-0.781	-0.293	0.062	-0.212	-0.133	-0.075	-0.159	-0.273
Past, Present and Future Activities	Mean score	13.01	12.90	13.06	12.65	13.02	13.00	13.73	13.47	13.44	12.88	13.45	12.59	13.26
	SD	3.15	3.41	3.32	3.45	3.62	3.97	2.83	3.33	3.22	3.22	3.26	3.27	3.23
	Floor (%)	0.4	0.5	0.4	0.4	0.9	2.3	0.7	0.8	0.2	0.6	0.8	3.1	0.4
	Ceiling (%)	2.0	2.1	2.5	1.6	3.5	6.8	2.4	2.9	2.0	1.6	3.4	3.1	2.3
	Skewness	-0.200	-0.179	-0.176	-0.051	-0.012	-0.189	-0.123	-0.272	-0.217	-0.145	-0.072	-0.091	-0.213
	Kurtosis	-0.131	-0.365	-0.365	-0.415	-0.632	-0.548	-0.289	-0.171	-0.355	-0.373	-0.382	0.351	-0.258
Social Participation	Mean score	12.60	12.30	12.08	11.39	11.17	10.86	12.93	12.48	12.32	11.46	11.58	10.87	12.34
	SD	3.15	3.38	3.49	3.38	3.61	3.83	3.01	3.27	3.31	3.16	3.31	3.18	3.29
	Floor (%)	0.3	1.0	1.7	1.6	0.9	4.5	0.3	0.8	1.1	1.3	4.2	3.1	0.9
	Ceiling (%)	2.0	1.6	1.5	0.4	0.9	2.3	1.5	1.5	2.0	0.6	0.8	3.1	1.5
	Skewness	0.045	-0.123	-0.034	0.091	0.112	0.086	-0.165	-0.130	-0.018	0.094	-0.175	0.231	-0.072
	Kurtosis	-0.265	-0.372	-0.466	-0.680	-0.653	-0.545	-0.097	-0.103	-0.195	-0.254	-0.167	0.323	-0.296
Death and Dying	Mean score	12.59	13.81	13.64	13.95	14.02	14.43	13.89	14.45	14.73	15.21	15.14	15.06	13.92
	SD	4.90	4.67	4.90	4.73	4.66	5.22	4.84	4.83	4.50	4.55	4.45	4.09	4.86
	Floor (%)	9.7	4.6	6.5	4.9	4.4	11.4	5.3	5.1	2.9	2.9	3.4	6.3	5.8
	Ceiling (%)	11.0	16.0	17.3	15.1	16.7	18.2	17.5	20.8	19.5	23.4	21.2	15.6	18.0
	Skewness	-0.158	-0.365	-0.352	-0.480	-0.397	-0.753	-0.411	-0.605	-0.602	-0.768	-0.798	-0.925	-0.428
	Kurtosis	-1.040	-0.940	-0.979	-0.809	-0.859	-0.515	-0.931	-0.772	-0.697	-0.541	-0.299	-0.054	-0.933
Intimacy	Mean score	14.50	14.25	14.45	14.13	14.59	14.41	14.73	14.93	14.53	14.20	14.61	14.28	14.59
	SD	3.34	3.52	3.49	3.49	3.50	3.80	3.00	3.27	3.33	3.01	3.05	4.27	3.33
	Floor (%)	0.6	0.8	0.4	0.8	1.8	2.3	0.4	0.3	0.4	0.3	0.8	6.3	0.5
	Ceiling (%)	8.9	8.6	12.7	6.5	10.5	6.8	8.5	13.5	8.3	5.4	7.6	15.6	10.0
	Skewness	-0.424	-0.358	-0.144	-0.476	-0.522	-0.541	-0.445	-0.368	-0.436	-0.256	-0.404	-0.630	-0.395
	Kurtosis	-0.127	-0.327	-0.549	-0.184	-0.230	-0.240	0.397	-0.125	-0.176	-0.241	0.039	-0.194	-0.142
Overall	Mean score	79.50	79.91	79.76	77.89	78.42	78.32	83.14	83.20	82.45	80.72	81.69	79.44	81.27
	SD	13.30	14.34	14.34	14.62	14.61	16.06	12.28	13.33	12.86	12.00	13.41	11.50	13.57
	Floor (%)	0.1	0.2	0.2	0.4	0.9	2.3	0.1	0.2	0.2	0.3	0.8	3.1	0.00
	Ceiling (%)	0.1	0.3	0.2	0.4	0.9	2.3	0.1	0.2	0.4	0.3	0.8	3.1	0.00
	Skewness	-0.082	-0.047	-0.026	-0.074	0.044	0.134	0.026	-0.164	0.155	0.007	-0.118	0.229	-0.073
	Kurtosis	-0.181	-0.452	-0.218	-0.324	-0.706	-1.022	-0.463	0.231	-0.343	0.063	-0.304	-0.442	-0.239
	Min.	40.00	36.00	35.00	40.00	47.00	25.00	52.00	37.00	51.00	45.00	44.00	58.00	35.00
	Percentiles													
	10	63.00	61.00	61.00	58.00	58.50	57.00	67.00	67.00	66.00	66.00	63.90	63.30	64.00
	20	69.00	67.00	68.00	65.00	65.00	62.00	72.00	72.40	71.00	70.00	71.00	68.20	70.00
	30	72.00	72.00	72.00	70.80	70.50	68.50	76.00	76.00	75.00	74.90	74.00	73.90	74.00
	40	77.00	76.00	75.00	74.00	74.00	72.00	79.00	80.00	79.00	78.00	78.60	76.00	78.00
	50	80.00	80.00	80.00	78.00	78.00	76.00	83.00	83.00	82.00	81.00	82.00	79.00	81.00
	60	83.00	84.00	84.00	82.00	84.00	83.00	86.00	87.00	85.00	83.00	84.00	81.80	85.00
	70	87.00	88.00	87.00	86.00	86.50	90.50	90.00	90.00	89.00	87.00	89.30	86.00	89.00
	80	91.00	92.00	92.00	91.00	92.00	94.00	94.00	94.00	93.00	91.00	93.20	89.60	93.00
	90	97.00	99.00	99.00	96.40	98.00	101.50	99.00	101.00	99.20	96.00	101.10	95.70	99.00
	Max.	113.00	114.00	117.00	114.00	110.00	110.00	119.00	120.00	116.00	115.00	110.00	104.00	120.00

*Population representative data

Table 2. Item analyses and internail consistency of the WHOQOL-OLD-TR (n= 6951)*

Domain	Mean (SD)	Floor (%)	Ceiling (%)	Skewness	Kurtosis	Cronbach's alpha (CI 95%)	Correlation coeffi-cients / (Corrected Item-Total Correlation)	If Item Deleted Cronbach's Alpha values
Sensory Abilities	14.04 (3.96)	0.8	7.6	-0.279	-0.776	0.898 (0.894-0.902)	-	-
	Item 1 (Impairments to senses)						0.845	0.841
	Item 2 (Loss of sensory abilities)						0.852	0.838
	Item 10 (Problems with sensory functioning)						0.788	0.863
	Item 20 (Rate sensory functioning)						0.616	0.921
Autonomy	13.54 (3.24)	0.2	2.5	-0.143	-0.258	0.744 (0.734-0.754)	-	-
	Item 3 (Freedom to make own decisions)						0.600	0.651
	Item 4 (Feel in control of your future)						0.543	0.683
	Item 5 (People around you are respectful of your freedom)						0.534	0.688
	Item 11 (Able to do things you'd like)						0.477	0.719
Past, Present and Future Activities	13.28 (3.24)	0.4	2.2	-0.262	-0.239	0.815 (0.807-0.821)	-	-
	Item 12 (Satisfied with opportunities to continue achieving)						0.672	0.747
	Item 13 (Received the recognition you deserve in life)						0.632	0.767
	Item 15 (Satisfied with what you've achieved in life)						0.671	0.748
	Item 19 (Happy with things to look forward to)						0.561	0.801
Social Participa-tion	12.35 (3.32)	1.0	1.4	-0.131	-0.334	0.800 (0.793-0.808)	-	-
	Item 14 (Have enough to do each day)						0.473	0.816
	Item 16 (Satisfied with the way you use your time)						0.693	0.714
	Item 17 (Satisfied with level of activity)						0.738	0.688
	Item 18 (Satisfied with opportunity to participate in community)						0.572	0.773
Death and Dying	13.98 (4.62)	4.7	16.1	-0.448	-0.786	0.890 (0.875-0.884)	-	-
	Item 6 (Concerned about the way you will die)						0.815	0.818
	Item 7 (Afraid of not being able to control death)						0.843	0.806
	Item 8 (Scared of dying)						0.813	0.817
	Item 9 (Fear pain before death)						0.521	0.931
İntimacy	14.49 (3.34)	-0.403	-0.099	0.5	9.3	0.898 (0.89-0.90)	-	-
	Item 21 (Feel a sense of companionship in life)						0.746	0.914
	Item 22 (Experience love in your life)						0.837	0.881
	Item 23 (Opportunities to love)						0.826	0.885
	Item 24 (Opportunities to be loved)						0.827	0.885
Overall	81.71 (14.57)	0.0	0.0	-0.139	-0.233	-	-	-

*overall data pool

Table 3. Correlation matrix (convergence) among the domains of the WHOQOL-OLD.

	Total Score	Sensory Abilities	Autonomy	Past, Present and Future Activities	Social Participation	Death and Dying	İntimacy
Total Score	1.000						
Sensory Abilities	0.643	1.000					
Autonomy	0.725	0.323	1.000				
Past, Present and Future Activities	0.810	0.340	0.667	1.000			
Social Participation	0.747	0.343	0.575	0.716	1.000		
Death and Dying	0.482	0.252	0.080	0.141	0.069	1.000	
İntimacy	0.726	0.299	0.513	0.629	0.528	0.142	1.000

ces such as CFI=0.95, NFI=0.96, and RMSEA=0.055 for the comparison of the WHOQOL-Old-TR and the original scale structure (Supp. Figure 1).

Convergence of the dimensions among each other is presented in table 3. Past, Present and Future Activities, Autonomy, Social Participation and intimacy dimensions show high convergence among themselves whreas Sensory Abilities and Death and Dying dimensions did not any significantly.

Known groups' validity analyses tested the effect of age, gender, and health condition of the respondents. The greatest Cohen's effect size figure was obtained in the social participation dimension for age in favor of the younger age group. In death and dying and autonomy dimensions for gender in favor of men, and in the social participation dimension for health condition in favor of "well" respondents. Past, present, and future activities and intimacy dimensions were not statistically sensitive to age; intimacy was not statistically sensitive to gender; and autonomy was not statistically sensitive to health status as a result of the Known Groups Analyses ($p<0.001$) (table 4).

Differential item functioning analyses and Rasch analysis are presented in Table 5. According to the item analyses, the item difficulty values ranged from 0.48 to 0.68. The discrimination values of the items were between 0.49 and 0.90. For all items, both item difficulties and discrimination were at stable levels. The range of item reliability values were 0.98–0.99, and person reliability values were between 0.77–0.87 for all dimensions. Item discrimination index scores were between 8.70–28.73, and person discrimination index scores were in the range of 1.84–2.63. Person reliability was 0.91, and item reliability was 0.99 as the goodness of fit reliability criterion for the entire scale in Rasch analyses. The PSI was 3.18 and the item separation index was 22.50. On the other hand, infit values were between 0.61 and 1.70, and outfit values were between 0.58 and 1.82 (table 5).

When the results of DIF analysis and MH chi-square analysis were evaluated together in terms of classification, it was understood that the items did not have DIF in terms of gender, age, and educational status: sP-DIF value strictly less than 0.05 indication no DIF for all of the items of the WHO-QOL-OLD (table 5). Item characteristic curves (ICC) are presented in Supplementary Figure 2. The distribution of the responses of the intimacy scale revealed fewer than five descriptors for all items (Supp. Figure 2).

Table 4. Known Groups Validity

	Age			Gender			Health Condition		
	65-74 (n:4215)	75 and over (n:2736)	ES * (%)	Women (n:3496)	Men (n:3335)	ES * (%)	Well (n:1304)	Ill (n:4059)	ES * (%)
	Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)	
Sensory Abilities	14.3(3.9)***	13.6(4.0)***	17.2	13.8(4.0)**	14.1(3.9)**	7.8	14.4(3.8)***	13.7(4.0)***	18.2
Autonomy	13.7(3.1)***	13.3(3.2)***	11.2	13.2(3.2)***	13.8(3.0)***	21.5	13.5(3.0)	13.3(3.1)	-
Past, Present and Future Activities	13.3(3.2)	13.2(3.3)	-	13.0(3.3)***	13.5(3.1)***	13.3	13.3(3.2)***	12.9(3.2)***	13.6
Social Participation	12.7(3.2)***	11.8(3.4)***	24.7	12.2(3.4)**	12.4(3.2)**	5.1	12.6(3.2)***	12.0(3.3)***	16.6
Death and Dying	13.6(4.7)***	14.5(4.5)***	18.8	13.4(4.7)***	14.4(4.5)***	22.5	14.4(4.4)***	13.8(4.8)***	11.5
İntimacy	14.5(3.3)	14.4(3.4)	-	14.4(3.4)	14.5(3.2)	-	14.5(3.1)**	14.3(3.4)**	6.0
Total Score	82.2(14.3)**	80.9(14.9)**	8.6	80.1(15.0)***	82.8(13.8)***	18.8	82.7(13.1)***	80.1(14.9)***	18.1

* Cohen's d (as an effect size method) is defined as the difference between two means divided by a standard deviation for the data. Effects size 0.2 refers to a weak effect; 0.5 to moderate effect; 0.8 refers to good effect and values above 1.0 refers to very satisfactory effect.
**p<0.05, ***p<0.001

DISCUSSION

Although some articles have been published about the norm values of the WHOQOL in the literature, as far as we know, no article has been published on the norm values of WHOQOL-OLD, which was developed as the older adults' module of the WHOQOL-Bref in any community or country. For this reason, the only option was to compare the norm value we produced in this study with the data of population-based studies using the WHOQOL-OLD module for different purposes in the literature. In all dimensions, higher dimension scores were obtained in males than females in all age groups except aged 90 years and older. The social participation dimension score decreased after the age of 80 for both men and women, while the autonomy dimension score dropped significantly after the age of 85 only for women.

The dimension scores obtained in this study were like the scores of the WHOQOL-OLD Turkish validation study (2) and were lower than the scores obtained in developed societies (12-14), whereas closer dimension scores were obtained with the other developing countries such as India, Iran, Brazil, and Mexico (15-18). When we compared the dimension scores obtained from this study with the findings of the multicenter international development study published by Power et al. (1), the mean dimension scores we obtained were lower than the scores obtained from the international study in all dimensions except the intimacy dimension, which is about the same as in the development study. The highest dimension score was the intimacy dimension score, which was close to or higher than that obtained in different cultures as well (12,13,16, 19-21). During the development of WHOQOL-OLD, it is noteworthy that the death and dying dimension score, which is sensitive to different cultures, was lower than most Western cultures but higher than that of Eastern cultures (16,22,23,15). Previous studies have shown that, death is perceived differently in Eastern and Western societies (24). In this respect, the fact that our death and dying dimension score was between Western and Eastern societies is consistent with Turkey's geographical and cultur-

Table 5. WHOQOL-OLD Rasch & Differential Item Functioning Analysis

Dimentions	Item Numbers	Item Analysis		Rasch Analysis in Dimentions					DIF Analyses								
									Sex (male-female)			Age (65to74-75to94)			Education(graduated*-not)		
		Item difficulty (0-1)	Discrimination (0-1)	Difficulty by dimentions	Infit	Outfit	Item - Person Reliability	Item – Person Separation Index	χ^2	E.S.[95% CI]	Class	χ^2	E.S.[95% CI]	Class	χ^2	E.S.[95% CI]	Class
Sensory Abilities	Q1	0.65	0.89	-0.30	0.69	0.65	0.99 - 0.87	28.73 – 2.63	7.49[b]	0.03(0.01, 0.05)	AA	11.68[b]	0.04(0.02, 0.06)	AA	3.28[a]	0.02(-0.00, 0.05)	AA
	Q2	0.65	0.90	-0.31	0.65	0.58			0.32[a]	-0.01(-0.03, 0.02)	AA	5.33[b]	0.03(0.00, 0.05)	AA	1.40[a]	-0.01(-0.04, 0.01)	AA
	Q10	0.67	0.84	-0.49	0.93	0.85			0.70[a]	0.01(-0.01, 0.04)	AA	1.32[a]	0.01(-0.01, 0.04)	AA	7.65[b]	-0.04(-0.07, -0.01)	AA
	Q20	0.54	0.64	1.10	1.70	1.82			5.20[b]	-0.04(-0.07, -0.01)	AA	25.48[b]	-0.08(-0.11, -0.05)	AA	3.56[a]	0.03(-0.00, 0.07)	AA
Autonomy	Q3	0.68	0.63	-0.51	0.84	0.81	0.99 – 0.77	21.22 – 1.84	17.21[b]	0.06(0.03, 0.09)	AA	11.82[b]	0.05(0.02, 0.08)	AA	3.18	0.03(-0.00, 0.07)	AA
	Q4	0.52	0.56	0.44	1.01	1.02			0.07[a]	0.01(-0.03, 0.04)	AA	4.95[b]	-0.04(-0.07, -0.01)	AA	0.03	0.00(-0.03, 0.04)	AA
	Q5	0.64	0.56	-0.19	1.00	0.99			10.91[b]	-0.05(-0.09, -0.02)	AA	1.94[a]	0.02(-0.01, 0.06)	AA	0.50	0.02(-0.03, 0.06)	AA
	Q11	0.55	0,49	0.25	1.16	1.18			0.45[a]	-0.01(-0.05, 0.02)	AA	4.85[b]	-0.04(-0.08, -0.01)	AA	5.96	-0.05(-0.10, -0.01)	AA
Past, Present and Future Activities	Q12	0.56	0.70	0.16	0.90	0.90	0.99 – 0.83	17.76 – 2.20	6.80[b]	0.04(0.01, 0.07)	AA	0.61[a]	0.01(-0.02, 0.04)	AA	3.80	-0.03(-0.06, 0.01)	AA
	Q13	0.62	0.66	-0.35	0.99	0.98			10.04[b]	-0.04(-0.07, -0.02)	AA	15.71[b]	0.06(0.03, 0.09)	AA	0.36	-0.02(-0.05, 0.02)	AA
	Q15	0.62	0.70	-0.31	0.89	0.88			1.94[a]	0.02(-0.01, 0.05)	AA	6.52[b]	0.03(0.01, 0.06)	AA	7.76	0.05(0.02, 0.08)	AA
	Q19	0.52	0.58	-0.50	1.22	1.24			0.41[a]	-0.01(-0.04, 0.02)	AA	39.58[b]	-0.10(-0.14, -0.07)	AA	0.03	-0.00(-0.04, 0.03)	AA
Social Participation	Q14	0.48	0.49	0.30	1.39	1.40	0.99 – 0.81	13.76 – 2.13	71.69[b]	-0.16(-0.19, -0.12)	AA	71.82[b]	-0.16(-0.20, -0.12)	AA	0.01	-0.00(-0.04, 0.04)	AA
	Q16	0.57	0.72	-0.36	0.80	0.80			19.31[b]	0.06(0.03, 0.08)	AA	30.94[b]	0.08(0.05, 0.10)	AA	7.42	-0.04(-0.07, -0.01)	AA
	Q17	0.54	0.77	-0.13	0.69	0.69			1.99[a]	0.02(-0.01, 0.04)	AA	33.66[b]	0.07(0.05, 0.10)	AA	0.00	-0.00(-0.03, 0.03)	AA
	Q18	0.50	0.59	0.18	1.11	1.12			20.18[b]	0.08(0.04, 0.11)	AA	0.11[a]	0.11(-0.03, 0.04)	AA	4.19	0.04(0.00, 0.08)	AA
Death and Dying	Q6	0.65	0.87	-0.19	0.75	0.76	0.99 – 0.79	26.53 – 1.93	0.27[a]	-0.01(-0.03, 0.02)	AA	0.12[a]	-0.00(-0.03, 0.02)	AA	3.33	-0.03(-0.06, 0.00)	AA
	Q7	0.67	0.91	-0.29	0.61	0.60			5.82[b]	-0.03(-0.05, -0.01)	AA	0.42[a]	-0.01(-0.03, 0.01)	AA	0.26	-0.01(-0.04, 0.02)	AA
	Q8	0.68	0.89	-0.33	0.69	0.67			0.00[a]	-0.00(-0.03, 0.03)	AA	2.18[a]	0.02(-0.01, 0.04)	AA	4.53	0.03(0.00, 0.07)	AA
	Q9	0.50	0.55	0.81	1.88	1.82			3.18[a]	0.04(-0.00, 0.08)	AA	0.12[a]	-0.00(-0.05, 0.04)	AA	0.01	0.00(-0.05, 0.05)	AA
İntimacy	Q21	0.63	0.79	0.40	1.35	1.24	0.98 – 0.86	8.70 – 2.57	31.30[b]	0.06(0.04, 0.09)	AA	14.43[b]	-0.04(-0.07, -0.02)	AA	14.48	-0.05(-0.08, -0.03)	AA
	Q22	0.66	0.89	-0.04	0.84	0.74			1.57[a]	0.01(-0.01, 0.03)	AA	0.06[a]	0.00(-0.02, 0.02)	AA	4.14	-0.02(-0.05, -0.00)	AA
	Q23	0.67	0.88	-0.30	0.88	0.78			9.04[b]	-0.03(-0.05, -0.01)	AA	4.78[b]	0.02(0.00, 0.04)	AA	15.49	0.05(0.02, 0.07)	AA
	Q24	0.66	0.88	-0.06	0.90	0.80			24.98[b]	-0.05(-0.07, -0.03)	AA	5.19[b]	0.02(0.00, 0.04)	AA	7.70	0.03(0.01, 0.06)	AA

***at least primary school graduate** **Item Reliability**=0.99 **Person Reliability**=0.91 **Item Separation Index**=22.50 **Person Separation Index**=3.18

a: p>0,05 b: p<0,05 E.S.[95% CI]: Effect Size [95% Confidence Interval] Class: DIF analysis classification, AA: No-DIF

al characteristics as a transitional culture between East and West. As a matter of fact, the absence of any item from the death and dying dimension in the short version (WHOQOL-AGE), in which the WHOQOL-OLD and the main scale WHOQOL-BREF were combined, indicates that this dimension differs at the global level (25).

Considering the distribution characteristics of the WHOQOL-OLD dimension scores and the total scale score, floor and ceiling effects were within acceptable limits in all dimensions, except for the death and dying dimension. The death and dying dimension showed a 16% ceiling effect, which is slightly above the acceptable upper limit of 15%. The distribution of all dimensions of the scale conforms to the normal distribution in the context of skewness (<1.0) and kurtosis (close to 0.0). The alpha values indicating the internal consistency of the WHOQOL-OLD dimensions were between 0.74–0.90, which is quite satisfactory in agreement with many previous studies using the WHOQOL-OLD module (2,12,1,22,26). When the "if item deleted alpha values" were evaluated, the 20th item in the sensory abilities dimension, the 14th item in the social participation dimension, the 9th item in the death and dying dimension, and the 21st item in the intimacy dimension negatively affected internal consistency of the dimensions they were in. However, the correlations of these potentially problematic items (based on the results of alpha analyses) with the dimension scores they belonged to, were in the range of 0.47–0.75, which is quite satisfactory. According to the Turkish national WHOQOL-OLD data pool analysis, some items (i.e., items 9 and 20) that seemed to be potentially problematic were also found to be problematic items as a result of the analysis of Turkey data in the development phase of the scale (2). Similar results were obtained for items 9 and 20 in the Rash analyses, which gave infit and outfit values far from 1.0 (1.88/1.82 for Q9; 1.70/1.82 for Q20, respectively, for infit and outfit values presented in Table 5). These two items were sound in terms of the infit values in the German WHOQOL-OLD validation study (26).

Classical construct validity analyses consisted of factor analyses, convergent-divergent analyses and known groups validity analyses. According to the results of the correlation matrix of the dimensions, the highest correlated dimension with the overall scale score was the past present and future activities dimension, which was reported as a key facet of QoL with strong interconnections to other QoL facets by Brinkhof et al (13). The past, present, and future activities dimension gave high collinearity (VIF value was higher than 2.0) with other dimensions in the linear regression analysis (not presented here), and the items of this dimension combined with the items of the social participation dimension to form a single dimension in the explanatory factor analysis. This makes one think that the activities of the past, present, and future are close to social participation by older Turkish adults. On the other hand, the pooled data of the Turkish version of WHOQOL-OLD showed that the Turkish version fits with the original scale structure (CFI and NFI> 0.90 and RMSEA <0.08) very well.

All of the dimensions of the WHOQOL-OLD could discriminate between younger and older age, male and female, and ill and well significantly except for the intimacy dimension, which was only sensitive to the health condition of the participant. The intimacy dimension score was higher than all other dimension scores, and it seems that older Turkish adults have been homogeneously distributed in society in terms of intimacy. The effect size values indicated that while the age of the person mostly affects the social participation and death and dying dimensions, the gender of the older adult highly affects autonomy and death and dying dimensions. Overall scale scores were significantly lower in females than in males, and lower in ill older adults than those are well.

It is an expected situation that has been shown in the literature that women have lower QoL scores

than men, the poor than the wealthy, and the ill than well (27). Hence, the disadvantaged situation of women compared to men in terms of the autonomy and death and dying dimension scores was very striking in this study.

When the results of the item analysis were examined, the item difficulty values were between 0.48 and 0.68, and the item discrimination values of the items were between 0.49 and 0.90, indicating acceptable values (all between 0.0–1.0) for all of the items. The distribution of item reliability values was between 0.98–0.99, and the distribution of person reliability values was between 0.77–0.87. Thus, both the PSI and the item separation index exhibited a sufficient discrimination. The item difficulty values were distributed close to zero for each item which indicates that all items had moderate difficulty values. On the other hand, the distribution of infit and outfit values were around 1.0, except for items 9 and 20, which were the potential problematic items of the WHOQOL-OLD-TR as mentioned above.

In the DIF analysis of each item for gender, age, and educational status, MH chi-square values were found to be nonsignificant in some items and significant in others, while the effect sizes calculated for these were found to be at low levels. For statistical significance in DIF analysis, ES (95%CI) was used and sP-DIF classification were made for delta statistics because chi-square statistics is affected by big sample sizes as in this study (11).

To conclude, WHOQOL-OLD Turkish norm values showed that in all dimensions, higher dimension scores were obtained in males than females in all age groups except 90 years and older. The social participation dimension score decreased after the age of 80 for both men and women, while the autonomy dimension score dropped significantly after the age of 85 only for women. Turkish older adults' QoL perceptions are considerably poorer than those of living in Western countries and more or less like other older adults in developing countries. Classical psychometric analyses of the Turkish WHOQOL-OLD repository data showed good internal consistency and generated acceptable fit values with the original scale structure. The Turkish version of the overall WHOQOL-OLD module can be considered as a valid and reliable scale suitable for application in the field of health. Nevertheless, the dimensions past, present, and future activities and social participation were combined in a single dimension in the exploratory factor analyses. The death and dying dimension and items 9 and 20 of the Turkish WHOQOL-OLD version showed weak psychometric properties that need further work (i.e., retranslation and/or cultural adaptation).

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SUPPLEMENTARY TABLES

Supplementary table 1. Studies contributing to the research data pool

	Project title (*applied to the national WHOQOL center*)	Year	Authors	Type of data	Sample size	Status of disseminating/publishing
1	Evaluating of the effect of regular monitoring of the elders through home visits in the primary health care serviceson the health related quality of life	2014	Aylin Sena BELİNER Aliye MANDIRACIOĞLU	Community-based	97	Doctoral Dissertation
2	The relationship between Quality of Life and Cognitive Functions, Anxiety and Depression among Hospitalized Elderly Patients	2015	Ayşe Semra DEMİR AKÇA	Clinical-based	243	Published Article doi:10.9758/cpn.2015.13.2.194
3	Frequency of application the healthcare organization more than one due to same reason, depression frequeny, life quality among 65 age and over individuals which living in the centre of Burdur and related factors	2016	Aysun GÜZEL Fatih KARA	Community-based	765	Doctoral Dissertation
4	Factors affecting quality of life and depression levels in the population aged 65 and over living in the distirct of Palandöken in Erzurum	2018	Banu BEDİR Elif Okşan ÇALIKOĞLU	Community-based	480	Speciality Thesis
5	Investigation of flexibility among geriatric subjects with different age groups, sex and physical activity levels	2016	Elvan KELEŞ İbrahim Engin ŞİMŞEK	Community-based	120	Master's Thesis
6	The relationship between quality of life and adaptation to aging in elderly people	2020	Selin KÜÇÜKKAYA Fatma Nevin ŞAHİN	Community-based	444	Master's Thesis
7	Yaşlılarda Yaşam Kalitesi ve Yaşam Doyumu ile İlişkili Faktörler	2016	Gizem UZUN	Community-based	109	Unpublished
8	Huzur Evinde Kalan Yaşlılarda Yaşam kalitesinin Değerlendirilmesi.	2012	Gönül GÜRBÜZ Asiye DURMAZ AKYOL	Nursing Home	99	Unpublished
9	Is There a Correlation Between the Quality of Life of Old People and Their Attitude to Aging?	2022	Gülengül MERMER Aysun UYSAL TORAMAN	Nursing Home	147	Published Article doi:https://doi.org/10.31067/acusaglik.944893
10	Gazimağusa Bölgesinde Yaşayan 65 Yaş Ve Üzeri Bireylerin Sağlık Profili, Yaşam Kalitesi Ve Bakım Verme Yükü Hemşirelik Alan Projesi	2016-2017	Handan SEZGİN	Community-based	762	Unpublished
11	Yaşlıların beslenme şekilleri ve yaşam kalitesi	2012	Hande ŞAHİN Semra AKAR ŞAHİNGÖZ	Community-based- Nursing Home	99	Unpublished
12	The relationship of nutritional habits with telomere lenght and adrenomedullin levels in aging	2021	Hatice Kübra GÜZELDERE Meral AKSOY	Community-based	120	Doctoral Dissertation
13	Association Between Quality of Life and Nutritional Status of Nursing Home Residents or Community Dwelling Elderly.	2021	Hilal ŞİMŞEK Aslı UÇAR	Community-based-Nursing Home	100	Published Article DOI:10.14744/etd.2020.74150
14	The evaluation of the life qualities of people over 65 years old living in Samsun in Tekkeköy	2011	Hülya DOĞAN Şennur DABAK	Community-based	361	Doctoral Dissertation
15	Toplum İçinde Yaşayan 80 Yaş Üstü Ve 80 Yaş Altı Yaşlı Bireylerde Grup Egzersizlerinin Etkilerinin Karşılaştırılması		Hülya DONAT TUNA Nursen İLÇİN	Clinical-based	16	Unpublished study

16	The Effects Of Myofascial Release Technique Combined With Core Stabilization Exercise In Elderly With Non-Specific Low Back Pain: A Randomized Controlled, Single-Blind Study	2019	İsmail ÖZSOY Nursen İLÇİN	Clinical-based	43	Published Article DOI: 10.2147/CIA.S223905
17	Covid 19 Ulusal Kısıtlar Döneminde Geriatrik Bireylerde Fonksiyonel Düzey, Fiziksel Aktivite Düzeyi, Depresyon Ve Yaşam Kalitesi Arasındaki İlişkinin İncelenmesi	2021	Mine PEKESEN KURTÇA	Community-based	118	Unpublished
18	Assessment of physical function, quality of life, daily life activities of geriatric individuals with type 2 diabetes mellitus and their relationship with nutrition	2017	Mustafa CEMALİ Zafer ERDEN	Nursing Home	68	Master's Thesis
19	Huzurevinde Yaşayan Yaşlı Bireylerin Ağrı Düzeyleri ve Ağrı İnançlarının Yaşam Kalitesine Etkisi	2014-2015	Nevin DOĞAN Songül GÖRİŞ	Nursing Home	108	Unpublished
20	Depression, quality of life, and influential factors in the elderly	2012	Nihal BAKAR Rabia HACIHASANOĞLU AŞILAR	Community-based	450	Master's Thesis
21	The effect of applied reminiscence therapy on the quality of life older adults in living nursing home	2015	Nilay ERCAN ŞAHİN Oya Nuran EMİROĞLU	Nursing Home	136	Doctoral Dissertation
22	Macula dejenerasyonu ve diyabetik gözü olan yaşlı hastalarda hastalık algısı, depresyon, anksiyete ve yaşam kalitesi ile ilişkisi	2018	Ömer ŞENORMANCI	Clinical-based	74	Unpublished
23	Nutritional status and effecting factors among elderly individuals in Edirne city center.	2016	Özge CEMALİ Hamdı Nezıh DAĞDEVİREN	Community-based	1000	Master's Thesis
24	An analysis of factors affecting the life quality of above 65 years of age elders at the nursing home	2013	Recep YAĞCIOĞLU Aliye MAVİLİ AKTAŞ	Nursing Home	216	Master's Thesis
25	Care Dependency and Quality of Life in Older Adult Patients	2021	Saide FAYDALI	Clinical-based	350	http://www.internationaljournalofcaringsciences.org/docs/34_gulnar_original_14_1.pdf
26	Validity of the Turkish Occupational Self Assessment for Elderly Individuals	2018	Serkan PEKÇETİN	Community-based	117	Published Article DOI:10.1177/1539449217743457
27	The effects of telerehabilitation application with elderly on sleep quality, life guality, level of depression and physical parameters in different time periods of the day	2022	Tolunay KESKİN Nursen İLÇİN	Community-based	30	Master's Thesis
28	The risk factors associated with falls in the elderly living in nursing homes and their own homes	2014	Zeynep BULUT DOĞAN Nuray KIRDI	Community-based- Nursing Home	160	Master's Thesis
29	Kayışdağı Darülaceze Müdürlüğünde yaşamını sürdürmekte olan sakinlerin yaşam kalitelerinin değerlendirilmesi	2008	Ayşe KARAN Nurten ESKİYURT	Nursing Home	119	Unpublished study

Supplementary table 2. Baseline characteristics for the Turkish WHOQOL-OLD data pool

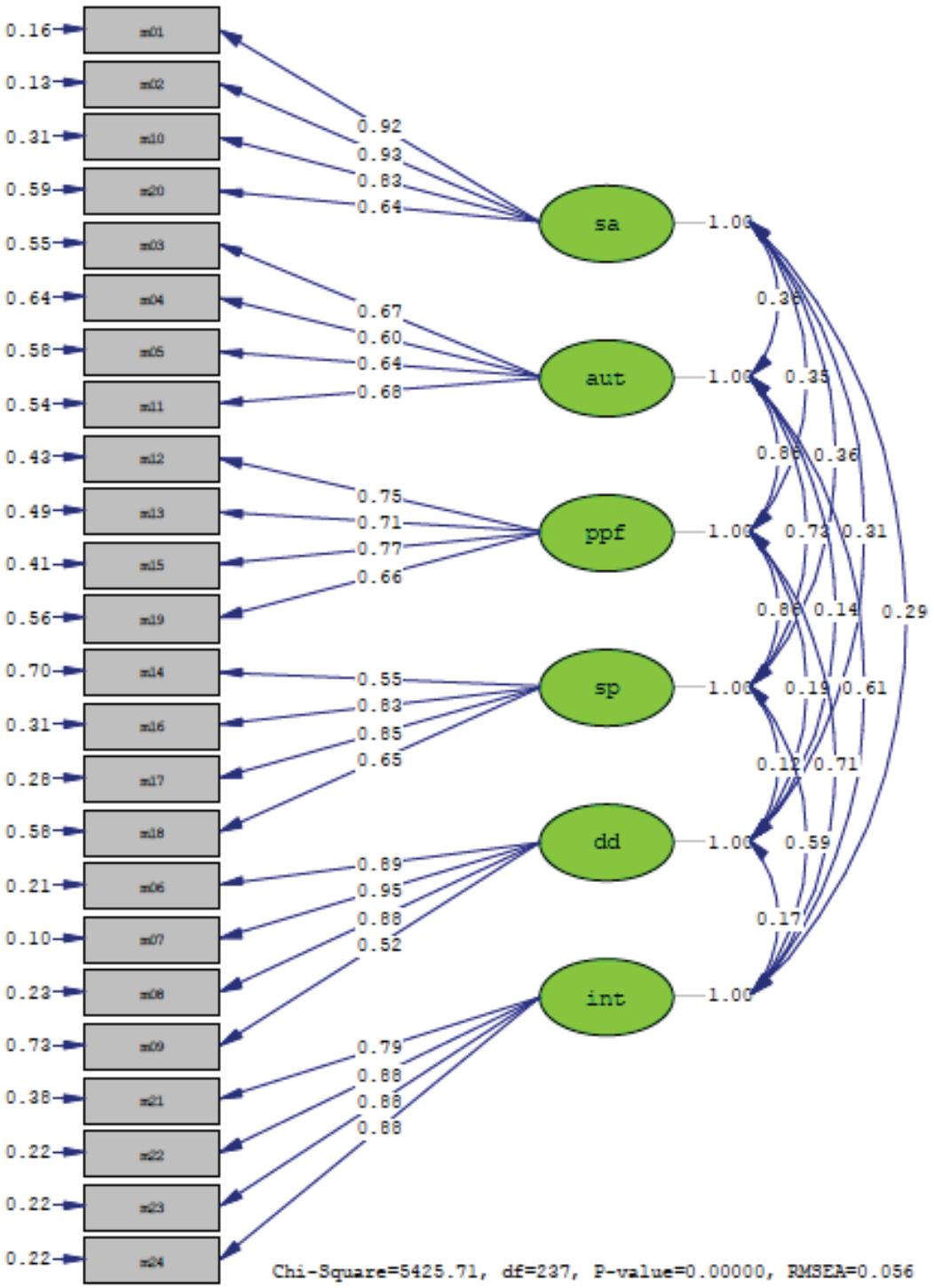
Sociodemographic Characteristics		Number	Percent
Age	Mean±SD	73.2±6.8	
Gender	Women	3496	51.2
	Men	3335	48.8
Marital Status	Married	3183	52.4
	Not Married	1068	17.6
	Widow	1828	30.1
Education Status	Unqualified	1604	27.0
	Primary School	2330	39.2
	Middle School	890	15.0
	High School	704	11.8
	University	420	7.1
Working Status	Working	183	4.8
	Not working	1479	38.5
	Retired	2182	56.8
Social Security	No	461	8.8
	Yes	4769	91.2
Smoking	No	3974	85.5
	Yes	673	14.5
Alcohol Drinking	No	3296	93.3
	Yes	236	6.7
Drug Use	No	670	23.8
	Yes	2148	76.2
Health Condition	Well	1304	24.3
	Ill	4059	75.7

Supplementary table 3. Exploratory factor loadings of the WHOQOL-old-TR (Varimax rotation solution)

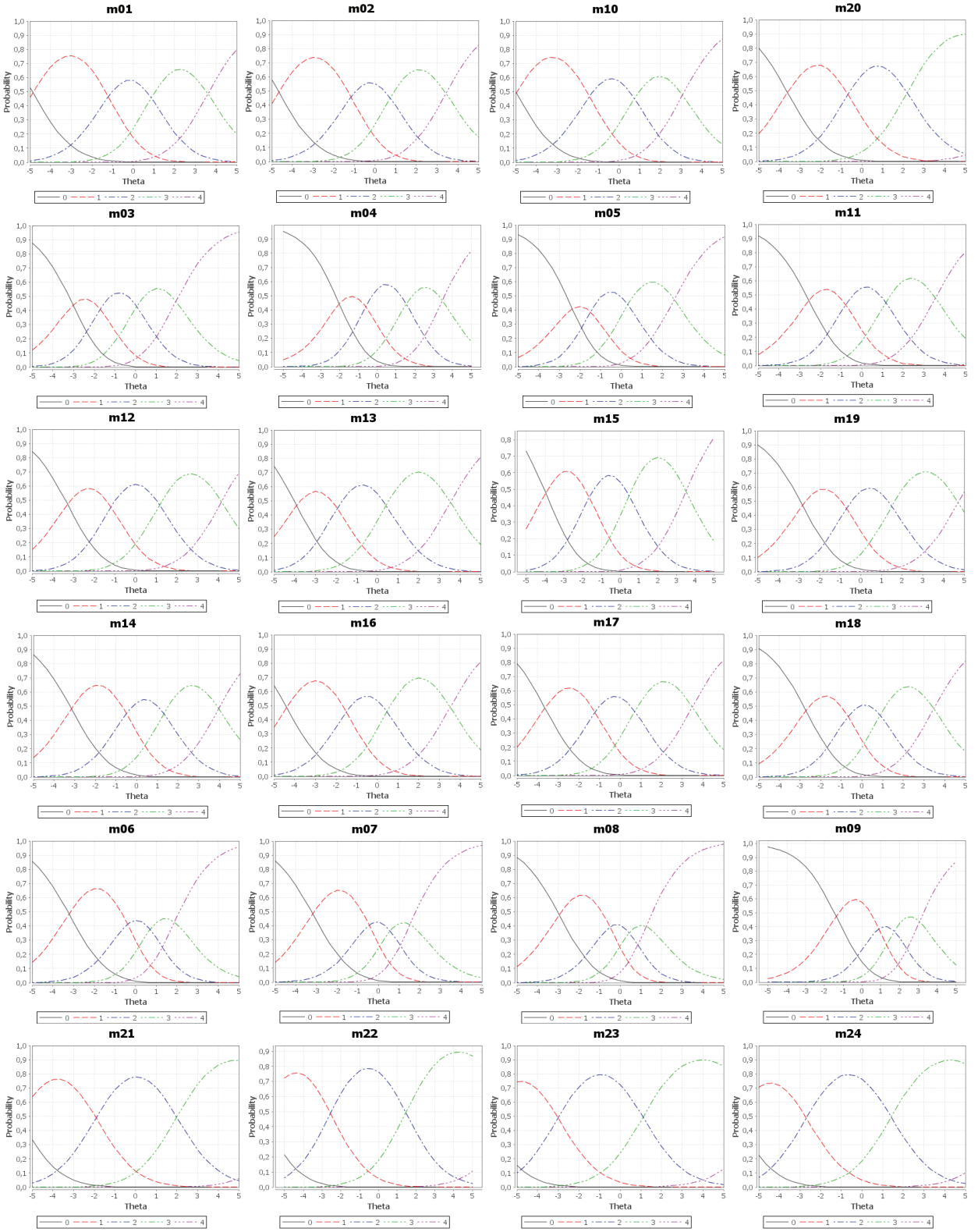
Items	Domain	Components				
		1	2	3	4	5
Q1	Sensory Abilities	0,103	0,090	**0,902**	0,127	0,083
Q2		0,137	0,095	**0,899**	0,139	0,082
Q10		0,117	0,091	**0,858**	0,157	0,079
Q20		0,279	0,111	**0,702**	-0,001	0,117
Q3	Autonomy	0,230	0,138	0,146	0,087	**0,751**
Q4		0,270	0,092	0,093	-0,082	**0,689**
Q5		0,181	0,309	0,058	0,020	**0,699**
Q11		**0,576**	0,103	0,141	0,020	0,419
Q6	Death and Dying	0,037	0,034	0,137	**0,899**	0,044
Q7		0,033	0,048	0,155	**0,914**	0,045
Q8		0,047	0,035	0,147	**0,896**	0,059
Q9		-0,012	0,065	-0,022	**0,688**	-0,067
Q12	Past, Present and Future Activities + Social Participation	**0,600**	0,224	0,129	0,055	0,399
Q13		**0,489**	0,367	0,016	0,086	0,393
Q14		**0,637**	0,089	0,095	-0,077	0,101
Q15		**0,653**	0,294	0,112	0,129	0,251
Q16		**0,770**	0,216	0,142	0,058	0,140
Q17		**0,798**	0,173	0,169	0,020	0,126
Q18		**0,678**	0,176	0,086	0,012	0,054
Q19		**0,633**	0,283	0,102	0,018	0,161
Q21	Intimacy	0,305	**0,751**	0,134	0,045	0,174
Q22		0,297	**0,828**	0,119	0,066	0,175
Q23		0,267	**0,847**	0,088	0,066	0,145
Q24		0,263	**0,847**	0,101	0,050	0,164

*Extraction Method: Principal Component Analysis. Rotation Method: Varimax with Kaiser Normalization.

Supplementary Figure 1. Confirmatory factor model for the six WHOQOL-OLD dimensions (standardized loadings).



Supplementary Figure 2. Item Characteristics Curves (ICC) of the WHOQOL-OLD



RESEARCH

IS DYNAMIC THIOL/DISULFIDE HOMEOSTASIS ASSOCIATED WITH THE PROGNOSIS OF GERIATRIC PATIENTS WITH SEPSIS IN THE INTENSIVE CARE UNIT?

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Abstract

Introduction: Sepsis is an important cause of mortality, especially in geriatric patients hospitalized in the intensive care unit. Our study aims to evaluate the effectiveness of thiol / disulfide homeostasis in determining the mortality of geriatric patients admitted to intensive care unit due to sepsis.

Materials and Method: Our study was designed prospectively in patients aged 65 years and older with geriatric sepsis hospitalized in the intensive care unit between January 2018 and March 2019. Thiol-disulfide homeostasis was measured at the time of hospitalization. Demographic and clinical characteristics and thiol – disulfide homeostasis levels were compared in patients with mortality and surviving.

Results: 252 geriatric patients with sepsis were included in the study. A total of 148 (58.7%) of the patients died, 104 (41.3%) were discharged alive. In the group with mortality, native-thiol, total-thiol and disulfide levels were found to be significantly lower compared to the surviving group ($p < 0.05$). In geriatric patients with sepsis; levels of native-thiol less than 209 µmol / L, total-thiol lesss than 248 µmol / L and disulfide being less than 20.4 µmol / L was found as the cut-off value for mortality ($p=0.0001$).

Conclusion: This study showed that low native-thiol, total-thiol and disulfide levels may be associated with mortality in patients with geriatric sepsis hospitalized for the first time in the intensive care unit.

Keywords: Aged; Intensive Care Units; Sepsis; Sulfhydryl Compounds.

INTRODUCTION

Sepsis is the leading cause of morbidity and mortality in patients hospitalized in the intensive care unit (ICU) (1). Older patients have a higher risk for mortality (2). In addition to the age factor in patients developing sepsis, determining other risk factors for patient mortality in ICU is imperative to sepsis prognosis (2,3). Age, vital sign assessment, and other scoring systems are used for evaluation of the mortality data of patients hospitalized in ICU. It is difficult to determine patient mortality in ICU owing to various causative agents and underlying diseases that lead to ICU hospitalization. Therefore, additional parameters are crucial for the evaluation of ICU mortality (3).

Activation of free radicals, reactive oxygen species (ROS), oxidant, and pro-oxidant systems are associated with negative clinical outcomes in aging individuals with sepsis (4); both advanced age and sepsis increase the morbidity and mortality (4,5). Therefore, evaluation of oxidant systems in patients hospitalized in ICU could aid determination of sepsis prognosis (5).

The plasma thiol level is usually measured by using the classical 5,5′-dithiobis-(2-nitrobenzoic) acid (DTNB) and Ellman reagent. This compound is stoichiometrically decreased by free thiols in an exchange reaction, forming disulphide and releasing one molecule of 5-thionitrobenzoic acid. Dynamic thiol/disulfide homeostatis is critical for a number of processes: antioxidant protection, detoxification, signal transmission, apoptosis, regulation of enzymatic activity, transcription factor regulation, and cellular signaling mechanisms (6). Low thiol levels are associated with decreased inflammatory processes, decreased antioxidant activity, and adverse clinical outcomes (7). Furhtermore, dynamic thiol disulphide homeostasis is being increasingly implicated in many disorders. There is also a growing body of evidence demonstrating that an abnormal thiol disulphide homeostasis state is involved in the pathogenesis of a varietyof diseases, including diabetes, cardiovascular disease, malignancy, rheumatoid arthritis, chronic kidney disease, infection diseases, neorological diseases, and liver disorder. Therefore, determination of dynamic thiol disulphide homeostasis can provide valuable information on various normal or abnormal biochemical processes (6).

In this respect, evaluation of thiol/disulfide homeostasis, which is one of the oxidant systems, may be effective in the prognosis of severe sepsis in geriatric patients admitted to ICU (5). There are no previous studies evaluating thiol/disulfide homeostasis in geriatric patients with sepsis. Therefore, the aim of our study was to evaluate the possible relationship of thiol/disulfide homeostasis with mortality in geriatric patients (aged ≥65 years) hospitalized in ICU.

MATERIALS AND METHOD

Ethics committee approval and study design

This study was planned prospectively in geriatric patients (aged ≥65 years) with sepsis; they were hospitalized in the ICU in the Health Sciences University, Anesthesiology and Clinical of Critical Care, Ankara Numune Education and Research Hospital between January 2018 and March 2019. Inpatients were diagnosed with sepsis based on their clinical findings as well as according to the "Third International Consensus Definitions" criteria (8). ICU patients who were <65 years of age and diagnosed with causes other than primary sepsis (trauma, intoxication, metabolic disorders, cardiovascular, and respiratory reasons, etc.) were excluded from the study. Patients' age, sex, number of comorbid disease (diabetes mellitus, hypertension, malignancy/immunodeficiency, respiratory system disease, heart disease, renal disease, central nervous system disease), acute physiology chronic health evaluation (APACHE II) score, sepsis-related organ failure assessment (SOFA) score, duration of mechanical

ventilation (MV), ICU stay, and mortality data were recorded (9,10).

This study was approved by the ethics Committee at Ankara Numune and Research Hospital (date: 28/12/2017, no: E-17-1478). Verbal and written consent was obtained from patients or their legal representative before the study. Our study was conducted in accordance with the Helsinki Declaration principles. In this study, while sampling the geriatric elderly patient group, the definition of "elderly" for age ≥65 years was taken into account, which is the criteria of World Health Organization and the Organization for Economic Co-operation and Development (11,12).

Blood sampling and determination of white blood cell counts and serum levels of C–reactive protein and thiol–disulfide

Venous blood samples were obtained for the determination of white blood cell (WBC) counts, C-reactive protein (CRP) levels, and thiol-disulphide homeostasis status during hospitalization. WBC count was determined with a Cell-Dyn 3700 automated hemocytometer (Abbott, Abbott Park, IL, USA) by drawing the blood into tubes containing ethylenediamine tetra-acetic acid. Serum was separated after blood samples were centrifuged at 1200 rpm for 15 minutes. Serum samples were stored at -80°C until use for thiol-disulfide analysis. Serum CRP concentrations were measured on the Roche Modular P analyzer with a Tinaquant CRP (Latex) high-sensitive immuno-turbidimetric assay (CRP latex HS, Roche kit, Roche Diagnostics, GmbH, Mannheim, Germany). Serum total thiol and native thiol levels were determined by the automated method developed by Erel and Neselioğlu (Roche cobas-c501 automated analyzer, Mannheim, Germany) (6). Thiol/disulfide homeostasis tests were performed using the automatic and spectrophotometric method. The principle of the thiol/disulfide measurement method is the reduction of dynamic disulfide bonds (-S-S-) to functional thiol groups (-SH) with $NaBH_4$. The unused $NaBH_4$ remnants were completely dissociated using formaldehyde; this prevented further reduction of the 5,5'-dithiobis-2-nitrobenzoic acid (DTNB) as well as the disulfide bonds that were formed by the reaction with DTNB. The modified Ellman reagent was used to measure the total thiol content in samples. After serum extraction, it took approximately 12 minutes to measure all the parameters. Dynamic disulfide content was calculated by taking half of the difference between the amount of total thiol and native thiol. Ratio formulas (Index 1: disulfide/native thiol ratio, index 2: disulfide/total thiol ratio, and index 3: native thiol/total thiol disulfide) were used to calculate the dynamic disulfide content.

Data analysis

Statistical analysis of the patient data was performed using SPSS software 17.0 (SPSS, Chicago, IL) and p values <0.05 were considered significant. The conformity of the data to the normal distribution was evaluated with histogram and Kolmogorov-Smirnov test. Mann-Whitney's U-test was used to compare for non-parametric continuous variables and the chi-square test was used to compare for categorical variables. The results were specified as the mean and standard deviation (SD) for normally distributed continuous variables, median and interquartile range (IQR,25-75) for continuous variables with abnormal distribution. Categorical variables were expressed as frequency and percentage distribution. The thiol / disulfide homeostasis were compared between the mortality groups and the surviving group using multiple logistic regression. The odds ratios (ORs) and 95% confidence interval (CI) were defined in multiple logistic regression analysis. Diagnostic screening tests were used to determine the cut-off for thiol/disulfide homeostasis; additionally, receiver operating characteristic (ROC) curve analysis was also performed (sensitivity, specificity, positive predictive value, and negative predictive value). The area under the curve (AUC) was calculated.

RESULTS

During the study period, 793 patients were admitted in our ICU. According to the inclusion criteria, 252 (31.7%) patients were included in the study; 148 (58.7%) patients died and 104 (41.3%) were discharged. The total mean age of 252 geriatric patients included in the study was 78.2 ± 10.1 (mean ± SD) years. Patients who succumbed to mortality were higher in age, experienced a greater number of comorbid diseases, and had higher APACHE II and SOFA scores; in addition to this, the patients had increased duration of MV and ICU stay. The results were similar between the groups in terms of gender (Table 1). Results were similar between groups with mortality and surviving in terms of WBC counts and indices -1, -2, and -3 (p>0.05). In the surviving group, native-thiol, total-thiol, and disulfide levels were found to be significantly higher and CRP significantly lower, than those in the mortality group (p<0.05) (Table 2).

In addition to thiol / disulfide homeostasis, confounding factors such as age, comorbid disease, and CRP levels can also impact mortality. After adjusting for confounding factors using multiple logistic analysis, patients with mortality had lower levels of native-thiol [OR = 5.15, 95% CI (1.745–8.322), p = 0.002], total-thiol [OR = 2.09, 95% CI (1.119–4.244), p = 0.005], and disulfide [OR = 3.65, 95% CI (2.124–8.103), p < 0.001] than those surviving.

The cut-off value for mortality in geriatric patients with sepsis was 209 (μmol/L) for native-thiol, ≤248 (μmol/L) for total-thiol, and ≤20.4 (μmol/L) for disulfide. The AUC level between 0.7-0.9 is assumed to have moderate accuracy in predictive value. In our results, we found that AUC levels of native-thiol, total-thiol, and disulfide were between 0.7 ile 0.9 which were assumed as moderate accuracy (13). The results are presented in Table 3 as AUC, p-value, sensitivity, specificity, positive predictive value, and negative predictive value. ROC analyses for native-thiol, total-thiol, and disulfide mortality prediction are given in Figure 1.

DISCUSSION

In geriatric patients hospitalized for sepsis, native-thiol, total-thiol, and disulfide levels were significantly lower in the mortality group than in the

Table 1. Comparison of demographic and clinical features of the geriatric patients

Variables	Surviving (n=104)	Mortality (n=148)	P value
Age, (years), [a]	76.1±10.9	81.1±8.0	<0.001*
Male gender, n (%)	46 (44.2)	64 (43.2)	0.489
Comorbid disease, [b]	1 (1-3)	2 (1-4)	<0.001*
APACHE II score, [b]	24 (17-28)	29 (19-38)	<0.001*
SOFA score, [b]	7 (6-10)	10 (8-16)	<0.001*
Duration of MV, (days), [b]	5 (3-18)	7 (4-28)	0.015*
ICU stay, (days), [b]	15 (6-83)	17 (7-96)	0.001*

[a] mean ± standard deviation, [b] median (interquartile range (IQR, 25-75))

*Statistically significant p values are highlighted.

APACHE II: acute physiology and chronic health evaluation score, SOFA: sepsis-related organ failure assessment score, ICU: intensive care unit, MV: mechanical ventilation

Table 2. Comparison of laboratory features of the geriatric patients.

Variables	Surviving (n=104)	Mortality (n=148)	P value
WBC (x10^3/μL), [a]	10 (5-12)	12 (6-14)	0.416
CRP (mg/L), [a]	75 (41-110)	161 (51-214)	<0.001*
Native-thiol, (μmol/L) [b]	218.8±102.9	158.4±71.1	<0.001*
Total-thiol, (μmol/L) [b]	264.1±110.1	192.7±74.3	<0.001*
Disulfide, (μmol/L) [b]	22.5±5.3	17.1±7.0	<0.001*
Index-1, [b]	12.2±5.1	13.5±9.2	0.151
Index-2, [b]	9.5±3.1	9.9±5.2	0.531
Index-3, [b]	80.9±6.2	80.2±10.5	0.531

[a] median (interquartile range (IQR, 25-75)), [b] mean ± standard deviation
*Statistically significant p values are highlighted.
WBC: white blood cell, CRP: C-reactive protein level

surviving group. In addition, the level of native-thiol (<209 μmol/L), total-thiol (<248 μmol/L), and disulfide (<20.4 μmol/L) was determined as the cut-off value for mortality. Our results support the information that thiol is an important antioxidant, and decrease in the native-thiol, total-thiol, and disulfide levels shortens the cellular life span, which leads to increase in the mortality rate (5). To the best of our knowledge, this is the first study that provides data concerning the relationship between thiol/disulfide homeostasis and clinical outcome of sepsis in geriatric patients hospitalized in ICU.

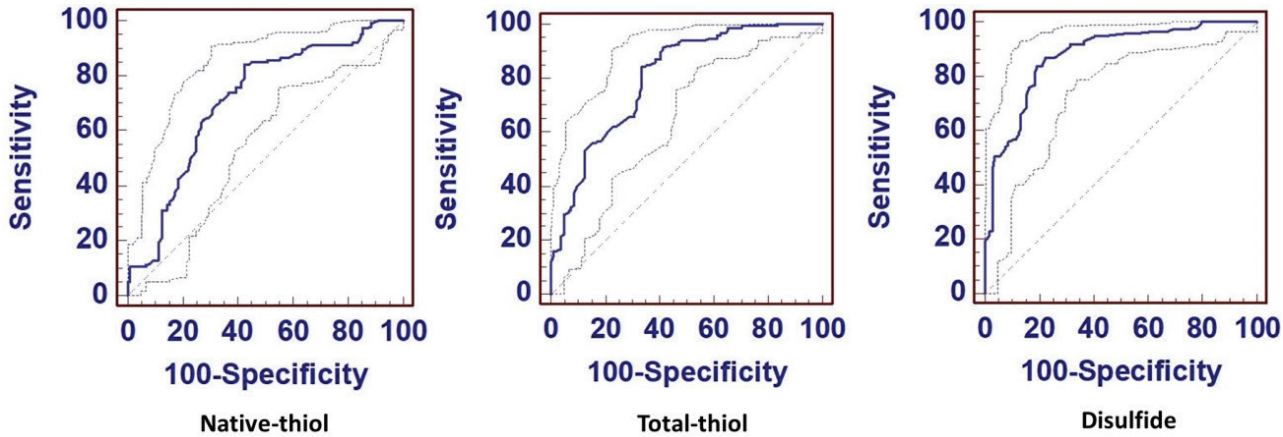
The aging of the population is a global phenomenon; the population aged 65 and above is growing faster than all other age groups. As the population demography changes, there will likely be an increase in the number of geriatric patients admitted to the ICU. According to literature, elderly patients account for 26-51% of ICU admissions. In addition, mortality rates in patients hospitalized in ICU vary between 20% and 58% (11,14,15). In patients with

Table 3. The area under the curve, cutoff level, sensitivity, specificity, PPV, and NPV of native-thiol, total-thiol and disulfide for mortality

	AUC	95% Confidence interval	p values	Cutoff level	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Native-thiol (μmol/L)	0.713	0.653-0.768	0.0001	≤209	84	61	74	72
Total-thiol (μmol/L)	0.803	0.749-0.850	0.0001	≤248	84	70	78	75
Disulfide (μmol/L)	0.878	0.831-0.916	0.0001	≤20.4	87	78	84	81

AUC: area under the curve, PPV: positive predictive values, NPV: negative predictive values

Figure 1. ROC curve for native-thiol, total-thiol and disulfide levels, predicting mortality in intensive care unit



ROC: receiver operating characteristic

sepsis, the rate of mortality increases with age; hence, age is considered as an independent predictor of mortality (16). Therefore, patients with an average age of 78.2 years were included in our study, which explains why the patient mortality rate in our study was close to the upper limit of 58.7%. Studies have suggested that there are different predictors of mortality in geriatric ICU patients. APACHE II and SOFA scores have been frequently used for this purpose, and as in our results, increased scores were associated with an increased mortality rate (11,14,15,17,18). However, available evidence is still not sufficient for physicians to determine clinical results and mortality rate in geriatric patients (11). Therefore, new studies are needed to predict clinical outcomes in elderly patients who are at a risk for mortality.

Although the pathophysiology of sepsis is not fully understood, clinical studies have revealed an imbalance between oxidants and antioxidants (19). Lorente et al. demonstrated that antioxidant capacity in sepsis determines the course of the disease and indicates a possible relationship between the total antioxidant capacity and mortality (20). Other causes of increased mortality in patients with sepsis are uncontrolled inflammatory response against pathogens, persistent oxidative stress, impaired oxygen use due to mitochondrial dysfunction, energy deficiency, and organ failure. Organ failure worsens the outcome of sepsis and is associated with 70% ICU mortality (17,21).

Based on existing scientific literature and our results, it can be concluded that low levels of native-thiol, total-thiol, and disulfide, which are indicators of antioxidant capacity, can help predict negative clinical outcomes, particularly mortality, in patients with sepsis (5,17,22,23). Oxidative stress contributes to the pathophysiology of sepsis by disrupting cellular redox homeostasis, which is the cause for lower thiol levels in patients who succumb to mortality. In addition, low disulfide levels in patients who succumb to mortality may be due to the reversible conversion of disulfide products to S-nitrosothiol and sulfenic acid (24), because when oxidative stress persistently occurs in a patient, irreversible sulfonic acid concentration increases and causes permanent loss of protein activity (25). Therefore, more research on the measurement of reversible and irreversible modifications is imperative.

Kozanhan et al. compared the status of thiol/disulfide homeostasis of 44 adult patients with sepsis with that of 44 control patients. While native-thiol, total-thiol, and disulfide levels were significantly lower in the sepsis group than in the control group, there was no difference between the groups in terms of indices -1, -2, and -3. Additionally, in the non-survivor group (18 patients), native-thiol, total-thiol, and disulfide levels were insignificantly lower than those in the survivor group (26 patients) (17). Ayar et al. compared 40 healthy children and 38 children with sepsis and reported that native-thiol, total-thiol, and disulfide levels and index-3 in the sepsis group were significantly lower than those in the control group, whereas indices -1 and -2 were higher in the sepsis group than in the control group. In addition, similar results were obtained when native-thiol, total-thiol, and disulfide levels and indices -1, -2, and -3 were compared between 27 survivor and 11 non-survivor patients (22). The probable reason for the similar results obtained may be the small number of patients included in the study. In our study, native-thiol, total-thiol, and disulfide levels in the mortality with sepsis and were significantly lower than those in the surviving group. Therefore, change in thiol/disulfide homeostasis may help us to better evaluate clinical outcomes of patients with sepsis. In order to reach this goal, sufficient number of patients should be included in the study. In another study evaluating the neonatal age group, similar results were obtained when native-thiol, total-thiol, index-3, index-2, disulfide, and index-1 levels were compared between the newborns with sepsis (66 patients) and the healty control group (51 newborn patients) (23). The balance of antioxidant and oxidant systems, including thiol/disulfide homeostasis, can change with age. Due to the age groups of the patients in these studies, thiol/disulfide homeostasis results may vary. Therefore, it would be more accurate to interpret the results according to age (5). In addition, other reasons for the difference in results obtained in terms of thiol/disulfide homeostasis may be due to difference in level of sepsis severity and the difference between the groups compared (control versus sepsis and mortality versus survivor).

Thiol/disulfide homeostasis levels normally vary during life-time. We see increase in the levels of native-thiol, total-thiol, and disulfide up to 3rd decades of age and then, these levels gradually starts to decrease from these decades up to 7th decades of life. The rate of diminish in the levels of native-thiol, total-thiol, and disulfide may increase due to secondary morbidities such as alcohol abuse, smoking, infections and genetic factor. Decrease in the levels of native-thiol, total-thiol, and disulfide increase the rate of mortality (5,6). The variables such as age, level of CRP and comorbid disease, were found to be higher in mortality group. Multiple logistic analysis was done in order to evaluate variables such as age, comorbid diseases and level of CRP which affect the mortality. Multiple logistic analysis revealed that low levels of native-thiol, total-thiol, and disulfide were isolated risk factors for mortality other than age, comorbid diseases and level of CRP. The levels of native-thiol, total-thiol, and disulfide do not change after 7th decades of life. Both of our groups have similar mean ages over 70. So this variable-age-does not directly explain the difference between groups. We speculate that the degree of severity of sepsis might effect the levels of native-thiol, total-thiol, and disulfide which increase the mortality. High levels of CRP due to severe sepsis and higher frequency in comorbid diseases may increase mortality. Multiple logistic analysis revealed these results. In conclusion, our study showed that low levels of native-thiol, total-thiol, and disulfide were found to be directly related with rate of mortality in geriatric-sepsis patients.

There is no previous study determining the cut-off values of native-thiol, total-thiol, and disulfide levels to predict mortality in geriatric patients with sepsis. According to our results, cut-off value of native-thiol for mortality in geriatric patients with sepsis was ≤209 (μmol/L); total-thiol, ≤248 (μmol/L);

and disulfide, ≤20.4 (μmol/L). In addition, the AUC value for all three parameters was between 0.7 and 0.9 and had a moderate accuracy predictive value (13). Our results are valid for geriatric patients with sepsis. To confirm our findings, further studies defining cut-off values for different age groups and AUC values are crucial.

Our study has few limitations. Thiol/disulfide homeostasis was tested at the time of the patient's hospitalization, and the values during patient's follow-up could not be measured. Therefore, the change in thiol/disulfide homeostasis during the follow-up for sepsis and its effect on clinical results are unknown. Additionally, thiol/disulfide homeostasis level could not be compared between sepsis and control groups owing to the absence of the control group.

CONCLUSION

Our study is the first to demonstrate the efficacy of thiol/disulfide homeostasis on the clinical outcome i.e. the prognosis of sepsis in geriatric patients hospitalized in ICU. Low levels of native-thiol, total-thiol, and disulfide were shown to be related with higher mortality in geriatric septic patients. Further studies with larger cohorts are needed to validate our current findings and to comprehensively understand the pathophysiology of oxidative stress in the sepsis process.

Conflict of Interest, Disclosure Statement

The authors declare that they have no conflicts of interest. The authors have indicated they have no financial relationships relevant to this article to disclose

Ethical Approval: All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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RESEARCH

HOW AWARE ARE FAMILY PHYSICIANS OF THE SOCIAL LIFE AND LONELINESS OF OLDER PEOPLE?

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Abstract

Introduction: The consequences of social isolation and loneliness on health and well-being in old age are increasingly being acknowledged. In this study, we examined how older patients perceive their social relationships and loneliness and explored family physicians' awareness of these issues.

Materials and Methods: This descriptive study evaluated social relations and the loneliness of older patients using the UCLA loneliness scale (UCLA-LS), the Nottingham Health Profile Social Isolation (NHP-SI) subscale, and a social relations questionnaire. The responses of these patients to loneliness and being socially active were compared with the reactions of family physicians to the same topics.

Results: Five family physicians and 200 older patients participated in this study. According to the patients' education levels and economic status, both scales exhibited significant differences. A significant correlation was found between chronic disease and UCLA loneliness on the scale, while a significant difference was found in the social isolation subscale according to those who lived with. Moreover, the family physicians clearly understood the relationship between living alone and their economic status.

Conclusion: This study revealed that the social isolation of older patients was affected by their education level, economic status, and who they lived with. It was also found that loneliness was affected by education level, financial situation, chronic disease, and disability.

Keywords: Family Practice; Aged; Loneliness; Social Isolation.

INTRODUCTION

It should be remembered that aging is an inevitable process, public perceptions of older people are different in every society, and biological processes differ between people. In addition to biological factors, diversity in psychological, social, and cultural conditions can also affect aging (1, 2). Therefore, given the increased proportion of older people in society, there is a need to design health and social services accordingly, and physicians should develop their professional competencies to meet this challenge (3).

Social problems and the chronic health care of older patients can be neglected when treating daily complaints. Moreover, older people are at risk of social isolation and loneliness due to economic-social losses, functional decline, the death of spouses, and changes in family structure (4,5). However, being socially connected is a requirement for psychological and emotional well-being and positively affects physical well-being and longevity (6).

The Age-Friendly Primary Health Care Center Guide developed by the World Health Organization (WHO) for primary health care center employees supports the health of older people (7). Moreover, physicians working in primary care should evaluate older patients within the discipline of family medicine to improve their health, provide treatment or care, and increase their quality of life (8,9). In this study, we examine older patients' perceptions of their social lives and loneliness and their family physicians' awareness of these issues.

MATERIALS AND METHODS

Study design

This descriptive study compares the senses of loneliness and social isolation of older patients and the responses of their family physicians. The study was carried out with five different volunteer family medicine specialists. A minimum of 40 patients were calculated from each family physician with 80% power and a 5% margin of error in the G-Power statistics program. Each family physician was visited once a week, and data were collected from 3–4 patients each day. Consecutive patients were excluded from the study because family physicians could have become familiar with the questionnaire and caused bias. The data collection process was completed between December 15, 2018, and February 15, 2019.

Participants

Patients who had been registered with each family physician for at least 6 months and who did not have any psychiatric disease or cognitive dysfunction (such as Alzheimer's or dementia) were included in the study.

Data collection tools

A sociodemographic data survey (UCLA-LS), the NHP-SI subscale, and a social relations questionnaire prepared by scanning the literature were applied to each patient and family physician.

Sociodemographic data survey

The sociodemographic data questionnaire included the following pieces of information: gender, age, education level, marital status, who they live with, how many children they have, profession, economic status, chronic diseases, how many months they have been registered with the family physician and the number of patients who had applied to the polyclinic that day. We also asked the following about the family physicians: age, number of years in the profession, duration of employment in their current Family Medicine Unit, proportion of patients aged over 65 years, and the speed of referrals of patients aged over 65 years during the previous 6 months.

UCLA Loneliness Scale

This 20-item scale is designed to measure a person's sense of loneliness and social isolation. Patients rate each item on a scale from 1 (never) to 4

(usually), and the highest points are 80. The higher the total score, the higher the feeling of loneliness, and *vice versa*.

Nottingham Health Profile Social Isolation subscale

This is a 5-question subscale of the NHP. Since there is no threshold for measurement, each subcategory is evaluated within its own limits. Accordingly, low scores suggest a low impact of the complaint, while high scores reflect an increased effect of the complaint.

Social relations questionnaire

Based on questions used in similar studies in the literature, 5 questions were developed to evaluate the patients' levels of social participation and loneliness. These questions included the following topics: social participation (such as how often they were visited by their relatives at home last month), feeling lonely (even when with company), and having a relative to talk to if they need help (Annex 1).

Social relations questionnaire for family physicians to evaluate their patients

The family physicians were asked 6 questions about each patient. To facilitate comparisons with the patients' answers, the doctors were asked the same questions about their patients (i.e., who they lived with and levels of social participation and loneliness). The other 5 questions were the same as the patients' social relationship questions. (Annex 2)

Statistical analysis

In the statistical analysis, when descriptive statistics were provided for normal distribution conditions, student t-tests and ANOVA were employed to compare the two independent groups in continuous data. The data obtained from the study were evaluated using SPSS 15.0. If the normal distribution conditions were not met, Mann–Whitney U and Kruskal–Wallis tests were applied. For comparisons with categorical data, the kappa values were examined using a chi-square test.

Ethical procedure

Permission was obtained from the local University Faculty of Medicine Health Sciences Ethics Committee with 20478486-050.04.04 dated 04.10.2018. Each patient was informed about inclusion in the study, and their consent was obtained.

RESULTS

A total of 5 family physicians and 200 older patients participated in this study to investigate the awareness of family physicians about the loneliness and social participation levels of their registered patients.

Distribution of patient characteristics

The 200 patients comprised 103 females and 97 males, with a mean age of 72.47 ± 5.82 years. The other characteristics of the patients are displayed in Table 1.

The mean score of the patients on the UCLA-LS was 36.69 ± 6.71. The mean score obtained from the NHP-SI questionnaire was 12.47 ± 24.50. Further, 14.5% of the patients answered "yes" to the question of feeling lonely, 13.5% stated "I have difficulty establishing relationships with people," 8.5% said "I do not feel close to anyone," and 13.5% reported "I think I am a burden on people" (Table 2).

Assessment of characteristics in sociodemographic data using the scales

When the mean scores of the UCLA-LS and the NHP-SI subscale were compared according to the sociodemographic data of the patients, no statistical differences were found according to gender. However, there was a significant difference in both scales according to education level and economic status. Moreover, a vital relationship was revealed between the presence of a chronic disease and UCLA-LS. According to those who lived with the disease, a significant difference was found in the NHP-SI subscale. There was no significant differ-

Table 1. Distribution of Patient Characteristics

Features	S/Ort.	% (veya SS*)
Gender		
Femsle	103	51,5
male	97	48,5
Age		
Mean	72,47	5,822*
Education		
Illiterate	12	6
literate	17	8.5
Primary school	96	48
Middle School	32	16
High school	30	15
University	13	6.5
Marital status		
Married	152	76
Not married (widowed, divorced, never married)	48	24
Economical situation		
Equal to monthly income	73	36,5
Less than monthly income	120	60
More than monthly income	7	3,5
Chronic disease		
Yes	189	94,5
No	11	5,5
With whom she/he lives		
Alone	39	19,5
With his wife	122	61
With his wife and children	19	9,5
Other (caregiver, sibling, relative)	22	11
The length of time she/he was registered with the family doctor		
6-36 months	115	57,5
37-84 months	85	42,5
Child		
0-3	152	76
4-9	48	24

ence between the loneliness scale and with whom the patients lived (Table 3).

Correlation of sociodemographic data using the scales

The correlation between educational status and the presence of chronic illnesses and the mean total scores of the UCLA-LS and the NHP-SI subscale were significant. As education levels increased, loneliness and social isolation decreased. Moreover, levels of loneliness increased in the presence of chronic illnesses. The mean total scores of the UCLA-LS were significantly positively correlated with the mean total score of the NHP-SI total score mean ($r = 0.680$, $p < 0.001$).

Assessment of participation in social life and the perception of loneliness

When evaluating the social relations toward the patients, 42% of the patients stated that they never participated in social activities outside, and 18% felt lonely even when in the company of others. Patients' answers such as "I feel alone when I am with others or relatives" and "who is living with" were evaluated mutually, and a significant difference was found ($p = 0.009$).) The social isolation subscale score of patients whose relatives visited was significantly lower ($p < 0.001$). Further, the social isolation subscale scores were considerably lower for patients who visited other people's homes ($p < 0.001$).

Distribution of Family Physicians' Characteristics

Five family physicians (four female and one male) participated in the study, with a mean age of 39.8 years. The mean work time in the profession was 15.8 years and had been working in their current Family Medicine Unit for an average of approximately 4.8 years. The percentage of patients aged over 65 years in the general population was 5%–11%, while the referral rate of patients over 65 years of age to family physicians varied between 8% and 24% daily.

Table 2. Frequency of patients' responses to UCLA Total score, NSP-SI subscale total score, and NSP-SI subscale

		Median	Sd	Min./Max.
UCLA Loneliness Scale total score		36,69	6,71	28/61
NHP-SI subscale total score		12,47	24,50	0,00/100
Nottingham Health Profile /Social Isolation subscale				
	N (%)	**Median**	**Sd**	**Min./Max.**
I feel alone				
Yes	29 (14,5)	3,19	7,76	0,00/22,01
No	171 (85,5)			
I have difficulty interacting with people				
Yes	27 (13,5)	2,61	6,63	0,00/19,36
No	173 (86,5)			
I don't feel close to anyone				
Yes	17 (8,5)	1,71	5,62	0,00/20,13
No	183 (91,5)			
I think I'm a burden to people				
Yes	27 (13,5)	3,04	7,71	0,00/22,53
No	173 (86,5)			
It's hard to get along with people				
Yes	24 (12)	1,91	5,20	0,00/15,97
No	176 (88)			

Family physicians' perceptions

There were two significant variables in the assessment of whether the five family physicians knew about the social relationships and loneliness of the patients. The first was the relationship between the economic status of individuals over the age of 65 and doctors' ability to predict whether their patients lived alone ($p = 0.035$). The second was the doctors' predictions of whether these individuals were alone, according to the marital status of those in the group who did not live alone ($p < 0.001$). It was not statistically significant whether doctors knew their patients were truly alone in terms of gender, presence of chronic disease, and occupational and social participation parameters (Table 4).

Comparison of Family Physician and Patient Answers

The family physicians reported that 34 of 39 patients said they lived alone, 113 of 122 patients reported living with their spouses, 7 of 19 patients reported living with their children, and 3 of 20 patients reported living with their caregivers or other persons. The kappa value of this comparison was 0.636, and the p-value was <0.001. It is worth noting that the doctors predominantly knew who their patients were living with (Table 5).

Table 3. UCLA-LS, and NHP-SI subscale evaluation with Sociodemographic data of the patients

Features		N	UCLA-LS			NHP-SI		
			Med.	Sd	p	Med.	Sd	p
Gender	**Female**	103	36,05	6,38	0,171	9,94	21,15	0,133
	Male	97	37,36	7,02		15,15	27,47	
Education	**Illiterate**	12	43,91	8,24	**0,002**	34,86	33,44	**0,008**
	literate	17	35,23	4,23		6,56	10,48	
	Primary school	96	37,16	6,72		14,82	25,96	
	Middle School	32	35,18	6,68		8,06	24,79	
	High school	30	35,36	4,18		6,22	15,98	
	University	13	35,15	8,75		7,44	21,70	
Marital status	**Married**	152	36,42	6,99	0,241	11,71	23,20	0,093
	Not married	48	37,52	6,63		14,88	24,92	
Economical situation	**Equal to monthly income**	120	35,32	6,19	**0,038**	6,73	18,93	**0,003**
	Less than monthly income	73	37,55	6,96		16,52	27,24	
	More than monthly income	7	36,14	6,06		2,87	7,60	
Chronic disease	**Yes**	189	37,01	6,76	**0,000**	13,09	25,03	0,108
	No	11	31,18	1,40		1,76	5,83	
With whom she/he lives	**Alone**	39	38,15	7,73	0,157	15,36	25,83	**0,043**
	With his wife	122	35,91	6,27		10,84	24,91	
	With his wife and children	19	36,63	6,02		11,83	22,39	
	Other (caregiver, sibling, relative)	20	36,69	6,71		17,38	21,58	

DISCUSSION

The concepts of loneliness and social isolation in older people were assessed in detail using all their components. The rate of loneliness was between 40% and 50%, with females aged 80 years and over having relatively higher loneliness rates (10,11). In a study carried out in Spain, 36.7% of individuals over the age of 65 years lived alone, and 56% of men and 72% of women in this population reported that they felt increasingly lonely with age (12).Approximately 33% of the Dutch population over 55 years of age live alone, and 4% experience severe loneliness (13). In comparison, we found that 14.5% of the patients felt lonely, and that the mean loneliness score of 41% was above average. In Denmark, 17.6% of older patients who applied to a family physician felt lonely (14).

The total scores of our patients (from UCLA-LS and NHP-SI) correlated with their education level. It has been determined that as educational levels increase, loneliness and social isolation decrease. A similar relationship between education level and loneliness was found in Sweden and Iran (10,15). In Iran, 29% of patients felt lonely according to the UCLA-LS scale. Here, a high education level, high income level, and having a current job were inversely related to feelings of loneliness. Moreover, marital status, having several children, gender, place of residence, living in a nursing home, low-income level, and healthy self-assessment level were found to be positively associated with loneliness (15).

In New Zealand, a negative relationship was found between loneliness and physical health and psychosocial well-being (16). We found that lone-

Table 4. Evaluation of the loneliness status of their patients by family physicians

Features		Those who live alone			Those who do not live alone		
		Family physician's answer			Family physician's answer		
		Not alone	Alone	p	Not alone	Alone	p
Gender	Female	1	17	0,349	83	2	0,256
	Male	4	17		71	5	
Chronic disease	Yes	5	34	1	7	143	0,464
	No	5	34		0	11	
Economical situation	Equal to monthly income	17	0	**0,035***	56	0	0,084
	Less than monthly income	17	5		92	6	
	More than monthly income	0	0		6	1	
Marital status	Married	2	6	0,248	141	3	**0,000***
	Not married	3	28		13	4	
Visited by relatives in the last month	At least once a week	3	20	0,688	79	2	0,106
	Less than once a week	1	11		64	3	
	Never visited	1	3		11	2	
Visiting relatives in the past month	At least once a week	2	13	0,318	42	2	0,900
	Less than once a week	1	16		78	3	
	Never visits	2	5		34	2	
Participation in out-of-home activities in the past month	At least once a week	1	8	0,201	31	3	0,065
	Less than once a week	0	12		56	4	
	Never participated	4	14		67	0	

liness and social isolation decreased significantly with improvements in the patient's economic situation, and the UCLA-LS loneliness score was considerably higher in patients with chronic diseases. These results were similar to a study in Iran, where it was revealed that self-perceptions of loneliness decreased as financial situations improved (15). Hence, low-income levels, living alone, and having a chronic illness were determined to be factors that increased levels of loneliness in older patients (17,18).

Comparing with whom the patients lived and their social isolation status, it was determined that people living alone were significantly more isolated than other groups. It was also found that those who had never married, were widowed, or divorced, and those who lived in nursing homes were statistically and significantly more lonely compared to those who lived with their spouses or had children. The mean loneliness scores of older people living in two different nursing homes in Turkey were 51.10 and 39.05, compared to 40.43 and 45.36 for those living at home or in institutions, respectively (19). In Denmark, it was found that older people who lived alone were 3.5 times more likely to experience loneliness, while those with low levels of social participation were 4 times more likely to feel alone. Furthermore, females were 1.8 times more likely to feel alone (20).

The frequency of being visited by relatives at home and visiting relatives were positively related to the patients' NHP-SI scores. It was also observed that as the frequency of mutual visits increased, the

Table 5. The overlap between the answers of the Family physician / patient for the question of whom the patients live with

Who Lives With						kappa	p
Patient's Answer	Family Physician's Answer						
	Alone N (%)	With his wife N (%)	With his wife and children N (%)	Other N (%)	Total		
Alone	34 **(82,9)**	2 %1,6	2 %6,1	1 %100	39	0,636	**0,000***
With his wife	2 (4,9)	113 **%90,4**	7 %21,2	0 %0,0	122		
With his wife and children	0 (0,0)	7 %5,6	12 **%36,4**	0 %0,0	19		
Other (caregiver, sibling, relative)	5 (12,2)	3 %2,4	12 %36,4	0 **%0,0**	20		
Total	41	125	33	1	200		

perception of social isolation decreased. A prospective study conducted with 334 older people (mean age of 72.6 years) in Germany predicted that being socially isolated was associated with low levels of outside physical activity and more depressive symptoms. Here, depression, living alone, and low social participation levels were determined as the three most effective parameters associated with feelings of loneliness (6). However, only 15.2% of our patients who were experiencing loneliness shared this situation with their doctors.

The responses of the family physicians and patients to the question of who the patients lived with significantly overlapped, with 14.5% of the patients reporting that they lived alone compared to family physicians, estimating that 21.5% lived alone. The family physicians knew 82.9% of those who lived alone in their answers. They also knew 47.4% of the patients who reported living alone and 81.9% of not-alone patients (14). In a similar study conducted in Denmark, 17.6% of patients said that they were lonely, while the family physicians stated that 23.2% of their patients felt lonely.

Generally, we found that the family physicians did not know about the patients' social relationships/social participation, whether they felt lonely when with others, or whether they had a relative to talk to when they needed support. In another study in which the social participation of patients was examined, the patients were analyzed by grouping them into two levels. The doctors knew that the involvement of patients in social activities was low and moderate, at 56.4%, and the higher ones were known by 62.8%. It was also found that family physicians were more unsuccessful in identifying whether patients felt alone if they were not living alone and thought their social participation was high (14).

In this paper, when the doctor and patient answers about who the patients lived with were compared, the family physicians correctly predicted that 82.9% lived alone. In a qualitative study in the Netherlands, it was determined that family physicians never asked patients about loneliness. This apparent contradiction could be because the family physicians included in our study had been working with the same patient group for a long time or because the study in the Netherlands was carried out in a limited group due to the employed methodology (13).

Strengths and Limitations

The strength of this study was guaranteed by examining five different Family Medicine Units, one of which was rural. In addition, we did not include consecutive applied patients to avoid familiarity with

the family physician's questions. The selection of family physicians from volunteers could have been a weakness of the study. This is because the sample did not reflect all family physicians' patients, since only patients who could come to the family physician and answer the questionnaire were included in the study.

CONCLUSIONS

This study revealed that social isolation was affected by the education level and economic status of the patients and with whom they lived. Furthermore, loneliness was affected by education level, financial situation, and the presence of a chronic disease. These results suggest that family physicians should be aware of their older patients' perceptions of loneliness and social isolation and should create an environment in which they can share these concerns. Considering that elderly patients who are socially isolated and living alone may require health institutions more frequently, family physicians should pay special attention to the social isolation and loneliness of the elderly.

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RESEARCH

ASSOCIATION BETWEEN C-REACTIVE PROTEIN/ALBUMIN AND C-REACTIVE PROTINE/PROTEIN RATIOS AND POOR OUTCOMES IN PALLIATIVE CARE PATIENTS WITH PRESSURE ULCERS

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Abstract

Introduction: Pressure ulcers are a significant cause of mortality and morbidity in older adult patients. Inflammatory processes accompany pressure ulcers. C-reactive protein and procalcitonin tests are sufficiently sensitive to show inflammation.Determining the ratios of these tests to each other may show a better performance in diagnosing and predicting the prognosis

Materials and Method: In this retrospective observational study, the records of patients with stage 2 and higher stage pressure ulcers who were followed up in the Adult Palliative Care Unit between January 1, 2019, and December 31, 2019 were reviewed. The National Pressure Injury Advisory Panel staging system was used for pressure ulcer staging. The patients were followed up for one year after hospitalization.

Results: The study included 151 patients with pressure ulcer who met the study criteria [80 (52.9%) female; 71 (47.1%) male] with a mean age of 74.7±12.6 years, and a mean length of hospital stay of 50.7±53.25 days. The one-year mortality rate was 70.8% (107/151).C-reaktif protein/albumin ratio and C-reaktif protein/total protein ratios were found to be significantly higher in the group with mortality ($p<0.05$). A ROC analysis revealed a cut-off value of 30.05 for the prediction of mortality in CRP, as the point at which the sum of the sensitivity and specificity values is the highest. The value of 35.2 predicting mortality for C-reaktif protein albumin ratio is the point at which the sum of the sensitivity and specificity values is the highest.

Conclusion: C-reaktif protein albumin ratio and CRP protein ratios demonstrated better prognosis and mortality prediction performance than CRP, albumin and total protein alone.

Keywords: Pressure Ulcer; Palliative Care; C-Reactive Protein.

INTRODUCTION

Pressure ulcers (PU) typically occur on the skin covering bony prominences and areas of the body that are subject to pressure. PUs are a common condition, especially in bedridden patients with limited mobility and older adults, with two-thirds of those who develop PUs being aged over 70 years (1). In addition to being a leading cause of both morbidity and mortality, PUs are responsible for disabling symptoms and so result in significant healthcare costs (1-2). In fact, the mortality rate associated with PUs has been reported to be 66% within a 12-week median follow-up period (3).

An inflammatory process usually accompanies the formation of PUs. C-reactive protein (CRP) and procalcitonin tests have been found to be sufficiently sensitive for the identification of the inflammation (4). The level of CRP, which is an essential acute-phase protein, is most commonly used for the identification of inflammation in daily practice. Procalcitonin is a calcitonin-related gene product expressed by human epithelial cells in response to bacterial infections (5), and it can be used as a blood infection biomarker for guiding antibiotic therapies in the presence of pulmonary infections (6). Moreover, procalcitonin is an important inflammatory marker for the monitoring of infections, especially in sepsis patients. Prior studies have examined the use of various inflammatory markers for prognostic purposes in relation to several diseases (7, 8), with CRP, albumin, procalcitonin, and protein tests being found to be easily accessible and highly applicable in hospital environments.

A high CRP/albumin ratio has recently been shown to associated with a poor prognosis and increased mortality in patients with various diseases, including sepsis, chronic obstructive pulmonary disease (COPD), liver cirrhosis, restless leg syndrome, inflammation, postoperative complications of abdominal surgeries, and certain malignancies (9,10,11). The CRP/albumin ratio is also a useful indicator of both mortality and morbidity in critically ill patients (12). The prediction of mortality based on the ratios of these parameters is known to be more accurate than the use of any one of them alone (13), although to the best of our knowledge no prior study has investigated the association between PUs and patients' CRP/protein, CRP/albumin, and/or CRP/procalcitonin ratios.

In light of prior findings, the present study examines the association between the CRP/protein, CRP/albumin, and CRP/procalcitonin ratios and mortality in patients with PUs.

MATERIALS AND METHODS

Approval for this retrospective observational study was obtained from the local clinical research ethics committee (No: 2020/10-111).

This study involved a retrospective review of patients with stage 2 or higher PUs who were followed up at the Adult Palliative Care Unit between January 1, 2019 and December 31, 2019. The National Pressure Injury Advisory Panel's staging system was used for the PU staging (14). Of the 195 patients initially reviewed, 44 with stage 1 PUs were excluded from the study due to the possibility of subjectivity in relation to their diagnosis. The remaining patients were followed up for one year after hospitalization. Patients with stage 2 and higher PUs were followed up and survived and non-survived were compared. The required data were retrieved from the electronic hospital information management system and the patients' files. After discharge, the patients were contacted by telephone to establish survival.

The patients' demographic characteristics, comorbidities, length of hospital stay (LOS), and presence of percutaneous enterogastrostomy or other catheters were recorded. The patients' initial laboratory parameters (from within 48 hours of their admission for palliative care) were also recorded from their charts and the electronic hospital information system. Any patients with data missing from their follow-up files were excluded from the study.

The reference values were 0–5 mg/l for CRP, 3.5–5.5 g/dl for albumin, 0–0.5 ng/ml for procalcitonin, and 5.5–8.8 g/l for protein. The CRP/albumin ratio (CAR) was calculated by dividing the CRP level by the albumin level, while the CRP/procalcitonin ratio (CPR) was calculated by dividing the CRP level by the procalcitonin level, and the CRP/protein ratio (CPrR) was calculated by dividing the CRP level by the protein level.

Statistical analyses

All the statistical analyses in this study were conducted using PASW Statistics (version 18.0, SPSS Inc., Chicago, USA) software. The demographic data were presented as the frequency and percentage, while the continuous variables were presented as the mean and standard deviation. A chi-square test was used to compare the categorical variables between the two groups. A Mann-Whitney U test and Student's t-test were used to perform pairwise comparisons of the non-normally and normally distributed continuous data, respectively. A receiver operating characteristic (ROC) analysis was conducted to identify the cut-off values for the ratios. A p-value of <0.05 was considered to be statistically significant.

RESULTS

A total of 195 patients were initially assessed for potential inclusion in this study, although 44 were subsequently excluded due to their decubitus ulcer level and/or missing data. As a consequence, a total of 151 patients with PUs who met the eligibility criteria were included in the study. The final sample comprised 80 (52.9%) females and 71 (47.1%) males. Moreover, the mean age was 74.7±12.6 years, the mean LOS was 50.7±53.2 days, and the one-year mortality rate was 70.8% (107/151). The patients' demographic characteristics and laboratory results are summarized in **Table 1**. The most common comorbidities in both groups (survived and exitus) were found to be similar, including infection (42.4%), cerebrovascular event (35.8%), hypertension (27.8%),

Table 1. Patients' demographic characteristics and laboratory results

Parameters	Exitus mean (SD)	Survived mean (SD)	p*
Age (years)	77.5 (11.0)	71.9 (14.2)	**0.022**
Length of Stay (days)	56.3 (73.7)	45.1 (98.8)	0.537
CRP (mg/dl)	79.4 (61.8)	65.2 (75.1)	0.274
Protein (g/dl)	5.4 (0.8)	5.7 (0.8)	0.082
Albumin (g/dl)	2.6 (0.5)	2.8 (0.5)	0.069
Procalcitonin	0.9 (1.7)	1.6 (4.5)	0.361
Glucose (mg/dl)	134.7 (93.5)	135.6 (65.3)	0.949
BUN (mg/dl)	31.3 (24.4)	24.3 (23.2)	0.103
Creatinine (mg/dl)	0.8 (0.5)	0.8 (0.7)	0.762
ALT (U/l)	27.1 (22.6)	27.6 (25.4)	0.920
AST (U/l)	29.9 (24.1)	30.9 (29.7)	0.856
Sodium (mmol/l)	137.5 (8.2)	136.9 (6.7)	0.607
Potassium (mmol/l)	3.8 (0.6)	3.7 (0.8)	0.402
TSH (uIU/ml)	1.4 (1.3)	1.8 (1.8)	0.257
Vitamin D (ng/ml)	13.7 (9.9)	15.1 (11.5)	0.560
WBC (/1000)	10.1 (5.7)	8.8 (3.7)	0.099
HGB (g/dl)	10.4 (2.2)	10.7 (1.6)	0.368
PLT (/1000)	158.7 (133.7)	193.5 (148.1)	0.180

and neurodegenerative diseases such as dementia or Parkinson's disease (15.3%) (**Table 2**). A comparison of the patients' genders and comorbidities is presented in **Table 3**.

The CAR and CPrR were found to be significantly higher in the group with mortality ($p<0.05$) (**Table 4**), although there was no statistically significant difference in terms of the CRP between the two groups.

The ROC analysis showed that a value of 30.05 when predicting mortality using the CRP represented the point at which the sum of the sensitivity and selectivity values was the highest (sensitivity 79.1%, specificity 46.2%). Furthermore, a value of 35.2 when predicting mortality using the CAR was the point at which the sum of the sensitivity and selectivity values was the highest (sensitivity 46.5%, specificity 79.2%). In addition, a value of 16.2 when predicting

Table 2. Frequency of patient comorbidities

Parameters	n	%
Infection	64	42.4%
Cerebrovascular Event	54	35.8%
Hypertension	42	27.8%
Neurodegenerative Disease	41	27.2%
Diabetes Mellitus	28	18.5%
Congestive Heart Failure	25	16.6%
Cancer	24	15.9%
Malnutrition	10	6.6%
Urinary Catheter	146	96.7%
Central Venous Catheter	79	52.3%
Percutaneous Endoscopic Gastrostomy	51	33.8%

Table 3. Comparison of patients' gender and comorbidities

Parameters		Exitus, n (%)	Survived, n (%)	p*
Gender	Male	22 (31.0)	49 (69.0)	0.638
	Female	22 (27.5)	58 (72.5)	
Hypertension	No	32 (29.4)	77 (70.6)	0.924
	Yes	12 (28.6)	30 (71.4)	
Diabetes Mellitus	No	38 (30.9)	85 (69.1)	0.320
	Yes	6 (21.4)	22 (78.6)	
Cerebrovascular Event	No	29 (29.9)	68 (70.1)	0.784
	Yes	15 (27.8)	39 (72.2)	
Cancer	No	32 (25.2)	95 (74.8)	**0.014**
	Yes	12 (50.0)	12 (50.0)	

Table 4. Comparison of the CRP, protein, CRP/albumin and CRP/protein results

Parameters	Cut-off value	AUC (95% CI)	p	Sensitivity %	Specificity %
CRP (mg/dl)	30.1	0.621 (0.527-0.716)	0.020	79.1	46.2
CRP/albumin	35.2	0.640 (0.543-0.737)	0.007	46.5	79.2
CRP/protein	6.3	0.633 (0.538-0.728)	0.011	74.4	50.9

mortality using the CPrR was the point at which the sum of the sensitivity and specificity values was the highest (sensitivity 41.9%, specificity 79.2%).

DISCUSSION

The present study sought to identify a laboratory value that can be used alongside the CRP level and inflammation-related parameters to predict mortality in elderly patients with PUs. As there are many factors that influence the CRP level (e.g., infection, rheumatologic disease, cancer, etc.) (15), we explored the ratios of the laboratory values that are less affected by the inflammatory factors assessed when following up PUs. As elderly patients may experience a decrease in their inflammatory response, the CRP level alone may fail to fully indicate the severity of the inflammation in cases of PUs (16).

CRP is recognized as a significant laboratory parameter when it comes to the prediction of survival and mortality (17). The CRP test is sensitive to tissue damage, acute infection, and inflammatory conditions, and the CRP level is known to increase in cases in which tissue damage and inflammation occur together, as is common with PUs (18). Procalcitonin is an acute-phase reactant that increases in patients with infectious diseases such as sepsis, pneumonia, and PUs (19,20). The CAR provides data concerning both inflammation and malnutrition (1), which is why it is commonly used in practice as a prognostic indicator for several diseases, especially during the follow-up of critical patients hospitalized for intensive care or palliative care (2). Indeed, high CRP levels are an important predictor of mortality in critically ill patients (21).

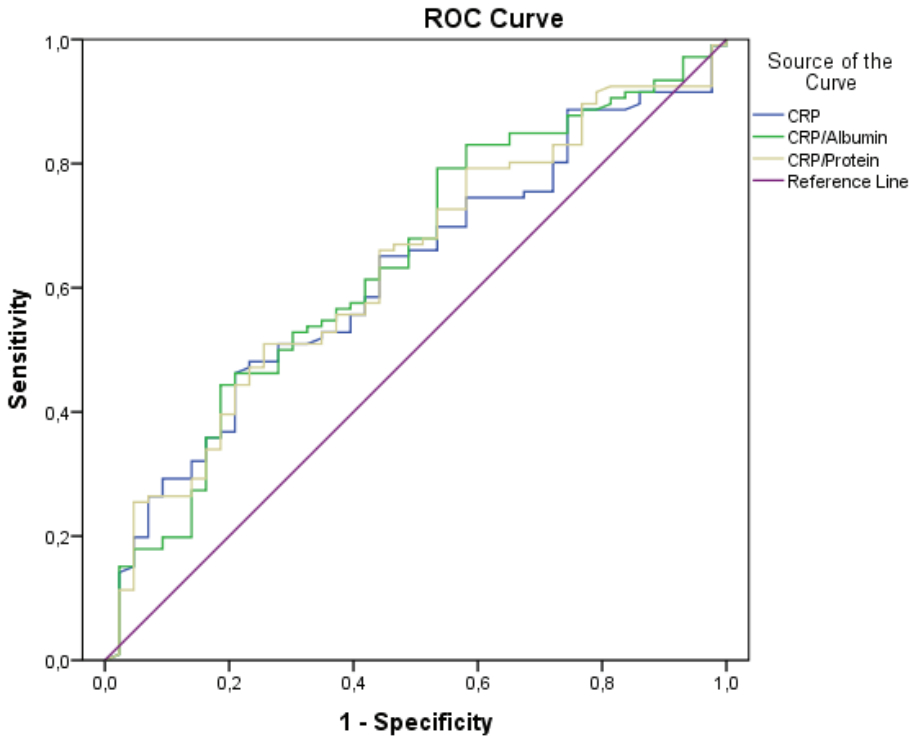
In a previous study, Amano et al. identified a significant relationship between the CRP levels, symptoms, and daily life activities of advanced cancer patients receiving palliative care (22). Ranzani et al. conducted a study involving 334 patients hospitalized in the intensive care unit for a minimum of 72 hours with a diagnosis of sepsis and septic shock, and they found both the CRP level and the CAR to be independent risk factors for mortality (9). Oh et al. reported that a one unit increase in the CAR leads to an 11% increase in the 30-day mortality risk among critically ill intensive care patients, while they identified the albumin level alone as a more reliable parameter than the CAR when it comes to predicting 30-day mortality (12).

CONCLUSION

In the present study, the CAR and CPrR were identified as useful predictors of mortality in patients with PUs, although the contribution of the CPR was found to be more limited. Based on the findings of this study, it can be concluded that the CAR and CPrR can be used as predictive parameters concerning the prognosis and mortality of patients with PUs. While this study found that the CPR could contribute to the determination of patients' prognosis and mortality, its effect was statistically insignificant. This finding may be attributable to the relatively small number of patients involved in the study and/or the impact of PUs and nutritional status on patients' albumin levels.

Limitations

It must be acknowledged that the findings of this study were based on limited data due to its retrospective and single-center design, which limits the generalizability of the results. In addition, the participating PU patients were largely older adults with multiple comorbidities, which may have influenced the results.



Area Under the Curve					
Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
CRP	0.621	0.048	0.020	0.527	0.716
CRP/Albumin	0.640	0.050	0.007	0.543	0.737
CRP/Protein	0.633	0.049	0.011	0.538	0.728
a. Under the nonparametric assumption					
b. Null hypothesis: true area = 0.5					

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RESEARCH

STAFF-BASED INDIVIDUALIZED CARE INVENTORY: PSYCHOMETRIC PROPERTIES OF THE TURKISH VERSION

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Abstract

Introduction: The Individualized Care Inventory–short form is a 22-item self-report measure with four sub-dimensions: knowing the resident, residents' autonomy and choice, staff-to-resident communication, and staff-to-staff communication. The inventory is used for in the context of dementia care. The present study aimed to assess the inventory's psychometric properties with a sample of formal caregivers from nursing homes.

Materials and Methods: The study was conducted with 184 formal caregivers from 13 different nursing homes in Istanbul between July and September 2020. This study used translation and back translation for the scale's language equivalence and expert opinion for the content validity. The reliability and validity were tested by exploratory and confirmatory factor analysis, test-retest correlation analyses and internal consistency.

Results: The content validity index for the inventory was 0.93. In the construct validity analysis, four sub-dimensions corresponding to the original factor structure were derived for the inventory. Cronbach's alpha values for the factors, namely knowing the resident (α = 0.618), autonomy and choice of the resident (α = 0.768), and communication (α = 0.713) were satisfactory. The tests-retests was conducted in a 15–25-day intervals, and all sub-dimensions were positively correlated (r: 0.236–0.390) ($p < 0.05$).

Conclusion: The Turkish Individualized Care Inventory is a valid and reliable tool that can be used to measure the individualized care approaches of formal caregivers in nursing homes.

Keywords: Dementia; Patient-Centered Care; Long-Term Care; Psychometrics.

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INTRODUCTION

Individualized care, in contrast to routine or task-oriented care, focuses on meeting the needs of a particular patient at a particular point in time (1) and encompasses the values and principles of holistic care, including respect for individuality, attention to nursing needs, promotion of independence, partnership and negotiation of care, and equity and fairness (2). The critical, common themes characterizing individual-centered care are patient participation and inclusion, communication between the patient and healthcare worker, and the conditions of the place where healthcare is provided (3).

Caring for people with dementia living with multiple chronic conditions and/or functional limitations involves enhancing safety, quality of care, and quality of life through individualized care (IC). Individualized care is a standard practice that takes into account the individuality of the patients and encourages their participation in daily activities and decision making (4). IC promotes the wellbeing, health outcomes, individual functioning, autonomy, and satisfaction of the patient by tailoring the care activities, preferences, and choices to each individual's unique characteristics (5).

To promote person-centered care (PCC) practices and research in geriatric care, it is necessary to ensure that evaluations are carried out using specific measurement tools with appropriate psychometric properties. Since the difficulties and complexities in providing IC for older people, especially people with dementia, are evident (6), Individualized Care Inventory (ICI) which is easy to use, have been developed to measure and understand the individualized care approaches in long-term care environments. Other observational tools, such as Dementia Care Mapping (7) and Resident-centered Assessment of Interactions with Staff and Engagement (RAISE) (8), require large amounts of time to implement and are thus difficult to use with large sample sizes. Furthermore, the Individualized Care Scale (ICS) was developed by Suhonen and colleagues (2007) for older people's care settings but not specifically for dementia care (9). ICS's intended use was in acute care, within a framework of nursing science, and thus would be more appropriate in such settings. Notably, a comparative study of ICI and ICS instruments revealed that a combination of these two tools would be more comprehensive and informative in assessing individualized nursing care for older people (10). While the ICS has already been adapted to the Turkish population by Acaroglu and colleagues (11), a psychometric evaluation and a cultural adaptation of the ICI are required to ensure that both instruments can be used in combination in Turkish older adult care settings.

The ICI was designed to measure the approaches of staff caring for people with dementia based on the following domains: knowing the residents, upholding patient autonomy and choice, and maintaining staff-to-resident and staff-to-staff communication (4). The inventory enables self-evaluations of formal caregivers' individualized care approaches with the aim of enhancing person-centered care (12). Notably, the psychometric properties of the English-Canadian (4) and Chinese (12) versions of the ICI have been examined. Furthermore, O'Rourke and colleagues analyzed the inventory to determine and compare the structures of registered nurses and licensed practical nurses' responses; the formal caregivers involved in the study interpreted and responded to ICI items in a similar manner, indicating the research and practical suitability of this inventory for both groups (13).

Thus, research indicates that interventions aiming to improve person-centered care in long-term care facilities could use the ICI to assess the approaches of formal caregivers working in dementia care. However, it is essential that researchers and managers in the field are equipped with accurate measures to evaluate the effectiveness of individualized care approaches and interventions. To this end, the purpose of the present study was to evaluate the validity and reliability of the short 22-item ICI

for dementia care with a sample of Turkish-speaking formal caregivers providing dementia care in nursing homes.

MATERIALS AND METHODS

Design

A cross-sectional design was adopted to test whether the psychometric properties of the staff-based ICI are suitable for the inventory's use with Turkish-speaking formal caregivers and nurses in long-term care facilities. The STROBE checklist was used for this article (14).

Participants and Data Collection

This methodological and cross-sectional study was conducted to assess the reliability and validity of the Turkish staff-based individualized care inventory (ICI). Physical copies of the self-administered survey forms were sent to 13 nursing homes (12 privately owned and one municipality-owned) in Istanbul by post between July and September 2020. The nursing homes' bed capacities varied from 20 to 120, and the bed allocations were not exclusively for people with dementia but also included other residents without dementia. Nurses, elderly care technicians, and certified caregivers of people with dementia were asked to participate in the study. For validation studies, the larger the sample size, the better; however, the subject-to-item ratio is also suitable for determining sample size if it is intuitively more useful for the researchers and allows for utilizing samples of appropriate sizes (15). Accordingly, the optimal sample size of this study was calculated based on the number of items in ICI, that is, 22. The researchers aimed to reach a sufficiently large sample size with a subject-to-item ratio between 5:1 and 10:1. Subsequently, a total of 184 participants from the 13 facilities were included in the study, resulting in a subject-to-item ratio of 8.4:1, which fell within the targeted range. Retests were conducted with 101 participants from the same facilities in 15–25-day intervals.

Staff-Based Individualized Care Inventory

The ICI was developed by Chappell and colleagues (2007) to evaluate healthcare staff's perceptions of individualized care provided to people with dementia (4). The inventory has four dimensions: (i) knowing the person or resident (IC-know), (ii) providing opportunities for autonomy and choice (IC-autonomy), (iii) ensuring staff-to-staff communication (IC-communication-SS) and staff-to-resident communication (IC-communication-SR). The long (47 items) and short (22 items) versions of the ICI were developed by Chappell et al. after a factor analysis. The responses for IC-know, IC-communication-SS, and IC-communication-SR were collected using a four-point Likert-type scale (1 = strongly disagree, 2 = somewhat disagree, 3 = somewhat agree, 4 = strongly agree) and a five-point Likert-type scale for IC-autonomy (1 = very frequently, 2 = frequently, 3 = occasionally, 4 = seldom, 5 = never). The same scoring type was used for both short and long versions.

The current study used the short version of the ICI. The following four sub-dimensions and their Cronbach's alpha values were considered: IC-know (0.75), IC-autonomy (0.84), IC-communication-SR (0.67) and IC-communication-SS (0.77) (4).

IC-know refers to the staff's own perceptions of how well they know the individuals they are caring for, and the six-item IC-know scale results in scores between 6 and 24. The eight-item IC-autonomy scale measures the general environment in which the staff work, and the possible scores fall between 8 and 40. The three-item IC-communication-SR scale focuses on how the staff communicates with the residents, with possible scores between 3 and 12. Finally, the five-item IC-communication-SS scale reflects the way the staff communicate with one another and with their supervisors, with possible scores lying between 5 and 20. Higher scores indicate better results in each domain. Notably, the domains in the original version of the ICI were found to be highly correlated with one another, with Pearson's r ranging from 0.85 to 0.94 (4).

Translation Procedure

The original questionnaire was independently translated from English to Turkish by three individual researchers and one professional translation office and then back-translated into English by another translation office. The back-translated version was then compared with the English version of the ICI to ensure that the items had no differences in meaning and to confirm the items' conceptual meaning, clarity, and terminology.

Data Analysis

For the statistical data analysis, IBM SPSS Statistics (version 26) and IBM SPSS AMOS (Analysis of Moment Structures) (version 26) were used. Missing data accounted for less than 1% of all the data, and case mean substitution was used to replace the missing values—a technique generally recommended for the same (16).

Next, content validity was evaluated. The translated final version of the ICI was submitted to a panel of six specialists who were informed about the scale and the concepts involved. These experts in geriatric nursing or dementia care were asked to evaluate the 22 items of the inventory, compare the items with those of the original instrument, and evaluate each item on a four-point scale (4 = very relevant, 3 = relevant with some adjustment to phrasing, 2 = only relevant if phrasing is profoundly adjusted, and 1 = not relevant). The content validity index (CVI) was calculated based on the number of experts who provided a rating of 3 or 4 for each item, and the total scores were divided by the total number of experts. A CVI score of 0.80 or above was considered acceptable (16).

Descriptive statistics (mean, frequency, and percentage) were used to describe the participants' sociodemographic and job-related characteristics. To determine the construct validity of the scale, an exploratory factor analysis (EFA) and a confirmatory factor analysis (CFA) were carried out. In the reliability tests conducted, internal consistency was assessed using item–total correlations and Cronbach's alpha. Test-retest results were compared using Spearman's correlation.

Ethical Considerations

Written permission to use the ICI was obtained from the authors who developed the instrument. Permission to undertake the study was obtained from Koç University Clinical Research Ethical Review Board (NO: 2020.011.IRB1.002). Participants were informed of the purpose of the study and invited to participate. Participants were assured of their right to refuse to participate or to withdraw from the study at any stage.

RESULTS

Sample Characteristics

A total of 256 staff and care providers from 13 eligible facilities were asked to participate in the study, of which 184 agreed. The majority of participants were female (71%), with a mean age of 31 years; 49.5% were certified caregivers, 31.5% were nurses, and 18.5% were elderly care technicians. Most of the participants had attained a high school level of education (40.2%) and had an average of 6 years of job experience in elderly care and 4.2 years of job experience in dementia care. 72.8% of the staff had not undergone specific education for dementia issues or dementia care **(Table 1).**

Construct Validity

Construct validity for the Turkish version of the ICI was analyzed using EFA and CFA. Before conducting these analyses, the Kaiser–Meyer–Olkin (KMO) test and Bartlett's test were conducted. Specifically, the adequacy of the sample size was determined using the KMO value; the result was 0.706, indicating that the sample size was suitable for EFA. The results of the Bartlett's Test of Sphericity were statistically significant ($\chi^2 = 1200.455$, $p = 0.00$, $p < 0.01$). This result indicates the assumption of equal variances for the sample is true before running certain statistical tests.

Table 1. Sample Characteristics

Characteristics		n	%
Age	18-25 age	76	41.8
	26-36 age	47	25.8
	37-56 age	59	32.4
Gender	Female	130	71
	Male	53	29
Education	Primary school	37	20.1
	High school	74	40.2
	Vocational school	56	30.4
	University degree	13	7.1
	Graduate degree	2	1.1
Job title	Nurse	58	31.5
	Elderly care technician	34	18.5
	Certified Caregiver	91	49.5
Elderly care experience	0-2 Years	24	14.4
	2-4 Years	55	32.9
	4-8 Years	37	22.2
	8-12 Years	30	17.9
	12-18 Years	15	9.0
	>18 Years	6	3.6
Dementia specific education	Yes	46	27.2
	No	123	72.8

The EFA analysis revealed a four-factor structure for the scale. A principal component analysis was used as the extraction method, and the item loadings were between 0.40 and 0.82 after rotation (varimax). The four-factor structure was found to explain 47.153% of the total variance.

The model fit of the item–factor relationship derived by EFA was assured by CFA. CFA fit indices were used to reveal the adequacy of the model in this study, namely the chi-square fit, goodness-of-fit index (GFI), root mean square error of approximation (RMSEA), comparison of model fit indices (CFI), and normed fit index (NFI). The scale's fit indices were significant after modification ($\chi 2 = 294.97$; df = 155, $p = 0.00$; $p < 0.01$). The fit index values were as follows: GFI = 0.865; RMSEA = 0.070; CFI = 0.849; NFI = 0.736 **(Table 2).** Two items in the ICI were found to be meaningless based on their regression weights and $p < 0.05$ statistical significance level and were thus deleted. One of the deleted items was from the IC-know subscale, and the other was from the IC-autonomy subscale. Accordingly, the Turkish version of the ICI was reduced to 20 items. Modification processes were carried out by creating covariance matrices between the appropriate items. The fit indices of the model provided an acceptable level of validity after these modifications.

Reliability Analysis

The reliability of the inventory was evaluated using an item–total correlation test, Cronbach's alpha coefficient test, and test-retest correlation. The Cronbach's alpha values of the IC-know, IC-autonomy, and IC-communication subscales were 0.618, 0.768, and 0.718, respectively. Item–total correlation coefficients were corrected and calculated for the items of each dimension of the ICI. Average item-total correlations ranged between 0.194 and 0.543 for

Table 2. Fit Indices Obtained from CFA for the ICI

Fit Indices	Before Modification	After Modification
χ^2 / df	531.84 / 203 = 2.62	294.97 / 155 = 1.903
RMSEA	0.094	0.070
SRMR	0.093	0.081
CFI	0.679	0.849
GFI	0.792	0.865
NFI	0.577	0.736
AGFI	0.741	0.817

Abbreviations: CFA, confirmatory factor analysis; CFI, comparative fit index; df, degree of freedom; GFI, goodness of fit index; NFI, normed fit index; AGFI, adjusted goodness of fit index; SRMR, standardized root mean square residual; RMSEA, root mean square error of approximation; χ2, chi-square.

IC-know, 0.290 and 0.633 for IC-autonomy, 0.261 and 0.575 for IC-communication as a whole, 0.308 and 0.403 for IC-communication-SR, and 0.350 and 0.637 for IC-communication-SS **(Table 3).**

A total of 101 participants agreed to take the retest. The test-retest measurements were taken in intervals of 15–25 days. The correlation result was positive for the sub-dimensions (r = 0.236, 0.390) and statistically significant but with low correlation ($p < 0.001$, $p < 0.05$) **(Table 4).**

Table 3. Internal Consistency and Item-Total-Item Correlations of ICI

ICI and Sub-Domains	Cronbach Alpha	Item-Total Item Correlations	Mean Score ± SD
ICI total	0.779	0.142-0.742	67.46±8.09
IC-Know (5 items)	0.618	0.194-0.543	16.59±2.94
IC-Autonomy (7 items)	0.768	0.290-0.633	27.07±5.21
IC-Communication (8 items)	0.713	0.261-0.575	24.34±3.79
IC-SR Communication (3 items)	0.555	0.308-0.403	7.37±1.89
IC-SS Communication (5 items)	0.748	0.350-0.637	16.97±2.81

Table 4. Test-Retest Reliability Analysis of ICI

ICI Sub-Scales	Test Mean ± SD	Re-test Mean ± SD	r*	p
IC-Know	3.31 ± 0.58	2.96 ± 0.62	0.349	0.000
IC-Autonomy	3.59 ± 0.58	3.95 ± 0.65	0.390	0.000
IC-SR	2.4 ± 0.60	2.47 ± 0.64	0.236	0.018
IC-SS	3.39 ± 0.563	3.44 ± 0.44	0.346	0.000

*Spearman correlation test, n=101

DISCUSSION

To the best of our knowledge, this is the first study to evaluate the validity and reliability of the Turkish version of the ICI for dementia care in nursing home settings and to indicate the psychometric properties to use in dementia care practice and research. The reliability and validity tests revealed that the Turkish ICI's psychometric properties are similar to those of the original inventory.

Content validity was assessed by calculating the content validity index (CVI), which indicates good content validity if the value is above 80% (17). The content validity of the ICI was found to be 93.7%, which was excellent. Sample size recommendations for a reliability analysis vary from 200 to 1000 in the literature, and validity studies and factor analyses require 10 subjects per item to generate replicable results (18). Although the target was 5–10 subjects per item, only 184 people agreed to participate in this study due to restrictions and workload pressure during the COVID-19 pandemic period, resulting in an 8.4:1 subject-to-item ratio.

One of the most commonly used methods for assessing the reliability of a measurement tool is to evaluate the internal consistency of the scale. Accordingly, the reliability of the Turkish ICI and its sub-dimensions were evaluated, revealing moderate to good internal consistency. The internal consistency of the IC-communication-SR subscale was low. A low internal consistency means that there are items or sets of items which are not correlating well with each other. The low internal consistency for IC-communication-SR was also determined in adaptation of ICI to Chinese language (12). Notably, in the reliability and validity study of the Chinese version of the ICI, Cronbach's alpha values were as follows: 0.67 for "knowing residents," 0.72 for "resident autonomy," 0.63 for "resident-to-staff communication," and 0.80 for "staff-to-staff communication" (12). When the items of both subscales (resident-to-staff and staff-to-staff communication) were combined under the communication dimension in the Chinese version, Cronbach's alpha value (α= 0.79) was more acceptable (12) and close to the Turkish version's value of 0.779. Therefore, in the Turkish version of ICI resident-to-staff and staff-to-staff communication sub-dimension should be combined under communication sub-dimension for better Cronbach's alpha value.

The exploratory factor analysis in the present study revealed a four-factor structure similar to that of the English-Canadian and Chinese versions (4, 12). Furthermore, a confirmatory factor analysis was used to reveal the adequacy of the model fit of the Turkish version. Two items—one for IC-know and one for IC-autonomy—were deleted due to their low regression weights in the CFA. The resulting 20-item inventory was found to adequately fit the model after a few modifications of the items.

The item–total score correlations were generally acceptable. The time invariance of the ICI was evaluated using the test-retest correlation. The results of two measurements under the same circumstances but with an interval of 15–25 days were evaluated. The test-retest correlation result was positive for all domains (r = 0.236, 0.390), and a low but statistically significant correlation was found.

There are some limitations to the study that need to be addressed. First, test-retest reliability was analyzed following a 15–25-day interval, which was longer than the typical period and may have affected the results. The study was conducted during the COVID-19 pandemic, and the restrictions in place may have had a negative effect on the care approaches and responses of the caregivers. Thus, additional studies with larger samples are needed to further analyze the ICI and underlying attributes of individual care.

The present study evidences the usefulness of ICI for dementia care and can guide the development of individualized dementia care in Turkish nursing homes, in turn improving the quality and

effectiveness of nursing care in long-term care environments. The short 20-item ICI instrument is precise and focuses on the individualized care approaches required for caregivers to provide quality care. Furthermore, this assessment tool would be easy to use in busy, long-term care environments, and it may also be applicable to healthcare professionals in other settings.

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RESEARCH

THE PREDICTORS OF IN-HOSPITAL MORTALITY IN HYPERTENSIVE ELDERLY INTENSIVE CARE UNIT PATIENTS WITH CORONAVIRUS DISEASE 2019

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Abstract

Introduction: Advanced age is an important prognostic indicator for the mortality of coronavirus disease 2019, especially in patients over 65. Patients with chronic underlying conditions such as hypertension showed the worst outcomes. This study aimed to identify predictors of mortality in elderly hypertensive patients hospitalized in intensive care units.

Materials and Methods: Demographic, clinical, treatment, and laboratory data were extracted from electronic medical records and compared between survivors and non-survivors. Univariate and multivariate logistic regression methods were used to explore the indicators of in-hospital mortality.

Results: One hundred and ninety-eight patients with a median age of 75 years (65–94 years) were included in this study, of whom 95 were discharged from the intensive care units, and 103 died. Shortness of breath [hazard ratio (HR): 1.65, 95% confidence interval (CI): 1.04–2.61, p: 0.034], C-reactive protein (CRP)/albumin ratio (>51.32) (HR: 1.83, 95% CI: 1.12–2.97, p: 0.015), serum creatinine (>1.62 mg/dl) (HR: 2.04, 95% CI: 1.13–3.33, p: 0.001), aspartate transaminase (>34 u/l) (HR: 1.99, 95% CI: 1.28–3.09, p: 0.002), D-dimer (>781 ng/ml) (HR: 1.59, 95% CI: 1.04–2.43, p: 0.031), leukocyte (>12,000´ 10^3/µl) (HR: 1.68, 95% CI: 1.09–2.59, p: 0.018) and lymphocyte count, (≤660´ 10^3/µl) (HR: 1.76, 95% CI: 1.17–2.63, p: 0.006) were independent predictors for mortality in elderly hypertensive patients.

Conclusion: Using these predictors with cut-off values can identify patients at risk of death and needing aggressive intervention earlier in the disease course.

Keywords: Aged; COVID-19; Hypertension; Mortality; Patient admission; Prognosis.

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INTRODUCTION

The 2019 novel coronavirus disease (COVID-19), which emerged in December 2019 and was declared a pandemic in March 2020, remains a global public health concern. There is a wide spectrum of clinical presentations, ranging from asymptomatic status to respiratory failure requiring respiratory support to death. Specifically, older patients (>65 years) with comorbidities are at high risk of death, and older age may independently predict 60-day mortality after admission to the intensive care unit (ICU) (1, 2).

Several studies have shown that hypertension may be associated with a poor prognosis in COVID-19 (3-5). It has been reported that after adjusting for confounders, compared with non-hypertensive patients, hypertensive patients continue to have a two-fold increased risk of COVID-19 mortality (6). Nevertheless, the fact that hypertension is often associated with advanced age and other cardiovascular diseases in the general population and that this condition may contribute to COVID-19 causes its independent role to be debated. There is insufficient data on the factors determining prognosis, especially in elderly patients with hypertensive COVID-19.

This study aimed to identify predictors of in-hospital mortality among older hypertensive patients with COVID-19 by investigating the potential prognostic roles of age, gender, COVID-19 related symptoms, comorbidities, and specific laboratory markers on admission.

MATERIALS AND METHODS

Study design and participants

The training cohort participants were consecutive patients diagnosed with COVID-19 by at least two positive nasopharyngeal or oropharyngeal SARS-CoV-2 reverse-transcriptase-polymerase-chain-reaction tests (SARS-CoV-2 (2019-nCoV) with a qPCR Detection Kit and Bio-Speedy) in the Manisa Merkezefendi State Hospital (Pandemic Hospital). Among these patients, those aged ≥ 65 years who were diagnosed with hypertension before hospitalization, it was noted that at least one antihypertensive drug was used, and they were followed up in the ICU and were included in the study. Indications for ICU hospitalization were determined according to the COVID-19 treatment guideline of the Republic of Turkey Ministry of Health. Indications included uncontrollable fever, respiratory rate > 30/minutes, severe respiratory distress, SpO2 < 90% on room air, bilateral multilobar ground-glass opacities, intense consolidations on computed tomography, and need for mechanical ventilation due to respiratory failure. All data were extracted from the electronic medical records of patients hospitalized between April 1st, 2020, and December 31st, 2020. One hundred and ninety-eight patients with an outcome (discharged or dead) were enrolled in the study.

The study protocol was approved by the Manisa Celal Bayar University Clinical Research Ethics Committee (Decision No.85252386-050.04.04.04) and followed the Declaration of Helsinki. Written informed consent was not obtained because the data were anonymous, and the study was observational. However, patients or relatives were verbally informed that their data would be used anonymously for medical studies, and their permission was obtained.

Process of data extraction

We obtained demographic data, epidemiological characteristics, clinical features, disease severity, laboratory tests, and treatment results from the medical record system. Hypertension and treatment were stratified according to medical history or medications administered prior to infection. The laboratory data of patients within the first 24 h after admission to the hospital were evaluated. Data were collected and analyzed once all included patients died or were discharged from the ICU.

Statistical Analyses

Statistical analyses were performed using SPSS Statistics version 26.0 (IBM Corp. Released 2019.

IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). Figures were constructed using GraphPad Prism version 8.0.0 for Windows (GraphPad Software, San Diego, California, USA, www.graphpad.com). Categorical variables were summarized using frequencies and proportions and compared using Pearson's chi-square or Fisher's exact test in cases where applicable conditions were unmet. The Shapiro-Wilk test was used to check whether the continuous variables were normally distributed. Continuous variables were reported as mean values ± standard deviations (SD) or medians (minimum-maximum) for non-normally distributed data and compared using Student's t-test or the non-parametric Mann-Whitney U test. The predictive value of the variables was evaluated by measuring the area under the receiver operating characteristic (ROC) curve. The optimal threshold value for clinical stratification (cut-off value) was obtained by calculating the Youden index. The Kaplan–Meier method was used for univariate survival analysis, and the log-rank test was used to assess the statistical significance between the survival curves of the models. All variables with p values of ≤ 0.20 from the Cox univariate analyses were entered into a multivariate analysis using the backward stepwise Cox regression model. We considered a p-value < 0.05 as statistically significant for all analyses.

RESULTS

During the study period, 489 COVID-19 patients hospitalized in the ICU were evaluated. Of these, 307 were aged ≥65 years. Among the 307 patients, 198 diagnosed with hypertension and using at least one antihypertensive drug were included in the study. The baseline demographic and clinical characteristics of all participants at admission are presented in Table 1 based on ICU survival. The median age of the non-survivor group was significantly higher than that of the survivor group (77 vs. 74 years, p = 0.002). While 55.3% of the non-survivor group was male, 38.9% of the survivor group was male (P = 0.021). The prevalence of symptoms on admission, such as fever, headache, diarrhea, fatigue, muscle ache, or taste dysfunction, was also similar between the two groups. However, shortness of breath was more common among the non-survivors. Shortness of breath was the most common symptom in all the patients (62.6%). In contrast, cough and chest pain were more common among survivors. Renal failure was more common in the non-survivors than in the survivors (41.7% vs. 21.1%, p = 0.002). However, there were no statistically significant differences between the hemodialysis groups. However, the incidence of diabetes mellitus was twice as high in the survivors (42.1% vs. 20.4%, p = 0.001). The other comorbid conditions were similar in both groups. While 97.1% of the non-survivors required invasive mechanical ventilation, this rate was 48% in the survivor group (p < 0.001). Non-survivors had a shorter length of in-ICU stay than survivors did. The median length of stay in the intensive care unit for non-survivors was 8 (min-max, 1–33) days, while the median stay in the intensive care unit for survivors was 14 (min-max, 5–37) days (p < 0.001).

Laboratory parameters and medications used are listed in Table 1. Higher urea, serum creatinine, uric acid, aspartate transaminase, alanine transaminase, D-dimer, troponin, ferritin, leukocyte, CRP, and CRP/albumin ratios were the laboratory parameters measured in non-survivors. Albumin and lymphocyte levels were lower in the non-survivors than in the survivors. The use of angiotensin-converting enzyme (ACE)/angiotensin-receptor blockers (ARB) class drugs for antihypertensive treatment was higher in the survivor group (71.6% vs. 56.3%, p:0.026). In addition, the use of dihydroxycalcium canal blockers was higher in the survivor group (46.6% vs. 31.6%, p = 0.031). Both groups were similar in beta-blockers, non-dihydroxycalcium canal blockers, and aldosterone antagonists. It was observed that more favipiravir, immunosuppressive agents, and steroids were used in non-survivors than survivors during their stay in the intensive care unit.

Table 1. Baseline characteristics, laboratory parameters and medications of study population.

	Total (n:198)	Elder Hypertensive Survivors (n:95)	Elder Hypertensive Non-Survivors (n:103)	p-value
Age, years	75.0 (65.0-94.0)	74.0 (65.0-89.0)	77.0 (65.0-94.0)	**0.002**
Gender (male), n (%)	94 (47.5)	37 (38.9)	57 (55.3)	**0.021**
Body mass index, kg/m^2	24.9 (18.2-35.4)	25.3 (18.3-35.0)	24.4 (18.2-35.4)	0.245
Systolic blood pressure, mmHg	114.5 (70.0-196.0)	145.0 (75.0-190.0)	144.0 (70.0-196.0)	0.452
Diastolic blood pressure, mmHg	87.5 (30.0-126.0)	88.0 (45.0-126.0)	87.0 (30.0-120.0)	0.309
Symptoms at admission, n (%)				
Fever	109 (55.1)	52 (54.7)	57 (55.3)	0.932
Cough	59 (29.8)	35 (36.8)	24 (23.3)	**0.037**
Shortness of breath	124 (62.6)	49 (51.6)	75 (72.8)	**0.002**
Headache	9 (4.5)	5 (5.3)	4 (3.9)	0.641
Diarrhoea	17 (8.6)	12 (12.6)	5 (4.9)	0.051
Fatigue, tiredness	15 (7.6)	11 (11.6)	4 (3.9)	0.041
Palpitation	5 (2.5)	2 (2.1)	3 (2.9)	0.718
Muscle ache	20 (10.1)	12 (12.6)	8 (7.8)	0.256
Sore throat	5 (2.5)	3 (3.2)	2 (1.9)	0.672
Chest pain	5 (2.5)	5 (5.3)	0 (0.0)	**0.024**
Inability to taste	7 (3.5)	6 (6.3)	1 (1.0)	0.057
Comorbidities, n (%)				
Diabetes Mellitus	61 (30.8)	40 (42.1)	21 (20.4)	**0.001**
Anemia	51 (25.8)	21 (22.1)	30 (29.1)	0.259
Renal failure	63 (31.8)	20 (21.1)	43 (41.7)	**0.002**
Dialysis	20 (10.1)	6 (6.3)	14 (13.6)	0.090
Coronary Artery Disease	46 (23.3)	19 (20.0)	27 (26.2)	0.301
Peripheral vascular disease	4 (2.0)	4 (4.2)	0 (0.0)	0.051
Chronic heart failure (HFrEF)	24 (12.1)	10 (10.5)	14 (13.6)	0.509
COPD	33 (16.7)	15 (15.8)	18 (17.5)	0.750
Hyperlipidemia	21 (10.6)	12 (12.6)	9 (8.7)	0.374
Malignancy	11 (5.6)	4 (4.2)	7 (4.2)	0.427
CVA/TIA	19 (9.6)	8 (8.4)	11 (10.7)	0.590
Smoking	28 (14.1)	12 (12.6)	16 (15.5)	0.558
Invasive mechanic ventilation, n (%)	115 (58.1)	15 (48.0)	100 (97.1)	**<0.001**
Length of in-ICU stay (days)	10.0 (1.0-37.0)	14.0 (5.0-37.0)	8.0 (1.0-33.0)	**<0.001**

Laboratory parameters					
	Urea, mg/dl	65 (18-398)	54 (18-258)	85 (27-398)	**<0.001**
	Serum creatinine, mg/dl	1.1 (0.4-7.7)	0.9 (0.4-6.6)	1.3 (0.4-7.7)	**<0.001**
	Serum potassium, mmol/l	4.2 (2.6-7.2)	4.1 (2.6-6.3)	4.2 (2.8-7.2)	0.165
	Serum calcium, mg/dl	8.3 ± 0.7	8.4 ± 0.7	8.3 ± 0.8	0.342
	Uric acid, mg/dl	6.1 (1.8-66)	5.6 (2.1-15.6)	6.9 (1.8-66)	**0.022**
	Albumin, g/dl	3.3 (1.8-4.3)	3.5 ± 0.4	3.1 ± 0.5	**<0.001**
	Aspartate transaminase, u/l	34 (9-1190)	26 (9-296)	39 (14-1190)	**<0.001**
	Alanine transaminase, u/l	23 (2-1100)	20 (2-473)	25 (6-1100)	**0.004**
	D-dimer, ng/ml	718.5 (150-53286)	469 (150-3946)	1123 (150-53286)	**<0.001**
	Troponin, ng/ml	0.014 (0.002-12.769)	0.006 (0.002-12.769)	0.059 (0.002-1.969)	**<0.001**
	Ferritin ng/ml	411.7 (11.7-1661.3)	262.9 (11.7-1650)	625.5 (24.5-1661.3)	**<0.001**
	Haemoglobin, g/dl	11.3 ± 1.9	11.4 ± 1.9	11.2 ± 2	0.205
	Leukocyte, $x10^3/\mu l$	11200 (2800-45900)	9600 (2800-39300)	13400 (3400-45900)	**<0.001**
	Lymphocyte, $x10^3/\mu l$	980 (110-4040)	1120 (310-3380)	810 (110-4040)	**0.003**
	C-reactive protein (CRP), mg/dl	184.7 (30.5-414.2)	151.9 ± 719	220.5 ± 81.8	**<0.001**
	CRP/Albumin ratio	54.5 (7.8-170.3)	40 (7.8-126.8)	68 (9.1-170.3)	**<0.001**
Medications, n (%)					
	Acetylsalyclic acid	96 (48.5)	48 (46.6)	48 (50.5)	0.581
	Clopidogrel	26 (13.1)	11 (11.6)	15 (14.6)	0.535
	ACE-I / ARB	126 (63.6)	68 (71.6)	58 (56.3)	**0.026**
	Beta-blocker	59 (29.8)	26 (27.4)	33 (32.0)	0.473
	Dihidro-Calcium canal blockers	78 (39.4)	30 (31.6)	48 (46.6)	**0.031**
	Non-Dihidro-Calcium canal blockers	8 (4.0)	4 (4.2)	4 (3.9)	1.000
	Aldosterone antagonists	16 (8.1)	7 (7.4)	9 (8.7)	0.724
	Statin	20 (10.1)	12 (12.6)	8 (7.8)	0.256
	Hydroxychloroquine	192 (97.0)	93 (97.9)	99 (96.1)	0.684
	Azithromycin	131 (66.2)	61 (64.2)	70 (68.0)	0.577
	Favipiravir	117 (59.1)	49 (51.6)	68 (66.0)	**0.039**
	Immunosuppressive agent or steroid	77 (38.9)	30 (31.6)	47 (45.6)	**0.043**

Data are presented as the mean ± standard deviation or median (minimum-maximum) for continuous variables and as counts (%) for categorical variables.

HFrEF, heart failure with reduced ejection fraction; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; TIA, transient ischemic attack, ACE-i: Angiotensin-Converting Enzyme Inhibitor, ARB: Angiotensin Receptor Blocker

Statistically significant p values are shown in bold

Univariate associations between the baseline clinical characteristics and mortality are shown in Table 2. Mortality was higher in patients with hypertension aged > 81 years, with a median survival time of 10 days. On the other hand, it was determined that gender did not significantly affect survival. It was observed that 54.38% of the deaths in men and 58.69% in women occurred during the first 10 days of ICU follow-up. Furthermore, shortness of breath is associated with mortality, whereas cough is associated with survival. Interestingly, diabetes mellitus was associated with half-decreased mortality risk (hazard ratio (HR), 0.49; 95%CI, 0.33–0.74, p = 0.002). On the other hand, mortality was found to be 2.38 times higher in the presence of renal failure (p < 0.001). However, dialysis had no significant effect on the mortality rate.

The cut-off values of the laboratory parameters are listed in Figure 2. The best power to predict mortality was found for the serum CRP/albumin ratio, with an AUC of 0.77, followed by aspartate transaminase, troponin, C-reactive protein, and the other laboratory parameters. In the univariate analysis, the HRs for death during hospitalization was significantly higher for patients with concentrations of all evaluated tests, except for albumin and lymphocytes above the selected cut-offs (Table 2).

In the multivariate analysis, Shortness of breath (HR: 1.65, 95% CI: 1.04–2.61, p: 0.034), CRP/albumin ratio (>51.32) (HR: 1.83, 95% CI: 1.12–2.97, p: 0.015), serum creatinine (>1.62 mg/dl) (HR: 2.04, 95% CI: 1.13–3.33, p: 0.001), aspartate transaminase (>34 u/l) (HR: 1.99, 95% CI: 1.28–3.09, p: 0.002), D-dimer (>781 ng/ml) (HR: 1.59, 95% CI: 1.04–2.43, p: 0.031), leukocyte (>12,000 x10^3/µl) (HR: 1.68, 95% CI: 1.09–2.59, p: 0.018) and lymphocte, (≤660´ 10^3/µl) (HR: 1.76, 95% CI: 1.17–2.63, p: 0.006) were independent predictors for mortality in elderly hypertensive patients (Table 3).

DISCUSSION

COVID-19 patients over 65 are more likely to die (7, 8). Comorbidities can also significantly affect the prognosis of COVID-19. Hypertension plays a special role. Hypertension has also been reported in several studies and is a common underlying condition (9, 10). A meta-analysis by Tian et al. observed that hypertension increased the probability of death from COVID-19 by more than 2.5 times (11). Although there are data from many subgroups of COVID patients, we aimed to reveal the predictors of mortality in hypertensive patients aged ≥ 65 years who were followed up in the ICU. This retrospective cohort study identified several risk factors for death in elderly hypertensive adults hospitalized with COVID-19. In our study, 62.78% of the patients in the ICU were aged ≥ 65 years, and hypertension was present in 64.49% of the patients. A higher median age may explain our study's higher prevalence of hypertension. The fact that the cohort was composed of ICU patients is also a contributing factor. Although the number of male patients was significantly higher in the non-survivor group, we did not observe any significant association between mortality and sex.

The most common presenting symptom in the deceased patients was shortness of breath, an independent predictor of mortality in our study. Ghweil et al. reported a significant positive association between shortness of breath and COVID-19 progression to severe illness and death (12). Additionally, a meta-analysis reported similar findings and recommended dyspnea rather than fever as an indicator of poor outcomes in COVID-19 patients (13). The presence of shortness of breath at presentation may indicate extensive pulmonary involvement. The fact that cough has been observed less frequently in deceased patients and is associated with survival supports the speculation that a lack of a cough reflex may promote worse infection in elderly patients (14).

In our study, histories of renal failure and serum creatinine levels were significantly higher in patients who died than in those who survived. Such patients are known to have a proinflammatory state with functional defects in innate and adaptive immune cell populations and are at a higher risk of upper respiratory tract infection and pneumonia (15). In contrast, serum creatinine level at a cut-off of 1.62 mg/dl was an independent predictor of mortality. Furthermore, the risk of death doubled in patients with a serum creatinine value > 1.62 mg/dl. These data suggest that the kidneys may be a potential target in patients with COVID-19 (16). The novel coronavirus uses angiotensin-converting enzyme 2 (ACE2) as its cell-entry receptor. Recent RNA sequencing data of human tissues have shown that ACE2 expression in the kidney is approximately 100-fold higher than in the lungs (17). Therefore, deterioration in renal function may be caused by the entry of coronaviruses into kidney cells via an ACE2-dependent pathway. Renal involvement due to hypertension can cause this process to enter a vicious circle.

In the present study, serum levels of both ALT and AST were significantly higher, and serum levels of albumin were significantly lower in non-surviving patients. Additionally, we reported that elevated serum ALT and AST levels and low serum albumin levels were significantly associated with mortality. Still, only the AST level (>34 u/l) was an independent predictor of mortality. There is a strong and reasonable relationship between abnormal liver biochemistry and SARS-CoV-2 infection severity (18). It is unclear whether a liver injury results directly from a viral infection, due to potentially hepatotoxic drugs, or as a part of multi-organ dysfunction in COVID-19. Unlike ALT, AST can be released from the cardiac and body muscles and the liver. The fact that AST level is an independent predictor of mortality suggests that it may also reflect muscle and heart attitudes. Bloom et al. noted that an AST-dominant aminotransferase elevation is common in COVID-19, reflecting disease severity and appears to reflect true hepatic injury. Additionally, they found that AST levels correlated with markers of muscle injury, including lactate dehydrogenase and creatine kinase (19).

The CRP/albumin ratio is a newly defined, simple, useful, and inexpensive systemic inflammatory marker that combines the CRP and albumin levels. Several previous studies have demonstrated the prognostic value of CAR in COVID-19 patients (20, 21). We found that the 51.32 cut-off CRP/albumin ratio was an independent prognostic biomarker of mortality in our study population. Similar to our study, Güney et al. reported that CRP/albumin was significantly elevated compared to that in the non-severe group and that CRP/albumin was an independent risk factor for COVID-19 mortality (20). When the patients were divided into three groups according to their CRP/albumin levels from low to high, they found that the mortality in the highest group was 12.6 times higher than that in the lowest group. Our study found that mortality was 1.83 times higher, and the median survival time was 3 times less in patients with a CRP/albumin level above 51.32.

Abnormal D-dimer levels are thought to indicate hypercoagulation rather than consumptive coagulopathy. Hyperfibrinogenemia has been suggested to lead to fibrin polymerization, thrombus formation, and complications or adverse outcomes (22). Several studies have demonstrated the role of D-dimer as an effective predictor of COVID-19 mortality. Various thresholds for D-dimer values have been proposed, with most values ranging between 1000 and 2500 ng/mL (23, 24). However, we observed higher sensitivity and specificity at values below 1000 ng/mL, and the Youden index was maximum at 781 ng/mL. This study found that D-dimer levels of > 781 ng/mL were independently associated with fatal COVID-19 outcomes.

A wide range of hematologic parameter abnormalities have been reported with different disease severities, but marked changes were more com-

Tablo 2. Univariate association of baseline clinical characteristics and laboratory parameters to mortality in elder hypertensive COVID-19 patients

		Mortality n, (%)	Median Survival (days)	Hazard ratio	%95 CI	p-value (log rank)
Age, years	≤81 (n:151)	68 (45%)	19	2.13	1.31-3.48	<0.001
	>81 (n:47)	35 (74.5%)	10			
Gender	Male (n:94)	57 (60.6%)	13	0.74	0.50-1.10	0.127
	Female (n:104)	46 (44.2%)	19			
Body mass index, kg/m2	>27.92 (n:61)	23 (37.7%)	19	1.48	0.97-2.26	0.082
	≤27.92 (n:137)	80 (58.4%)	14			
Symptoms at admission						
Cough	Absent (n:139)	79 (56.8%)	13	0.52	0.35-0.79	0.004
	Present (n:59)	24 (40.7%)	20			
Shortness of breath	Absent (n:74)	28 (37.8%)	20	1.79	1.20-2.65	0.005
	Present (n:124)	75 (60.5%)	13			
Diarrhoea	Absent (n:181)	98 (54.1%)	15	0.55	0.27-1.10	0.175
	Present (n:17)	5 (29.4%)	-			
Fatigue, tiredness	Absent (n:183)	99 (54.1%)	15	0.42	0.21-0.83	0.071
	Present (n:15)	4 (26.6%)	-			
Comorbidities						
Diabetes Mellitus	Absent (n:137)	82 (59.8%)	14	0.49	0.33-0.74	0.002
	Present (n:61)	21 (34.4%)	26			
Renal failure	Absent (n:135)	60 (44.4%)	19	2.38	1.50-3.77	<0.001
	Present (n:63)	43 (68.2%)	9			
Dialysis	Absent (n:178)	89 (50%)	15	1.62	0.82-3.20	0.080
	Present (n:20)	14 (70%)	9			
Malignancy	Absent (n:187)	96 (51.3%)	16	1.92	0.68-5.38	0.079
	Present (n:11)	7 (63.6%)	11			
Coronary Artery Disease	Absent (n:152)	76 (50%)	17	1.40	0.86-2.27	0.116
	Present (n:46)	27 (58.7%)	12			

Laboratory parameters						
Urea, mg/dl	≤67 (n:105)	38 (36.2%)	21	2.56	1.72-3.80	<0.001
	>67 (n:93)	65 (69.9%)	11			
Serum creatinine, mg/dl	≤1.62 (n:139)	59 (42.4%)	19	2.84	1.76-4.57	<0.001
	>1.62 (n:59)	44 (74.5%)	8			
Serum potassium, mmol/l	≤5.1 (n:181)	88 (48.6%)	19	3.75	1.45-9.68	<0.001
	>5.1 (n:17)	15 (88.2%)	7			
Uric acid, mg/dl	≤5.6 (n:85)	36 (42.3%)	20	1.75	1.19-2.58	<0.005
	>5.6 (n:113)	67 (59.3%)	12			
Albumin, g/dl	≤3.2 (n:90)	63 (70%)	12	1.96	1.33-2.90	<0.001
	>3.2 (n:108)	40 (37%)	19			
Aspartate transaminase, u/l	≤34 (n:103)	33 (32%)	25	2.46	1.67-3.62	<0.001
	>34 (n:95)	70 (73.7%)	11			
Alanine transaminase, u/l	≤15 (n:58)	20 (34.5%)	26	1.66	1.08-2.54	0.033
	>15 (n:140)	83 (59.3%)	14			
D-dimer, ng/ml	≤781 (n:112)	40 (35.7%)	25	2.45	1.65-3.65	<0.001
	>781 (n:86)	63 (73.2%)	11			
Troponin, ng/ml	≤0.008 (n:78)	21 (26.7%)	26	2.49	1.68-3.70	<0.001
	>0.008 (n:120)	82 (68.3%)	12			
Ferritin ng/ml	≤496 (n:109)	38 (34.9%)	21	2.10	1.43-3.10	<0.001
	>496 (n:89)	65 (73%)	12			
Leukocyte, $x10^3/\mu l$	≤12,000 (n:108)	38 (35.2%)	26	2.30	1.55-3.40	<0.001
	>12,000 (n:90)	65 (72.2%)	11			
Lymphocyte, $x10^3/\mu l$	≤660 (n:58)	41 (70.7%)	11	1.82	1.18-2.83	<0.005
	>660 (n:140)	62 (44.3%)	19			
C-reactive protein (CRP), mg/dl	≤185.2 (n:100)	33 (33%)	25	2.62	1.78-3.82	<0.001
	>185.2 (n:98)	70 (71.4%)	11			
CRP/Albumin ratio	≤51.32 (n:88)	25 (28.4%)	33	2.93	1.9-4.32	<0.001
	>51.32 (110)	78 (70.1%)	11			

Only variables with p values of ≤0.20 are presented in the table

CI: confidence ınterval

Table 3. Cox regression analysis (backwards stepwise model) summarizing significant independent prognostic factors for mortality in elder hypertensive COVID-19 patients

Variable	Hazard Ratio	95% CI	p-value
Shortness of breath	1.65	1.04-2.61	0.034
CRP/Albumin ratio, (>51.32)	1.83	1.12-2.97	0.015
Serum creatinine, (>1.62 mg/dl)	2.04	1.33-3.13	0.001
Aspartate transaminase, (>34 u/l)	1.99	1.28-3.09	0.002
D-Dimer, (>781 ng/ml)	1.59	1.04-2.43	0.031
Leukocyte, (>12,000 x10^3/µl)	1.68	1.09-2.59	0.018
Lymphocte, (≤660 x10^3/µl)	1.76	1.17-2.63	0.006

CRP: C-reactive protein

Figure 1. Receiver operator characteristics curves to obtain cut-off values for parameters used in the multivariate analysis. (A) CRP/Albumin ratio, (B) Serum creatinine, (C) Aspartate transaminase, (D) D-dimer, (E) Leukocyte, (F) Lymphocyte

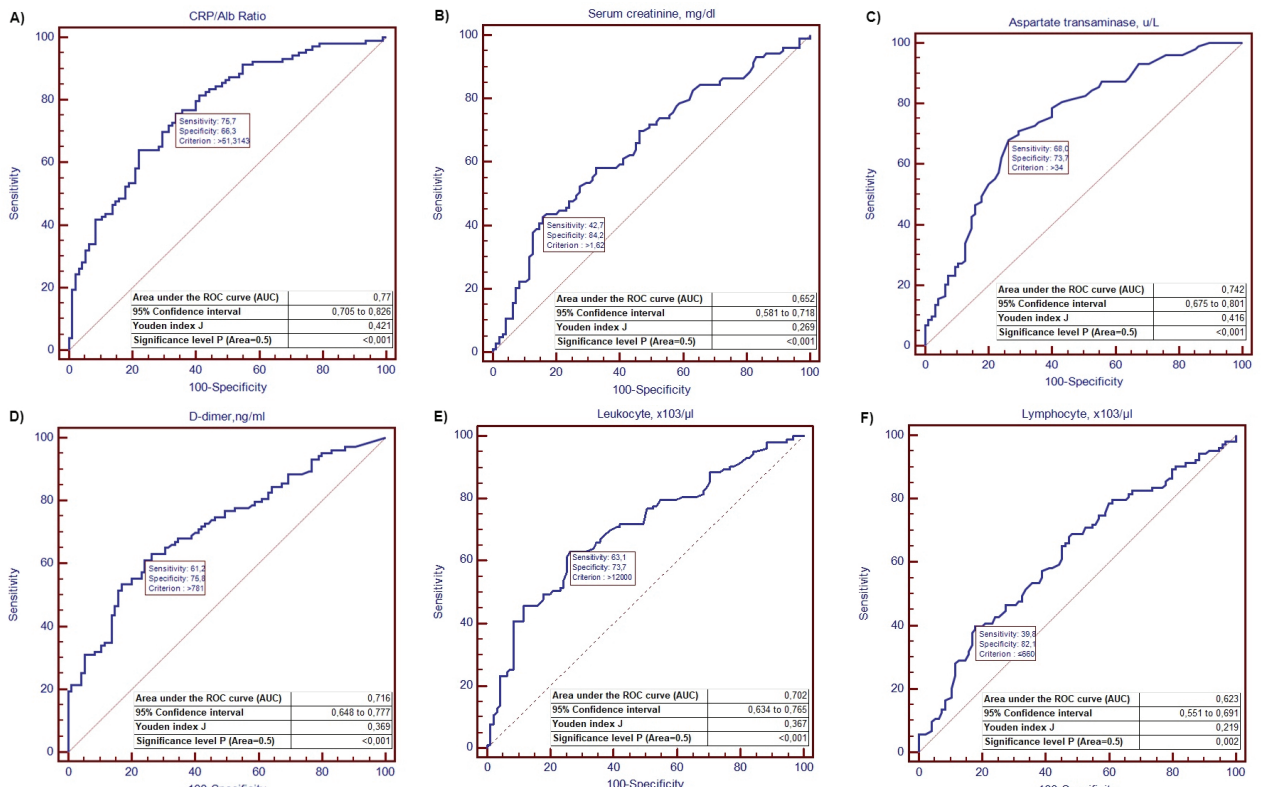
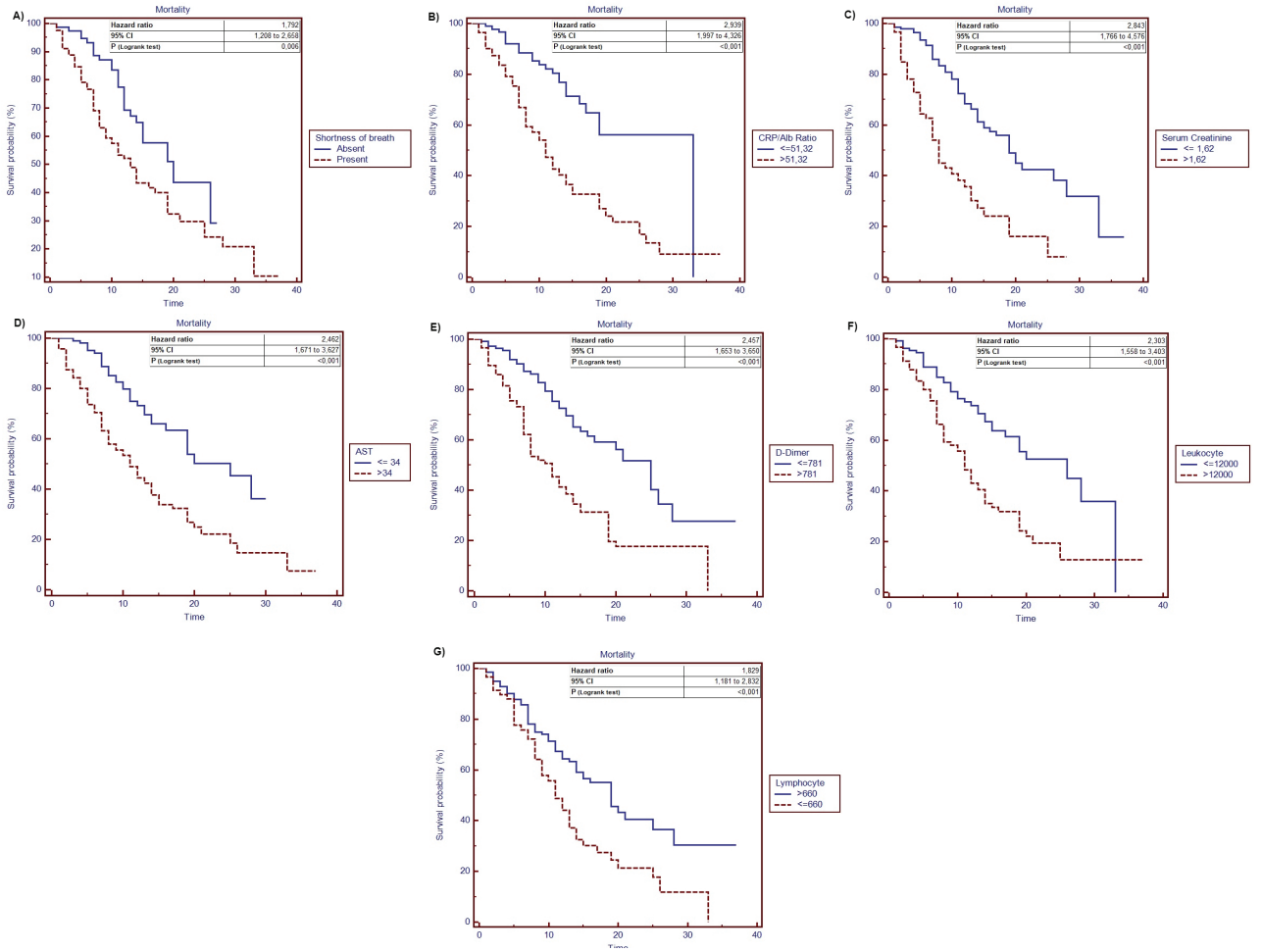


Figure 2. Kaplan–Meier survival curves for mortality from the time of intensive care unit admission. (A) Shortness of breath, (B) CRP/Albumin ratio (>51.32), (C) Serum creatinine (>1.62 mg/dl), (D) Aspartate transaminase (>34 u/l), (E) D-Dimer (>781 ng/ml, (F) Leukocyte (>12,000 x10^3/µl), (G) Lymphocte, (≤660 x10^3/µl). The timeline is expressed in days.



monly seen in samples from severe and critically ill patients. Our study observed that patients who died had significantly higher leukocyte and lymphocyte levels than survivors. Patients with severe and fatal disease have been shown to have significantly higher leukocyte and lower lymphocyte counts than non-serious diseases or survivors (25). We determined leukocyte levels > 12,000 x 10^3/µl as an independent predictor of mortality. Very low lymphocyte count (≤ 660 x 10^3/µl) was an independent predictor. The decrease in lymphocyte count is best explained by the role of both CD4 and CD8 T lymphocytes in eliminating virus-infected cells, and this is consistent with low lymphocyte counts being associated with poor case outcomes.

Limitations

Our study has some limitations. First, the data were collected from a single pandemic hospital and

cannot be generalized to all other regions. Second, due to the retrospective study design, the impact of selection bias cannot be completely ruled out. Third, not all laboratory tests were performed on all patients (lactate dehydrogenase, interleukin-6, and serum ferritin). Therefore, their role in predicting in-hospital mortality may have been underestimated. However, these limitations did not affect the reliability of the overall results. Finally, the data in this study permits a short-term assessment of the clinical outcomes of elderly hypertensive patients hospitalized in the intensive care unit. However, long-term prospective studies are needed, including patients who are followed-up and treated in the ward or as outpatients.

CONCLUSIONS

In the current study, hypertensive patients aged ≥ 65 years hospitalized for COVID-19 had high in-hospital mortality rates. The results of this study suggest that shortness of breath levels and some laboratory parameters may represent invaluable aids in identifying patients with a higher risk of mortality. In addition, these parameters can serve as a guide for clinicians in the early identification and management of at-risk patients.

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RESEARCH

LESS IS MORE: BETA-2 MICROGLOBULIN AS A FRAILTY MARKER IN COMMUNITY-DWELLING OLDER ADULTS

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Abstract

Background: Serum beta-2 microglobulin levels are commonly employed as prognostic and inflammatory indices, given their ease in assessment, reliability, and cost-effectiveness. Herein, we aimed to confirm the effectiveness of serum beta-2 microglobulin as a marker in geriatric patients and establish its role in frailty assessment.

Materials and Methods: This cross-sectional study included 81 participants aged>65 years. Serum beta-2 microglobulin levels were compared with erythrocyte sedimentation rate, C-reactive protein, procalcitonin, interleukin-1, interleukin-6, tumor necrosis factor Tumor Necrosis Factor-α, and vitamin D levels. To determine whether beta-2 microglobulin is an effective marker for frailty assessment, the study was divided into frail and non-frail patients, except for the acute infection group. Frailty was assessed using the Clinical Frailty Scale Version 9, and quality of life was assessed using the Quality of Life Scale Short Form-36.

Results: The mean age of the participants was 72.14±7.00 years. The frail group comprised 47.5% of the total patients. beta-2 microglobulin exhibited a strong positive correlation with C-reactive protein, Clinical Frailty Scale score, and comorbidity index, and a moderate positive correlation with Tumor Necrosis Factor-α and interleukin-6 levels. Conversely, beta-2 microglobulin and Short Form-36 exhibited a strong negative correlation. The Short Form-36 was the most effective in assessing changes in beta-2 microglobulin levels. The optimal beta-2 microglobulin cut-off value to assess frailty was 3.78 (sensitivity=75%; specificity=93.5%).

Conclusion: In the geriatric population, we detected a significant association between increased beta-2 microglobulin levels and frailty, as well as a significant relationship with decreased quality of life.

Keywords: Frailty Syndrome; Inflammation; Aged.

INTRODUCTION

Frailty is a syndrome related to a decline in physiological competence and capacity to maintain homeostasis, given the accumulation of cellular damage due to several factors over the course of a lifetime. Depending on their physiological and functional status, patients can be categorized into healthy, pre-frail, and frail groups (1). Moreover, frailty is known to be influenced by socioeconomic, psychological, and lifestyle factors such as diet, exercise, and genetic factors (2, 3). The incidence of diverse diseases is reportedly increasing with the gradual accumulation of aging-related cognitive and physical dysfunction. Therefore, frailty markedly impacts this heterogeneity, given that age-related functional changes differ among individuals. In the elderly population, frailty increases the risk of mortality, geriatric syndromes, and other negative health effects. Accordingly, the early detection of frailty can help reduce or postpone such risks. Lifestyle regulation is critical to maximally retain cognitive and physical functions and avoid frailty (3, 4). Assessing frailty levels is markedly important in geriatric patients who need to undergo rehabilitation. Scales are also commonly used to evaluate the quality of life and frailty. Frailty assessment is restricted by its complications in clinical practice, partly attributed to time-consuming testing methods. The identification of biomarkers depends on determining normal laboratory values in older individuals (5-7). Beta-2 microglobulin (B2M), a polypeptide, comprises the major histocompatibility complex class I and is encoded by a gene on chromosome 15. After initial isolation from the urine of patients with tubular proteinuria, B2M was found to be present in the serum (free form), as well as in urine and cerebrospinal fluid, after release from the cell surface or cytoplasm . Reportedly, healthy individuals exhibit relatively consistent B2M concentrations. Activation of the immune system induces the release of B2M from B and T cells into circulation (5-8).

It has been reported that B2M serum concentrations increase under various inflammatory and hematologic conditions. B2M levels have been associated with heart failure and hypertension and positively correlated with the incidence and mortality of cardiovascular diseases. Accordingly, B2M affords a considerable predictive value (8-10).

METHODS

Participants and Design

This study was carried out in Çukurova University, Department of Internal Medicine. When the power 80% confidence interval was accepted as 95% d=0.5, the number of people to be reached was found to be 84. 84 patients were included, and 3 patients were excluded from the study because they were diagnosed with myeloma. The study was completed with 81 people. In the first stage of the present study, we included 81 individuals, i.e., 52 females and 29 males. The enrolled individuals were divided into four groups: rheumatoid arthritis (RA; chronic inflammatory disease), osteoarthritis (OA; chronic non-inflammatory disease), acute infection (AI), and healthy individuals (HI). We noted no additional disorders or drug use impacting inflammatory markers in patients with OA and HI. Patients with AI exhibited urinary tract infection, cellulitis, soft tissue infection, sinusitis, and lung infection. Exclusion criteria were as follows: patients who were <65 years; patients with identified or known malignancy, stage 3 or 4 congestive heart failure, renal dysfunction, chronic liver disease, obesity (body mass index (BMI) >35 kg/m^2), and autoimmune disease; patients taking anti-inflammatory agents, antibiotics, or immunosuppressive medication. Given that AI impacts frailty, individuals with AI were excluded from the second stage of the study. The other individuals were categorized into two groups: frail and non-frail.

Measurement

Frailty assessment was performed using the 36-Item Short Form Health Survey questionnaire (SF-36) for all patients and the Clinical Frailty Scale (CFS-9).

SF-36

SF-36 is a commonly used scale for assessing the quality of life; it was initially used to assess the efficacy of treatments and subsequently employed to estimate patient mortality (11). SF-36 was created specifically for examining individuals who were physically unwell. In addition, SF-36 is highly sensitive to slight changes and can assess both positive and negative characteristics associated with health conditions (12, 13). The SF-36 questionnaire comprises 36 items divided into 8 areas: physical condition, role constraints (caused by physical and emotional issues), social function, mental health, vitality (energy), pain, and general perception of health (12-14). Considering questionnaire responses, the patients marked points on a scale. Each subscale received separate scores. In addition, SF-36 assesses negative features of health. The subscale ratings range from 0 to 100, with a high score indicating good health (12-14).

The Clinical Frailty Scale (CFS)

The CFS is a measurement method that can reveal clinical frailty in the geriatric population (15, 16).

1) Very fit: People who are robust, active, energetic, and motivated. These individuals commonly exercise regularly. They are among the fittest for their age.
2) Well: People who have no severe disease symptoms but are less fit than category 1. They exercise or are very active occasionally, e.g., seasonally.
3) Managing well: People whose medical problems are well-controlled but are not regularly active beyond routine walking.
4) Living with very mild frailty: Previously named "Vulnerable." While not dependent on others for daily help, symptoms often limit activities. A common complaint is being "slowed-up" and being tired during the day.
5) Living with mild frailty: These people usually have more evident slowing and need help in higher-order instrumental activities of daily living, such as finance, transportation, heavy housework, and medication management. Typically, mild frailty progressively impairs shopping, walking outside alone, meal preparation, and housekeeping.
6) Living with moderate frailty: People need help with all outside activities and housekeeping. Indoors, these individuals often have problems with stairs, need help with bathing, and may need minimal assistance with dressing.
7) Living with severe frailty: Completely dependent on both cognitive and physical personal care. However, they seem stable and not at a high risk of death (within 6 months).
8) Living with very severe frailty: Completely dependent on personal care and approaching end of life. Typically, they could not recover even from minor illnesses.
9) Terminally ill: Approaching the end of life. This category applies to people with a life expectancy of less than 6 months, and who are not otherwise living with severe frailty. (Many terminally ill people can still exercise until very close to death).

Scoring frailty in a patient with dementia: the degree of frailty corresponds to the degree of dementia. Common symptoms in mild dementia include forgetting details of a recent event, remembering the event itself, repeating the same question/story, and social withdrawal. In moderate dementia, recent memory is markedly impaired, although the individual seems to remember their past life events well. These individuals may need to be prompted to

perform personal care. Patients with severe dementia cannot perform personal care without assistance. In very severe dementia, individuals are often bedridden, and many are virtually uncommunicative.

Laboratory measurements

Blood samples were analyzed to determine levels of glucose, blood urea nitrogen, creatinine, uric acid, Na, K, P, chloride, total protein, albumin, bilirubin, alkaline phosphatase, gamma-glutamyl transpeptidase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total cholesterol, low-density lipoprotein, triglyceride, high-density lipoprotein, hemogram, parathyroid hormone (PTH), 25-OH vitamin D, serum iron, total iron binding capacity, serum B12 and folic acid levels, B2M, ferritin, C-reactive protein (CRP), thyroid-stimulating hormone, procalcitonin (PCT), interleukin (IL)-1, IL-6, and tumor necrosis factor-alpha (TNF-α) levels. In addition, complete urinalysis was performed. A Beckman Coulter DXC 800 instrument was used to perform the turbidimetric method for B2M.

Statistical analysis

Parametric data are presented as the mean ± standard deviation, whereas nonparametric data are presented as the median (interquartile range (IQR)). Data analyses were performed using SPSS 22.0 (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used for the normal distribution of data. T-test, Mann-Whitney U test, binary logistic regression test, multiple linear regression test (stepwise model), and ROC analysis were used in the data analyses. A *p*-value < 0.05 was deemed as statistically significant.

Ethics

An in-depth explanation of the study was provided to all patients, and informed consent forms were obtained. This study was approved by the Çukurova University Health Sciences Research Ethics Committee and Helsinki Declaration.

RESULTS

In the present study, patients who participated in the first phase had a mean age of 76.3±7.5 years, with 29 (35.6%) males and 52 (64.2%) females (min 65, max 99). The participants were divided into four main groups: patients with AI (22 patients, 27.2%), OA (20 patients, 24.7%), RM (20 patients, 24.7%), and HI (19 males, 23.4%). We detected no statistically significant difference between groups regarding the average age (p=0.008).

The mean B2M level of all groups was 3.8±1.3 mg/L (1.24-7.9 mg/L). We then analyzed the distribution of B2M levels across groups. The mean B2M levels were 4.68±1.29, 2.64±0.93, 4.37±1.05, and 3.53±0.90 mg/L in the AI, HI, RA, and OA groups, respectively.

The mean B2M levels of examined groups differed significantly (p = 0.0001). We noted that B2M levels were elevated during inflammatory conditions, such as AI and RA, when compared with those in HI, RA, and OA groups. We detected that differences between B2M levels in the AI and HI groups were statistically significant (p=0.0001). We also found a statistically significant difference between the RA and OA groups based on B2M levels (p =0.007).

In the AI group, CRP showed a 51% positive correlation with the B2M level. In other words, when B2M increases, the CRP value also increases. Similarly, we noted a positive association with CFS; in the AI group, we recorded an inverse correlation (66%) between the B2M level and the SF-36 quality of life scale. Accordingly, the average SF-36 score or the patient's quality of life decreases with increasing B2M levels.

In the second step (main part) of the study, the mean age of participants, except for the AI group, was 72.14±7.00 years (min: 65 years; max: 95 years). Among these patients, 30.5% (n = 18) were male and 69.5% (n = 41) were female. The frail group comprised 47.5% of the total patients.

Levels of B2M, sedimentation, CRP, PCT, IL-1, IL-6, and TNF-α, as well as the Charlson comorbidity index scores, were significantly elevated when compared with inflammatory indicators; however, quality of life and SF-36 scale scores were found to be significantly reduced (Table 1).

The logistic regression model used to estimate frailty was significant, with an accuracy rate of 94.9% and a predictive factor of 88.3%. Living with frailty (risk category CFS ≥ 4) was the dependent variable in the model, whereas B2M level, SF-36 score, age, and comorbidity index were independent variables. The risk of frailty increased by 1.61 times for every 0.476-unit decrease in the SF-36 score and by 13.9 times for every 2.6-unit increase in B2M levels, respectively (Table 2).

Considering the application of B2M levels for frailty screening or diagnostic testing, the ROC analysis revealed that the area under the curve (0.916) was a robust diagnostic tool (Table 3).

The optimal cutoff B2M value to assess frailty was 3.78, with a sensitivity of 75% and a specificity of 93.5%. Based on this cutoff value, the positive/false positive ratio was 11.53, or approximately one patient was misdiagnosed among every 12 patients. The false-negative/negative ratio value was 0.26, suggesting that for every five negatives, one false-negative patient was diagnosed (Table 4).

We assessed correlations between B2M and inflammatory markers and quality of life scale scores. Herein, we detected a robust positive correlation between B2M levels and CRP, CFS frailty score, and

Table 1. Comparison of parameters according to the frailty group

	Non-frail (n:31)	**Frail (n:28)**	**p**
Sex M/F (n)	12/19	6/22	
Parameters	X±S.D or Median (IQR)	X±S.D. or Median (IQR)	
CFS	2.06±0.81	4.57±0.63	<0.001
Age	67(10)	73(10)	0.125
B2-microglobulin	2.73(1.35)	4.17 (1.18)	<0.001
Sedimentation*	13.06±5.88	46.43±26.95	<0.001
CRP	0.24 (0.30)	1.82 (4.65)	<0.001
Procalcitonin	0.06 (0.08)	0.80 (1.04)	<0.001
Vitamin D*	20.72±11.27	18.15 (13.90)	0.512
IL-1	12.10 (28.70)	22.60 (43.90)	0.013
IL-6	32.70 (36.40)	190.40 (295.6)	<0.001
TNF-α	6.10 (7.3)	8.25 (2.33)	0.016
SF-36*	83.17±5.95	65.38±8.14	<0.001
BMI*	29.87±3.43	29.17±3.49	0.446
Comorbidty index	3(2)	5.5(2)	<0.001

Patients with acute infection are excluded. *Normally distributed

Table 2. B2-Microglobulin frailty estimation using B2M logistic regression analysis

	B	p	O.R.	95% C.I.for EXP(B)	
				Lower	Upper
Beta2-microglobulin	2.63	0.045	13.98	1.06	184.37
SF-36	-0.476	0.022	0.621	0.41	0.93
Age	-0.197	0.116	0.821	0.64	1.05
Comorbidity index	0.585	0.538	1.795	0.27	11.58

In this model, patients with acute infections are not included.

Table 3. The area under the curve for B2-microglobulin

Area	S.E.	p	95% Confidence Interval	
			Lower Bound	Upper Bound
0.916	0.037	<0.001	0.845	0.988

Table 4. Cutoff value for B2-microglobulin

Cut-off	Sensitivity	Specificity	Youden index	LR(+)	LR(-)
3.785	%75	%93.5	0.685	11.53	0.26

comorbidity index; a moderate positive correlation was observed with TNF-α and IL-6; a strong negative correlation was found with the SF-36 score.

Multiple linear regression was used to predict the association between B2M and sedimentation, IL-1, IL-6, TNF-α, CRP, PCT, vitamin D, BMI, comorbidity index, and SF-36. Notably, SF-36, comorbidity index, TNF-α, and CRP levels significantly contributed to the model. A stepwise approach was used for this model. The model described 83% of the changes in the B2M, and the most relevant factor related to changes in B2M levels was SF-36 (53.3%), followed by comorbidity index (7.2%), TNF-α (6%), and CRP (2.6%). For every unit increase in SF-36 score, B2-microglobulin decreased by 0.030 units (Table 5).

DISCUSSION

B2M has been confirmed as a significant mortality marker in geriatric individuals and has prognostic and predictive value, particularly in inflammatory conditions (17, 18). Herein, we determined whether B2M should be used as a marker for frailty assessment, as it involves an easy blood test that is relatively simple to perform (19) and can be used by physicians for routine measurement. Few studies have investigated the association between serum

Table 5. Predicting B2 microglobulin using the multiple linear regression model

Model	Unstandardized Coefficients		p	Collinearity Statistics	
	B	Std. Error		Tolerance	VIF
(Constant)	4.050	1.215	0.002		
SF-36	-0.030	.013	0.022	0.398	2.511
Comorbidity index	0.293	.074	<0.001	0.446	2.244
TNF-α	0.055	.019	0.005	0.934	1.070
CRP	0.051	.024	0.040	0.828	1.208

B2M levels and age and found that serum B2M levels increase with age. For instance, one study has reported that healthy adults with an average age of 40 to 86 years old exhibit elevated serum B2M levels with progressive aging. Similar findings have been reported in other studies (20-23). Additionally, B2M in the older Chinese population can reportedly affect both the frailty phenotype and index. Moreover, B2M was shown to be independently associated with baseline frailty in older adults (19, 24). The findings of the present study are consistent with a few previously reported studies, indicating that B2M levels increase with age. Serum B2M levels in the first stage of our study were higher in two groups, the RA and AI groups, and were likely related to inflammation. Based on these findings and minimal accumulated literature, B2M may be an elevated acute-phase marker during acute infectious conditions. In HI, excluding those with inflammatory and infectious disorders, increased serum B2M levels were unrelated to inflammatory conditions. As a notable feature of our study, we excluded participants with renal dysfunction, cancer, and AI, as these conditions would impact plasma B2M measurements. During the second and most important stage, the remaining participants were divided into two groups to represent frail and non-frail individuals, and the effect of B2M levels was examined based on frailty. We performed in-depth laboratory assessments and conducted two different assessment scales (CFS and SF-36). Comparing variables, the levels of B2M, CRP, IL-1, IL-6, TNF-α, sedimentation, PCT, and comorbidity index were significantly elevated in the frail group, whereas the SF-36 scores were significantly reduced. On analyzing B2M levels, we observed that this frailty marker was unrelated to other variables, and the optimal cutoff value for B2M to assess frailty was 3.78. Plasma B2M levels can be used to assess the degree of frailty in geriatric patients and, consequently, the need to establish essential medical care.

In the present study, frailty in a subset of the Turkish population was assessed using CFS, a validated test. To the best of our knowledge, this study is the first to develop a logistic regression model for estimating frailty and performing ROC analysis to determine whether B2M could be utilized as a marker for frailty assessment. In conclusion, B2M may be an important marker for predicting the risk of frailty in geriatric patients. A limitation of our study was its single-center, cross-sectional nature. Accordingly, large-scale, prospective, observational studies are required.

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RESEARCH

DIAGNOSTIC AND PREDICTIVE ROLE OF PLATELET/LYMPHOCYTE RATIO (PLR) IN PREDICTING OUTCOMES IN ELDERLY COVID-19 PATIENTS (A CROSS-SECTIONAL STUDY)

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Abstract

Introduction: In this study, we aimed to investigate the prognostic effects of platelet-to-lymphocyte ratio biomarker in the group of laboratory-confirmed Coronavirus Disease-19 (COVID-19) geriatric patients and compare them with the group of patients under 75 years of age.

Material and methods: The platelet-to-lymphocyte ratio were recorded for oxidative stress response when it is decided to transfer patients from the emergency room COVID-19/area to the COVID-19 /service, at the time of admission to intensive care unit due to arterial oxygen partial pressure (PaO2 mmHg) to fractional inspired oxygen (FiO2) < 200 mmHg, at the time of discharge from intensive care unit and exitus.

Results: It was found that the mean age of the survivors was significantly lower than those who had died (p = 0,016). In Post-hoc analysis, the platelet-to-lymphocyte ratio values at hospitalization of ≥ 75years old patients who had died were found to be significantly different compared to patients 75 < years (p = 0.006)who were survived and patients 75 ≥ years who had died (p = 0.043). Only hospitalization platelet-to-lymphocyte ratio value and age data were found to be associated with mortality. According to mortality;the cut-off value for platelet-to-lymphocyte ratio at the time of admission to the COVID-19/ service in patients 75 ≥ years at the time of admission to ICU in patients 75 < years was determined as 411.15 and 216.54, respectively.

Conclusion: The clinical use of the platelet-to-lymphocyte ratio may be a suitable marker in geriatric patients for determining disease severity and can be used as a predictive factor for determining the poor prognosis.

Keywords: Aged; Platelet Count; Lymphocytes; COVID-19.

INTRODUCTION

COVID-19 is a new disease which has become a global pandemic, and is caused by a novel coronavirus, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1,2). The disease is still not very well characterized, and factors associated with severe clinical course are not well known (1). Coronavirus disease has wide clinical parameters that require intensive care unit, ranging from asymptomatic carriers to mild pneumonia, respiratory failure requiring mechanical ventilation, sepsis, septic shock and multi-organ failure (usually in elderly and those with comorbidities) (2-4).

The production of reactive oxygen species (ROS) resulting in oxidative stress has been suggested to be the main cause of local or systemic tissue damage leading to severe COVID-19 (5).

It is important to identify markers suggestive of poor prognosis and mortality in COVID 19 patients in order to achieve important therapeutic goals. White blood cell (WBC) count, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and serum C reactive protein (CRP), which are biomarkers of peripheral blood-derived inflammation, have been investigated as independent predictors for the prognosis of systematic inflammatory diseases, particularly cardiovascular diseases and malignancies (6,7). Lymphopenia can be considered a cardinal laboratory finding with prognostic potential (8).

It has been suggested that a high platelet/lymphocyte ratio may indicate a more pronounced cytokine storm due to increased platelet activation (3). Therefore, PLR may have prognostic value in identifying severe cases and is associated with poor prognosis (8).

Studies provide optimal cutoffs for PLR for hospital stay and mortality in adult COVID-19 patients, but it is not known whether there are differences for the geriatric patient group. Identifying these factors associated with severe COVID-19 will assist physicians at all levels of healthcare in determining the patients for need of home care, hospital care, and admission to the intensive care unit (ICU). Thus, more rational use of scarce health care resources can be prioritized.

In this study, we aimed to investigate the prognostic effects of PLR biomarker in the group of laboratory-confirmed COVID-19 geriatric patients and compare them with the group of patients under 75 years of age.

MATERIAL AND METHODS

Ethical Approval

The current cross-sectional, retrospective investigation was conducted in compliance with the Declaration of Helsinki. The study was approved by the institutional Ethics Committee, which also gave consent for the use of electronic data (decision date: 14.02.2022, number: 26). Throughout the study, the authors followed good clinical practice guidelines.

Study Design

Three hundred fifty-one patients, who were admitted to the intensive care unit due to COVID-19 severe ARDS (PaO2/FiO2< 200 mmHg), were evaluated retrospectively in this study. Age and gender were all obtained from the hospital records. Patients were randomized into 4 groups: Group I: Survivor 75<years, Group II: Survivor 75≥ years, Group III: Died 75< years, Group IV: Died 75≥ years. The PLR values were recorded for oxidative stress response when it is decided to transfer patients from the emergency room COVID area to the COVID service, at the time of admission to intensive care unit due to PaO_2/FiO_2< 200 mmHg, at the time of discharge from intensive care unit and exitus.

Inclusion Criteria

Patients above 18 years who were admitted to the ICU due to COVID-19 severe ARDS (PaO2/FiO2< 200 mmHg) were included in this study.

Exclusion Criteria

Patients below 18 years, patients who did not require ICU follow-up were excluded from this study.

Statistical Analysis

Statistics were analyzed using SPSS version 21.0 (IBM Corp, Armonk, NY, United States) software. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, maximum) were used while evaluating the study data. The normality of the distribution of the data was investigated with the Kolmogorov-Smirnov test. Continuous variables were expressed as Mean±SD, interval variables as median (min, max), and categorical variables as numbers (percent). The Kruskal-Wallis test was used for comparisons between groups of more than two quantitative variables that did not show normal distribution. Mann-Whitney U test was used to find the group that created the post-hoc difference. Mann-Whitney U test was used for comparisons between two groups of quantitative variables that did not show normal distribution. Friedmann Test was used in dependent multiple group analyses. Wilcoxon sign rank test was applied to the paired groups to find the group that created the post-hoc difference. Pearson Chi-square test was used to compare categorical data. Logistic regression analyzes were applied to identify factors associated with mortality. First of all, single logistic regression tests were applied for factors such as PLR value at hospitalization, PLR value at admission to intensive care unit, PLR value at discharge, age, PLR difference between hospitalization and discharge, and PLR difference between hospitalization and admission to intensive care unit. Then, multiple logistic regression analysis was applied to the significant values. *Youden index* was used by performing AUROC analyzes in order to establish optimal cut-off values for mortality estimation. Statistical significance was accepted as $p<0.05$.

RESULTS

Within the scope of the study, 351 patients (175 males, 176 females) between the ages of 18-92 were analyzed for PLR values at the time of admission to the service, at the time of admission to the intensive care unit, and at discharge (exitus or discharge). 195 of the patients were under the age of 75 and the remaining 156 patients were over the age of 75.

In the statistical analysis, it was determined that the age and PLR values of the data did not comply with the normal distribution. When the patients who survived (n=194) and those who died (n=157) were compared; the mean age of patients who survived (66.6±17) was found to be significantly lower than those who had died (71.5±13.3) (p=0.016). There was no significant difference between survivors and those who had died in terms of gender (p>0.05). In terms of PLR levels at the time of admission to the service; It was found that the PLR level of the patients who survived (211.2±155.5) was significantly lower than that of the patients who had died (290.5±347.7) (p=0.017).

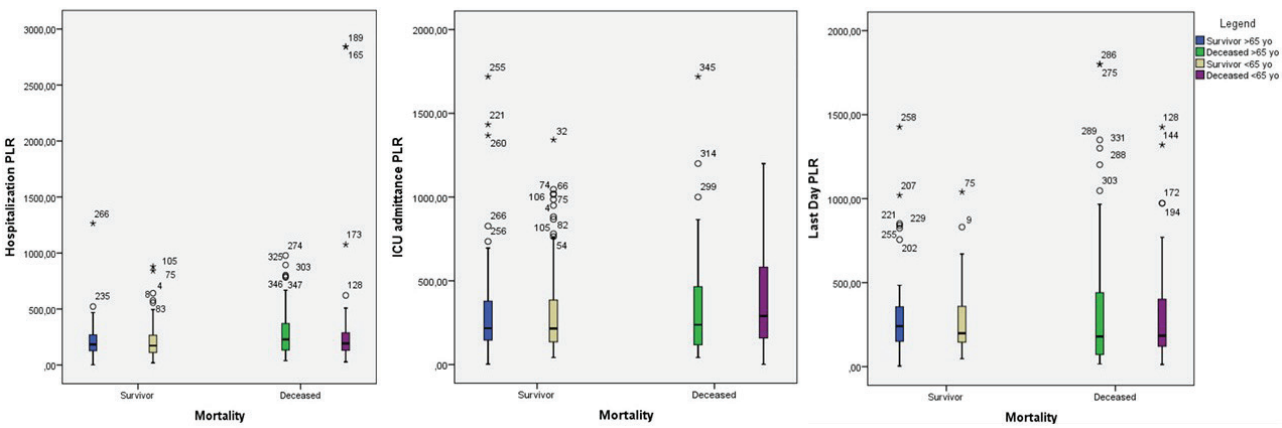
The difference between admission-discharge PLR values was found to be significantly higher in survivors compared to those who had died (p=0.019). It was found that the PLR value of patients at hospitalization were significantly different between the groups (p=0.040). In Post-hoc analysis, the PLR values at hospitalization of ≥75 years old patients who had died (Group IV) were found to be significantly different compared to patients under 75 years of age (p=0.006) who were survived and patients aged 75 years and over who had died (p=0.043). However, the PLR values of ≥75 years old patients who had died were similar to <75 years old patients who had died (p=0.117). (Table 1., Figure 1a-c.).

In the univariate logistic regression models made for the research of mortality-related data; only the PLR value at admission (p=0.01, OR:1.002 95% confidence interval 1.000-1.003) and age (p=0.004 OR: 1.021 95% confidence interval 1.007-1.036) data

Table 1. Demographic data and Platelet Lymphocyte Ratios (PLR) of the study population (n=351)

	Survivors (Age group)			Nonsurvivors (Age group)		
	Group I 75< (n=120)	Group II 75≥ (n=74)	Total (n=194)	Group III 75< (n=75)	Group IV 75≥ (n=82)	Total (n=157)
Age (in years) (Mean±SD)	56.8±14.0	82.6±4.6	66.6±17	60.7±10.7	81.4±5.3	71.5±13.3
Gender						
Male	65 (%33.5)	37 (%19.3)	102 (%53.1)	38 (%36.9)	35 (%22.3)	73 (%46.5)
Female (n,%)	55 (%28.6)	37 (%19.3)	92 (%47.9)	37 (%23.6)	47 (%29.9)	84 (%53.5)
Hospitalization PLR(Mean±SD)	209.5±150.4	214.6±163.5	211.2±155.5	294±455.7	287.4±207,5	290.5±347.7
ICU Admittance PLR (Mean±SD)	305.7±257.3	321.8±300.1	312.3±274.4	390.5±300.7	335.2±292.2	361.6±296.6
Last Day PLR (Mean±SD)	258.8±169.1	295.5±234.3	272.9±196.8	297.2±285.8	334.2±391.7	316.6±344.6

Figure 1a-c. a.PLR values of the groups at hospitalization, b. Admission, c. Last day



were found to be associated with mortality. The PLR values during hospitalization in patients older than 75 years of age, who had died (p=0.022, OR: 1.002, 95% confidence interval 1.000-1.004), and the PLR values at admission to intensive care unit in patients younger than 75 years of age, who had died (p=0.04, OR:1.001 95% confidence interval 1.000-1.002) were found to be associated with mortality. The PLR value of the cases with mortality at the time of hospitalization was found to be statistically significantly higher than the cases without mortality (p=0.007; p<0.01). According to mortality; the cut-off value for PLR at the time of admission to the COVID-19 service in patients 75 years was determined as 411.15 and over (sensitivity 24%, specificity 95%). On the other hand, the cut-off value for PLR at the time of admission to the intensive care unit in patients under 75 years of age was determined as 216.54 and over (sensitivity 68%, specificity 52%) (Table 2).

For young patients, the area under the curve for the PLR value at admission to ICU was 0.584 (0.498-0.669; p=0.049) in ROC analysis.The area under the curve for the PLR value at hospitalization for all patients was 0.574 (0.513-0.635; p=0.017). For elderly

Table 2. ROC analyzes associated with mortality and optimal cut-off values

	AUC (%95 CI)	Cut-off value	% Sensitivity	%Specificity	p
Hospitalization PLR (All Patients)	0.574 (0.513-0.635)	271.9450	51	64	0.017*
Hospitalization PLR (75≥)	0.594 (0.505-0.683)	411.1500	24	95	0.043*
ICU Admittance PLR (75<)	0.584 (0.498-0.669)	216.5400	68	52	0.049*
LastDay-Hospitalization PLR	0.573(0.508- 0.637)	-3.8550	71	53.5	0.019*

* p<0.05 , CI: Confidence interval, AUC: Area under curve, ROC: Receiver operating characteristic

patients, the area under the curve for the PLR value at hospitalization was 0.594 (0.505-0.683; p=0.043), (Figure 2.). The area under the curve for the difference in PLR value at hospitalization - discharge was 0.573 (0.508-0.637; 0.019), (Figure 3.).

DISCUSSION

In this study, the platelet lymphocyte ratio at the time of hospitalization, admission to the intensive care unit, and discharge from the intensive care unit (exit or discharge) in patients over 75 years of age, who were hospitalized due to SARS CoV-2 PCR test positivity within 3 months and then admitted to the intensive care unit because of moderate-to-severe ARDS, were compared with patients under 75 years of age. Optimal cut-off analysis for PLR was performed for disease progression and poor prognosis.

In COVID-19 patients, the lymphocyte count decreases and the neutrophil count increases due to inflammation. Studies have shown that the neutrophil lymphocyte ratio (NLR) and platelet lymphocyte

Figure 2. For elderly patients, the area under the curve for the PLR value at hospitalization (75≥) 0.594 (0.505-0.683; p=0,043).

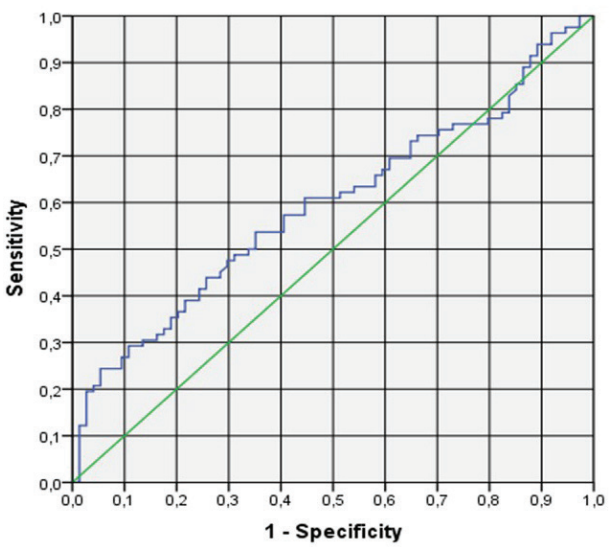
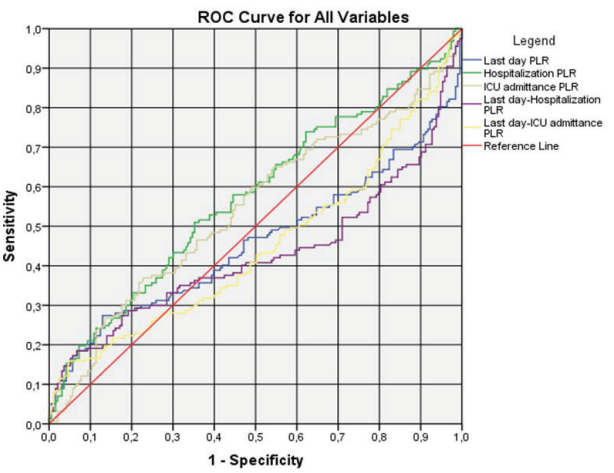


Figure 3. The area under the curve for the difference in PLR value at hospitalization - discharge was 0.573 (0.508-0.637; 0,019).



ratio (PLR) reflect inflammation more effectively and strongly than the individual lymphocyte, platelet, and neutrophil counts (9).

In the study of Seyit et al. PLR was found to be 156.47 ± 112.51 in positive SARS CoV-2 patients (n=110) presenting to the emergency department. The PLR value was found to be 109.14 ± 38.6 in those who were not infected at the same time. The rate of decrease in PLR indicates that the decrease in platelet count is greater than that of lymphocytes. This will require greater attention to thrombocytopenia in the follow-up of COVID-19 patients. The mean age of the patients in this study was 44.16 ± 18.56 years, and 75 of these patients were admitted to the service (10). In our study, patients with shortness of breath, respiratory rate >28/min, SaO2 <93% in room air, PaO2/FiO2 <300, who were admitted to the hospital due to >50% increase in lung infiltration within 24 to 48 hours and whose treatment was appropriate to continue in the service were included. Indications for admission to the service are the same as our protocol. In this study, the cut-off value for PLR at admission to the service was 102.8 (70% sensitivity, specificity 52%). In our patient group, the mean age of surviving patients (66.6±17) was significantly lower than those who had died (71.5±13.3) (p=0.016). Of the patients, 195 were under the age of 75 and 156 were over the age of 75. PLR value at hospitalization (p=0.01) and age (p=0.004) were found to be associated with mortality. It was found that the PLR level at the time of admission to the service was significantly lower in patients who survived at the end of study than in patients who had died (211.2±155.5 vs 290.5±347.7) (p=0.017).

PLR is widely used as a marker of changes in platelet and lymphocyte counts observed in the systemic inflammatory response and pro-thrombotic states (6,11,12). In cases accompanied by immune suppression and thrombosis such as neoplastic, cardiovascular, inflammatory rheumatic diseases; changes in PLR have been shown to have high predictive values in assessing the severity of systemic inflammation and response to treatment and have been associated with poor prognosis (6,7,9,11-14). Because of the presence of more neutrophils and fewer lymphocytes in severe COVID-19 patients than in non-severe patients, markers in routine blood tests have been the subject of research to monitor and predict the severity and prognosis of COVID 19 (14,15).

As in 351 patients (175 males, 176 females) aged between 18 and 92, whom we included in our study, coronavirus disease has wide clinical parameters that require intensive care unit, ranging from asymptomatic carriers to mild pneumonia, respiratory failure requiring mechanical ventilation, sepsis, septic shock and multi-organ failure (16).

As mentioned in many studies, coronavirus generally affects the elderly population (17). On the other hand, the second step of our study was that all patients included in the study were admitted to the intensive care unit due to the development of one or more of the severe pneumonia, moderate to severe ARDS, sepsis, septic shock, or multiple organ failure.

In the study of Asghar et al. which included all patients over the age of 18, the initial PLR value of the patients hospitalized in the service was found to be lower than the PLR value of the patients hospitalized in the intensive care unit (169.81±105.30 vs 271.84±179.47). In the same study, the PLR value of the patients who survived (n=78) was found to be lower than the patients who died (n=22) (186.38±130.34 vs 267.11±168.05) (18). These data were very similar to our study. In our patient group, PLR values at the time of hospitalization were similar in patients over 75 years of age and younger (287.4±207.5 / 294±455.7 respectively) (p=0.117). According to mortality, the cut-off point for the PLR value during hospitalization in patients over 75 years of age was determined as 411 and above (sensitivity 24%, specificity 95%). It was found that the hospitalization PLR values of the patients over 75 years of age who died (Group IV 287.4±207.5) were signifi-

cantly different compared to the surviving patients under the age of 75 (Group I 214.6±163.5). In most severe cases, different comorbid conditions such as diabetes, hypertension, heart failure and renal failure, have been found. The PLR value was found to be higher in patients with one or more of these comorbid conditions compared to non-severe patients (255.8±226.1 vs 436.5±329.2) (19). In our study, it was observed that the PLR values in patients over 75 years of age at service admission (p=0.022) and in patients under 75 years of age at intensive care unit admission were found to be higher in mortal patients when compared to survivors (390.5±300.7 vs 305.7±257.3) and found to be related to mortality. The cut-off value for mortality-related PLR in patients under 75 years of age was found to be 216 and above (sensitivity 68%, specificity 52%). In the last laboratory data at the time of discharge from the intensive care unit or at the time of exitus, which we took as the endpoint of our study, the final PLR value of the patients who survived was 272.9±196.8, while it was 316.6±344.6 for the patients who died. While the PLR value of the patients over the age of 75 who died was 334.2±391.7; it was found to be 297.2±285.8 in patients under 75 years of age. In the study of Asghar et al. while the final PLR value of the patients who survived was 305.63±466.06, it was found to be 340.48±428.64 in the patients who died. In that study, the cutoff value for ICU hospitalization was 153.65 (sensitivity 72.7, specificity 65.1), while the cutoff value for death was 153.65 (72.7 sensitivity, 59.5 specificity) (18). On the other hand, ICU admission was associated with mortality in patients younger than 75 years of age in our study (cutoff value 216.54, 68% sensitivity, 52% specificity).

CONCLUSION

The clinical use of the platelet-to-lymphocyte ratio may be a suitable marker in geriatric patients for determining disease severity and can be used as a predictive factor for determining the poor prognosis.

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RESEARCH

RETROSPECTIVE ANALYSIS OF GERIATRIC PATIENTS TREATED WITH DENTAL IMPLANTS AND IMPLANT-RETAINED PROSTHESES

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Abstract

Introduction: An increasing number of geriatric patients are being treated with dental implants instead of the conventional complete dentures for enhanced oral health-related quality of life. Therefore, this retrospective study assessed the survival rates and biological and technical complications of implants placed in partially and completely edentulous geriatric patients.

Materials and Method: Thirty-six elderly patients (65–80 years) rehabilitated with 105 dental implants and undergoing maintenance therapy at our private practice were included. Demographic data, including patient age, sex, systemic condition, and smoking status, were recorded. The new classification was used to define peri-implant status which was assessed based on bleeding on peri-implant probing, probing depth, suppuration, and peri-implant bone loss. Additionally, the cleanability of the prosthesis, screw-loosening, ceramic chipping, fracture of prosthesis, and their relationship with peri-implantitis were evaluated.

Results: The mean age of the patients at implant surgery was 67.8±3.3 years. The implant survival rate was 100% during the mean observation period of 38±26.5 months. Forty-two (40%) implants were diagnosed as healthy, 52 (49.5%) as having peri-implant mucositis, and 11 (10.5%) as having peri-implantitis. Smoking and poor oral hygiene were significantly associated with peri-implantitis ($p<0.01$). Peri-implantitis was also significantly more common around implants in function for >3 years ($p<0.01$).

Conclusion: According to new classification, peri-implantitis is not common in geriatric patients. Implant treatment and implant-retained prostheses can be safely used to improve the quality of life of elderly patients. However, clinicians should plan the surgery and prepare the prosthesis carefully as elderly people may need nursing or domiciliary dental care.

Keywords: Peri-Implantitis; Geriatric Dentistry; Oral Health; Quality of Life.

INTRODUCTION

Poor oral hygiene can cause caries, loss of periodontium, and ultimately, tooth loss (1). In the last few decades, dental implants have been the choice of treatment for tooth loss; they are placed in the bone to act as abutments for fixed or overdenture prostheses as an alternative to conventional removable ones. Dental implants have a reported 10-year survival rate of >95% in both partially and completely edentulous patients (2). Owing to the predictability and high survival rates of dental implants, their use in geriatric patients has been encouraged for improved oral health-related quality of life (3).

The use of implant-supported fixed and overdenture prostheses could enhance the chewing ability, social reintegration, and psychological well-being of geriatric patients (4). However, in geriatric patients, the presence of systemic conditions such as cardiovascular disease, diabetes mellitus, neurocognitive impairment (Alzheimer's disease and dementia), and loss of manual force and dexterity can jeopardize the healing and make dental implant therapy challenging (5). The surgical process, healing period during osseointegration, and survival rate of the implant should be carefully considered in this age group. Pathology in periodontium is inevitable in elderly individuals due to the loss of physiological integrity and impaired function. According to the recent ITI consensus report, implant therapy is not contraindicated in geriatric patients; however, comorbidities and autonomy should be considered (6).

Peri-implant mucositis is defined as the presence of inflammation in the peri-implant mucosa, and peri-implantitis is characterized by the loss of supporting bone in addition to the mucosal inflammation (7). Poor oral hygiene, history of periodontitis, cigarette smoking, lack of compliance during supportive periodontal therapy, and prosthesis-related factors (lack of cleanability and inappropriate fit of the implant-supported prosthesis) are established risk factors for peri-implant diseases (8). Technical complications, such as wear, chipping, fracture of the prosthetic material, and screw loosening, may also arise in patients with implant-supported prosthesis (9). The occurrence of technical complications is time dependent and may increase the chair-side time and affect the patients' quality of life (10).

Little information is available regarding the prevalence of peri-implantitis in geriatric patients. In most cases, peri-implant diseases are asymptomatic and are not perceived by patients (11). Peri-implantitis may also cause clinical symptoms such as bleeding, suppuration, and swelling (7,9). When left untreated, peri-implantitis eventually leads to implant failure. In patients aged ≥65 years, the prevalence of moderate or severe periodontitis is reported as 64% whereas, the corresponding value for peri-implantitis is 30% within the same age group (12). The management of peri-implantitis may be more complicated in geriatric patients because of the possible progression of the existing systemic disease, multimorbidity, and dependency for daily activities (13,14). Therefore, further treatment with maintenance therapy should be carefully planned in older individuals. Few studies have investigated the effect of preventive maintenance therapy on implant survival in geriatric patients. According to a systematic review, implant survival in patients >65 years is 96.3% and 91.2% at 3 and 10 years, respectively (15). A study on 133 patients aged >80 years reported a 5-year cumulative survival rate of 92.6%–99.7% in both jaws (12).

There is a limited data on the use of implant-supported fixed or overdenture prostheses and the complications affecting the quality of life in geriatric patients. Therefore, this study aimed to evaluate peri-implant health and disease, technical complications, and their relationship with peri-implantitis and implant survival in geriatric patients.

MATERIALS AND METHOD

This retrospective study included 113 dental implants of 40 patients who visited our private prac-

tice between October 2014 and July 2020 based on the following inclusion criteria: age >65 years, use of implant-supported prostheses for at least 6 months, and ongoing maintenance therapy. Four patients did not attend any of the follow-up visits. Therefore, the data of 105 dental implants of 36 patients were evaluated. The study design was approved by the local ethics committee of Gelişim University (2022/11-47). Informed consent was obtained from all patients at initial examination. The study was conducted according to principles stated in the Helsinki Declaration.

Data collection:

Demographic information regarding age, sex, general health status, medication, and smoking status was collected. Tooth loss resulting in partial or total edentulism was recorded. Clinical examinations were performed using a periodontal probe with a 0.5 mm diameter (University of North Carolina PCPUNC15, Hu Friedy Ins. Co, USA). Bleeding on peri-implant probing was assessed as the presence or absence of bleeding observed 30 s after probing and calculated as a percentage for each implant. Suppuration and peri-implant probing depths were also evaluated. To determine the peri-implant bone loss, digitalized panoramic radiographs were examined using the Image J program (Wayne Rasband, National Institute of Health, USA). The magnification was calculated by comparing the known implant length and that measured using the program. Bone loss on the mesial and distal sides of the implant was recorded in millimeters, and the most-affected side was used to diagnose peri-implantitis.

Definition of peri-implant diseases:

The new classification of periodontal and peri-implant diseases and conditions was used to define the peri-implant condition (1);

Peri-implant health: absence of signs of inflammation and bleeding on probing with normal or reduced bone support

Peri-implant mucositis: bleeding on probing with signs of inflammation

Peri-implantitis: radiographic evidence of bone loss ≥3 mm and/or probing depth ≥6 mm in conjunction with profuse bleeding (16).

Additionally, adherence to oral hygiene was evaluated by observational and behavioral (self-reported or observed behaviors, such as changes in toothpaste weight) outcomes and defined as inadequate in the absence of proper brushing and interdental cleaning (17). Implant survival, prosthesis cleanability, and technical complications (ceramic chipping, fracture, and screw loosening) were also recorded.

Statistical analysis:

Data analysis was performed using Statistical Package for Social Sciences (SPSS Inc., Release 24.0, for Windows, Chicago, IL, USA). Descriptive statistics (minimum and maximum values, median, mean, and standard deviation) were used to present the demographic information. Analysis of variance was applied to the three groups (peri-implant health, peri-implant mucositis, and peri-implantitis) with normal distribution, and Kruskal–Wallis H test was performed in the absence of normal distribution. To evaluate differences within groups, Bonferroni correction was performed ($p = 0.05/3=0.016$). Because the number of patients was small, the data were analyzed only at the implant level. The chi-square test was used to compare the data between the two groups. Pearson's correlation was used to examine the relationship between the variables and peri-implantitis.

RESULTS

Thirty-six patients (20 women and 16 men) with 105 implants were included in the data analysis. Their mean age was 67.8±3.3 years at implant surgery. If more than one surgery was performed, the age at the first surgery was used. Of the 36 patients, 8 (22.2%) had diabetes and 10 (27.8%) were smokers.

The mean number of teeth lost at the time of implant placement was 12.8±13. Thirty-two (88.8 %) patients had partial edentulism (Table 1).

Implant characteristics in relation to peri-implant health and disease

A total, 105 dental implants were evaluated in this study. Six of them (5.7%) supported overdentures, whereas most implants (94.3%) supported fixed prosthetic restorations. No implant failure was observed during the mean observation period of 38±26.5 months. The survival rate was 100%. Forty-two (40%) of the implants were diagnosed as healthy, 52 (49.5%) as having peri-implant mucositis, and 11 (10.5%) as having peri-implantitis. The data on peri-implant health and disease are presented in Table 2. The mean observation time and marginal bone loss were greater for the implants with peri-implantitis ($p<0.05$). Poor oral hygiene was

Table 1. Demographic data of elderly

Variable	
Mean age (years)*	67.8±3.3
Gender** Female Male	 20 (55.5%) 16 (44.5%)
Diabetes** Yes No	 8 (22.2%) 28 (77.8%)
Smoking habit** Yes No	 10 (27.8%) 26 (72.2%)
Tooth loss* (number)	12.8±13
Edentulism** Partial Total	 32 (88.8%) 4 (11.2%)

*Mean and standard-deviation

**n (%)

Table 2. Characteristics of study sample regarding peri-implant health and disease

	Peri-implant health (n=42)	Peri-implant mucositis (n=52)	Peri-implantitis (n=11)	p
Mean observation time (months) ±SD	24.1±23.7	44.3±24.9	61±15.7	**<0.01***
BOP (%)	-	52 (100)	11 (100)	0.42**
Suppuration (%)	-	13 (25)	6 (54.5)	0.34**
Mean PD (mm) ±SD	2±0.5	3±0.7	5.6±0.5	0.06*
Mean MBL (mm) ±SD	0.3±0.5	1.2±0.8	4.1±0.4	**0.02***
Prosthetic restoration Fixed Overdenture	 42 (100%) -	 49 (94.2%) 3 (5.8%)	 8 (72.7%) 3 (27.3%)	 0.52**
Cleanability of prosthesis Yes	 41 (97.6%)	 44 (84.6%)	 11 (100%)	 0.31**
Poor oral hygiene Yes	 8 (19%)	 34 (65.3%)	 4 (36.3%)	 **<0.01****
Screw loosening Yes	 5 (11.9%)	 18 (34.6%)	 1 (9%)	 0.62**
Ceramic chipping Yes	 2 (4.7%)	 13 (25%)	 1 (9%)	 0.42**

BOP: Bleeding on probing, PD: Probing depth, MBL: Marginal bone loss
* Kruskall-Wallis H test
**Chi-Square test

also significantly associated with peri-implantitis ($p<0.01$). Most prosthetic restorations (91.4%) were designed to enable proper oral hygiene, and minor technical complications, such as screw loosening and ceramic chipping, were observed in 24 (22.8%) and 16 (15.2%) of the implants, respectively.

As quality of life is affected by the progression of inflammation in the peri-implant tissues, the relationship between peri-implantitis and the other variables was evaluated (Table 3). Peri-implantitis was observed significantly more around implants in smokers and implants in function >36 months ($p<0.01$). No significant association was found between peri-implantitis and the other variables ($p>0.05$).

DISCUSSION

This study aimed to assess peri-implant health and disease in elderly individuals to determine their quality of life. In patients aged ≥ 65 years, the survival rate of dental implants over a mean observation period of >3 years was 100%. Additionally,

Table 3. Correlation table

	Peri-implantitis			
	Absent	Present	r	p
Age 65-70 ≥70	 75 (87.2%) 19 (100)	 11 (12.8%) -	-0.16	0.10
Gender Female Male	 51 (86.4%) 43 (93.5%)	 8 (13.6%) 3 (6.5%)	-0.11	0.24
Diabetes Present Absent	 20 (100%) 74 (87.1%)	 - 11 (12.9%)	-0.16	0.09
Smoking habit Yes No	 24 (77.4%) 70 (94.6%)	 7 (22.6%) 4 (5.4%)	0.25	**<0.01**
Tooth loss 1-14 15-28	 46 (95.8%) 48 (84.2%)	 2 (4.2%) 9 (15.8%)	0.18	0.05
Observation time (months) 6-36 ≥36	 61 (98.4%) 33 (76.7%)	 1 (1.6%) 10 (23.3%)	0.34	**<0.01**
Screw loosening Present Absent	 23 (95.8%) 71 (87.7%)	 1 (4.2%) 10 (12.3%)	-0.11	0.25
Ceramic chipping Present Absent	 15 (93.8%) 79 (88.8%)	 1 (6.3%) 10 (11.2)	-0.05	0.55
Overdenture prosthesis Present Absent	 3 (50%) 91 (91.9%)	 3 (50%) 8 (8.1%)	0.31	0.6
Cleanability of prosthesis Yes No	 85 (88.5%) 9 (100%)	 11 (11.5%) -	0.10	0.28
Poor oral hygiene Yes No	 42 (91.3%) 52 (88.1%)	 4 (8.7%) 7 (11.9%)	-0.05	0.6

peri-implantitis was observed in only 10.5% of the implants. The effect of implant-retained prostheses and removable dentures on the patients' quality of life has been evaluated before (18). Most studies showed that dental implants can be safely placed in geriatric patients and improve their quality of life (6,19). Consistent with the findings of these studies, we observed that implant-retained fixed or overdenture prostheses improve the patients' quality of life, have few biological and technical complications, and are therefore suitable alternatives to conventional removable dentures when treating geriatric patients.

Comparison of studies on peri-implant diseases is difficult because of the differences in methods and the criteria used to define health and disease. Peri-implant diseases were first defined in the year of 2008 in the consensus report from the 6th European Workshop on Periodontology (7). They defined peri-implantitis as the loss of implant-supporting bone in addition to mucosal inflammation. However, assessment of peri-implantitis based on its severity (probing depth and extent of bone loss) yielded substantial variance in its prevalence, from 11.3% to 47.1% (7). Owing to the discrepancy between studies and lack of a common definition of peri-implantitis, the American Academy of Periodontology and European Federation of Periodontology together developed a new classification system for periodontal and peri-implant diseases and conditions (1). In this study, the most recent classification was used to define peri-implant health and disease status. As a peri-implant inflammation decreases the life quality and may have a negative effect on systemic condition of a geriatric patient, a clinician should have a more accurate information before planning the treatment. Therefore, the adaptation of new classification overcomes the misdiagnosis of peri-implant diseases and gives us a more precise information. To date, very little information is available using the new classification to define peri-implantitis and its relation with other variables in geriatric patients. Gündoğar et al (10) used the same criteria to define peri-implant diseases in geriatric patients, and found a peri-implantitis prevalence of 30% whereas the considered value was 10.5% in this study. They reported that the marginal bone loss increased with increasing observation time, as was also observed in the present study. The higher levels of peri-implantitis were attributed to the long observation period, which was between 24 and 56 months in their study.

The strict selection criteria for ongoing maintenance therapy resulted with the analysis of 105 implants despite six years of data collection. Seki et al (20) found survival rate as 94.6% at the implant level in 56 implants of 23 patients. Lee et al (21) investigated the effects of 118 implants in 35 geriatric patients with a mean period of 32.7 months and observed peri-implant bone resorption as 0.27 mm. The mean observation time was significantly associated with peri-implant disease than with peri-implant health in this study. Jemt et al (22) reported that, over a 9-year observation period, implants showed additional bone loss. In another study by Karlsson et al (23) 20% of the implants showed additional bone loss of >2 mm during an observation period of 3.3 years. In a systematic review by Dreyer et al (24), the incidence of peri-implantitis ranged from 0.4% within 3 years to 43.9% within 5 years. In this study, peri-implant health was observed at a mean follow-up of 2 years. However, peri-implant mucositis was diagnosed with greater frequency as the observation period increased (44 months), and peri-implantitis was significantly more prevalent around implants with a mean observation time of 5 years.

Oral hygiene has a significant effect on peri-implant health. Poor oral hygiene is a risk factor for peri-implant diseases (6). In this study, poor oral hygiene was significantly associated with peri-implantitis. Smoking is a known risk factor for peri-implant mucositis (8). Despite overwhelming research, its association with peri-implantitis is still accept-

ed as a potential risk indicator (25). Peri-implantitis was more prevalent in geriatric smokers than in non-smokers in this study. To determine the cumulative effect of smoking on peri-implantitis in geriatric patients, more studies with a larger sample are needed.

Implant-retained overdentures have been found to be superior to complete conventional dentures in terms of patient satisfaction and oral health-related quality of life (17,18,26). However, the number of implants supporting the overdenture prosthesis was insufficient (n=6) in the present study to further analyze the biological and technical complications. Likewise, among the implants with peri-implantitis, one had screw loosening and one had ceramic chipping. The low rates of technical complications did not allow a comparison in this study.

In geriatric patients, the survival of the implants was 100%, and only 11 implants (10.5%) with a mean follow-up of 5 years had peri-implantitis. Thus, it can be concluded that the 100% survival rate and considerably low values of peri-implantitis helped improve the quality of life of patients aged ≥65 years. The favorable outcomes may be attributed to the facts such as the presence of a single periodontist who performed the surgeries, the high cleanability (91.4%) of the prostheses, and the continued maintenance program. The inclusion criterion of strict maintenance program is one strength of this study as it gives the opportunity to analyze clinical and radiological examinations as well as the systemic condition. Besides, the use of a new peri-implant classification is also another strength of this study that makes it a pioneer one. Zitzmann and Berglundh (7) recommended that when evaluating peri-implant inflammation, data from private or public dental clinics, apart from university clinic data, should also be included. This study presents data on geriatric patients treated at a private practice which can be considered as another strength. However, the small number of patients is a limitation of this study more likely due to the strict maintenance program. Another limitation is that only implant-based data could be analyzed. In a patient with multiple implants, inflammation of even a single implant can worsen the quality of life. Therefore, studies on peri-implant health and disease in the elderly in a private practice setting should also be performed using subject-based data.

In conclusion, the survival rate of implants over a mean follow-up of >3 years was 100% in geriatric patients. The implementation of new classification yielded results of peri-implantitis as 10.5% in implant level. Poor oral hygiene, smoking, and implants in function for more than three years were found to be associated with peri-implantitis. Implants can be safely placed and maintained with good oral hygiene to improve the oral health-related quality of life of geriatric patients.

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RESEARCH

UNDERGRADUATES' KNOWLEDGE, ATTITUDES, AND ANXIETY ABOUT AGING, AND INTEREST IN WORKING WITH OLDER ADULTS THE ROLE OF PARTICIPATION IN A COURSE ON AGING

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Abstract

Introduction: This study aimed to investigate the efficacy of attending a course on Aging Psychology on decreasing ageism and aging anxiety and increasing knowledge of and interest in working with older adults among undergraduate psychology students.

Materials and Method: The study participants included 160 college students aged between 19 and 30. A questionnaire including "the Facts on Aging Quiz", "the Anxiety about Aging Scale", "the Fraboni Scale of Ageism", a question of interest in working with older adults, and a Sociodemographic Information Form was administered at the beginning and end of the semester to two groups of students enrolled in two courses, namely, Aging Psychology and Introduction to Developmental Psychology II.

Results: Analyses partially supported the study hypotheses: Over the semester, ageism declined, whereas knowledge of aging increased. Ageist attitudes of participants who completed the Aging Psychology course declined more than those who completed the Introduction to Developmental Psychology II course. In addition, the level of knowledge of the participants who completed the Aging Psychology course significantly increased at the end of the semester, whereas that of the participants who completed the Introduction to Developmental Psychology II course did not change. The two groups of participants did not differ in aging anxiety and working interests with older adults over the semester.

Conclusion: Interventions in the level of knowledge on aging and the elderly through college courses increase the level of knowledge about aging and decrease ageist attitudes.

Keywords: Ageism; Attitude; Knowledge; Anxiety; Students.

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INTRODUCTION

Worldwide, life expectancy has increased, and the population is aging. The emergence of aging societies leads to various social changes, necessitates reconstructing beliefs about aging, and affects individuals' lifestyles. As in the rest of the world, there is an increase in the number of older adults in Turkey's population. Despite the increase in the elderly population, ageism continues to be a worldwide phenomenon (1). The changes in population distribution by age underline the need for individuals who have proper knowledge about, positive attitudes toward, and interest in working with older adults (2). Previous studies have shown that poor knowledge about aging is associated with both negative attitudes and feelings about aging and low interest in working with older adults (3, 4). It is expected that psychology graduates will be working with older adults on aging problems more than ever. Therefore, psychology students' attitudes toward and interest in working with older adults are important issues.

Turkey as an Aging Society

Since it was thought that Turkey had a young population, old age has not been regarded as a primary research concern in the last few years (5). As the world gets older, however, Turkey's population is also getting older Turkey's population is proportionally much younger than those of many other countries', the number of older adults in the population is increasing. The elderly population, those aged 65 and older, has increased by 24% in the last five years (6). The proportion of the elderly in the total population, 8.3% in 2016, has increased to 9.7% in 2021 (6).

Turkey is a collectivist society in many ways, and intergenerational contact is likely to be more common than in an individualistic society. Surprisingly, however, negative attitudes toward aging and older adults and psychological concerns about aging were higher in Turkey than in the United States, a comparatively individualistic society (7). The importance of studies on age discrimination has increased with the increase in the elderly population in Turkey. Older adults in Turkey face age discrimination in various aspects of life. A study comparing ageist attitudes in 15 Organization for Economic Cooperation and Development (OECD) countries found that the country with the highest ageism score was Turkey (8). A detailed examination of the results reveals that older people in Turkey experience age discrimination in various social areas, such as employment, health, environment, and social participation (8). Considering the changes in the structure of Turkey's population and age discrimination toward the elderly, the necessity of studies that will contribute to reducing the effect of ageism on the elderly has become more evident. To enhance the quality of elderly people's care, education on aging, which involves understanding the factors that influence the individual's perceptions of aging, both their own and others', can play an important role in the training of competent health professionals who will work with the elderly.

Knowledge About Aging, Aging Anxiety, and Ageism

Ageism refers to prejudice against one group based on their age and includes both stereotypes and discrimination based on age (9). While age-associated stereotypes about elders can be positive (e.g., older adults are wise) as well as negative (e.g., older adults are sick), negative stereotypes are more common (10).

Ageism is like racism and sexism; however, it has been distinguished from them because everyone can become a target of age discrimination (11). According to terror management theory (TMT; e.g., 12), ageism arises from the effort to distance oneself from older people via negative attitudes and behaviors due to the anxiety created by the awareness of one's mortality (12). Several studies have demonstrated that anxiety about aging, which is defined as a combination of concerns and anticipations of losses due to the aging process (13), is one

of the predictors of ageist attitudes toward elderly people (14, 15). Higher levels of anxiety about aging are associated with increasingly ageist attitudes toward older adults (14, 15).

Other research has found knowledge about the aging process to be another predictor of ageist attitudes; knowledge about aging is related to positive attitudes toward aging (3), and a lack of knowledge about aging is associated with higher levels of ageist behaviors (16). Students who take courses on aging during their university education have more knowledge about aging and less ageist attitudes and behavior than those who do not attend such courses (17). Additionally, a study conducted with nursing students found that watching documentaries about aging and being in contact with healthy older adults increased the level of knowledge about aging and positive behaviors toward the elderly (18). Turkish undergraduate nursing students who had completed a course on the health of elders exhibited significantly less ageist behavior than their peers (19). Although education about aging is effective in reducing ageist behavior, there are few courses on aging and ageism (15, 18) in university programs.

Psychology is one of the main professions through which people are cared for. Due to the aging population in Turkey, many members of this profession will be in contact with older people in their practice more than ever before. Providing training to psychology students to reduce ageism is important for the well-being of older adults. This study aimed to examine the effectiveness of the Psychology of Aging and the Introduction to Developmental Psychology II courses on psychology undergraduates to change their ageism, anxiety about aging, knowledge, and interest in working with older adults. It was expected that participants' ageist attitudes and aging anxiety would decrease, while their knowledge of aging and interest in working with older adults would increase at the end of the course.

MATERIALS AND METHODS

1. Sample

The participants were 160 psychology undergraduates who enrolled in courses related to aging at Aydın Adnan Menderes University in Turkey. Ninety-seven were second-year students who enrolled in Introduction to Developmental Psychology II (IDP), a course that discusses the physical, cognitive, and socioemotional development of adolescents and young, middle-aged, and older adults. Sixty-three were fourth-year students who enrolled in Psychology of Aging (PA), a course that discusses aging in late adulthood; these participants had already taken and passed the IDP course in their second year. The sample was 69.4% female and 31.6% male and ranged in age from 19 to 30 (M = 21.18, SD = 1.65). At least one of the grandparents was involved in the care of 41.9% of the participants when they were children.

2. Measures

Ageism. The participants' ageist attitudes toward elderly people were measured using the Fraboni Scale of Ageism (20). The Turkish adaptation of the reliability, validity, and psychometric properties of the Fraboni Scale of Ageism (FSA) was provided by Kutlu, Küçük, and Yıldız Fındık (21). The original scale had 29 items; however, four items (2, 8, 22, and 24) of the original FSA were excluded because they had low item-total correlations in the Turkish version (21). The FSA is a 25-item (e.g. "*Many elderly people just live in the past*") Likert-type scale ranging from 1 (strongly disagree) to 4 (strongly agree). Higher scores on the scale indicate a greater level of ageism. The Cronbach's a coefficient of the FSA is 0.84 (21). In this study, the Cronbach's alpha coefficients were 0.83 in the pretest and 0.86 in the posttest.

Knowledge about Aging. Palmore's 25-item True or False Facts on Aging Quiz 1 (FAQ1) was used to measure participants' knowledge of the physical, mental, and social effects of aging and common

myths about aging (22). The FAQ1 was adapted into Turkish by Maner, Mertan and Husnu (23). Each correct answer is scored one and the false answer is scored zero. Higher scores indicate a greater knowledge of aging. A sample item was "*The majority of old people – age 65- plus – are senile.*"

Anxiety about Aging. Participants' anxiety about aging was measured by a 20-item Likert-type (1 = strongly disagree to 4 = strongly agree) Anxiety about Aging Scale (AAS) (13). High scores on the AAS indicate a high level of aging anxiety. The AAS was adapted into Turkish by Aydın and Kabasakal (24). In adaptation study, the Cronbach's alpha coefficients was 0.85. A sample item was "*I worry that people will ignore me when I am old*". In this study, the Cronbach's alpha coefficients were 0.85 in the pretest and 0.83 in the posttest.

Interest in Working with Older Adults (IWOP). Participants' interest in working in a setting that provides services to old adults in the future was measured with a single question with 5-point, Likert-type answer options (1 not at all interested, 5 very interested).

Socio-Demographics. In the socio-demographic form, information was obtained about participants' gender, age, class, socioeconomic status, the frequency of contact with grandparents and whether grandparents were involved in their care when they were children. Social contact with grandparents was measured by asking, "How often are you in contact with your grandparents including face to face meetings, visits, phone calls, text messages, or electronic mail messages?" This question was asked four times for each grandparents. A total score was obtained by averaging the answers given. Participants give their answer based on 7-point scale (7= not alive to 1= Several times a day) (25).

3. Procedure

Data were collected during class time at the beginning (pretest) and end (posttest) of the semester, and extra credit points were offered as incentives for participation. The participants were told that two measurements would be taken in the study and they were asked to create a code name to match the pretest posttest data. Both courses spanned 14 weeks, with the IDP and AP course durations being 3 and 2 hours per week, respectively. Both courses had only theoretical content. In the first week of the courses, questionnaires were administered before the courses were introduced. In the IDP course, physical, social, and cognitive development processes were mentioned in adolescence for 3 weeks, young adulthood for 3 weeks, middle adulthood for 3 weeks, and late adulthood for 3 weeks. In the last week of the course, death and mourning topics were covered, and the posttest application of the study was made. Meanwhile, in the AP course, the late adulthood period was discussed in detail. First, the concepts of aging and late adulthood were mentioned, followed by the theories of aging, methodology of aging studies, physical changes and health in elderly people, cognitive processes, personality, resilience, role of individuals in the family and society, retirement, leisure-time activities, mental disorders, successful aging, and mourning and death topics. The two courses were given by the same instructor. The lecturer who teaches the course is a research assistant with a doctorate in developmental psychology.

4. Data Analysis

The analyses of the study were performed using the SPSS v. 22 program. Independent t-tests were employed to make comparisons between the two study courses (IDP and AP courses) in the pretest measures. Afterward, to address the associations between the study variables, Pearson correlation analysis was run separately for each course group. Furthermore, to determine whether the courses that the participants attended affected their level of knowledge about aging, ageist attitudes, aging anxiety, and interests in working with elderly people were tested using a repeated-measure analysis of variance (ANOVA). Since the ageism scores of men

were higher than those of women in previous studies (20), 2x2 repeated measures for last factor analysis of covariance (2-way ANCOVA) was conducted to examine whether the effectiveness of education differed according to gender.

5. Ethical Issues

This study was approved by the Social and Human Sciences Research Ethics Committee of Aydın Adnan Menderes University (reference number: 31906847/050.04.04-081001).

RESULTS

Independent samples t-tests were performed to explore the similarities and differences between the two courses (IDP and AP courses) in the pretest. No significant differences were found between the two courses in the pretest scores. Also, no significant differences were found between the two courses in the frequency of contact with grandparents and the involvement of their grandparents in their care when they were children. Moreover, the independent samples t-tests were performed to examine the gender-related similarities and differences in the pretest measurements. The FSA pretest scores showed a significant gender-related difference ($t_{(142)} = -2.56$; $p = .012$). The FSA scores of male students ($M = 67.86$; $SD = 9.66$) in the pretest were significantly higher than those of female students ($M = 63.20$; $SD = 10.36$) (Table 1). An additional independent samples t-test was conducted to determine whether there is a difference in pretest scores between those whose grandparents involve their their care as children and those whose not. It was found that there was no statistically significant difference.

The relationships between age and pre- and posttest FSA, FAQ1, AAS, and IWOP scores were calculated separately for the two study courses using Pearson's correlation analysis. The results of the correlation analysis for AP groups are as follows. The

Table 1. Demographic Variables and Pretest Scores Comparison Between Courses

		M	SD	M	SD	t
Education		Aging Psychology (AP, n = 63)		Developmental Psychology II (DP, n = 97)		
	FSA	63.66	11.27	65.33	9.68	.956
	FAQ1	13.72	2.68	13.30	2.85	-.886
	AAS	56.16	9.60	56.43	10.70	.160
	IWOA	3.73	4.77	3.06	.98	-1.338
Gender		Female (n = 111)		Male (n = 49)		
	FSA	63.20	10.37	67.87	9.66	-2.56*
	FAQ1	13.58	2.70	13.24	2.96	.677
	AAS	55.91	10.26	57.26	10.26	-.765
	IWOA	3.06	1.07	3.92	5.35	-1.619

Not 1. *p < .05, **p < .001

Not 2. FSA: Fraboni Scale of Ageism, FAQ1: The Facts on Aging Quiz, ASS: Anxiety about Aging Scale, IWOA: Interest İn Working With Older Adult

pretest FSA was moderately and positively correlated with the pretest ASS and posttest FSA. The pretest FAQ1 scores were negatively and moderately correlated with the pretest FSA and pretest AAS. Furthermore, a moderate positive correlation was noted between the pre- and posttest FAQ1. Lastly, the posttest FAQ1 was negatively and moderately correlated with the posttest FSA (Table 2).

The results of correlation analysis for the IDP group are as follows (Table 3). The pretest IWOP scores showed a weak negative correlation with age and pretest FSA. The pre- and posttest IWOP scores showed a positive and weak relationship. A moderate positive correlation was noted between the pre- and posttest AAS and between the pretest AAS and posttest FSA scores. The pretest FSA scores are moderately positively correlated with the posttest FSA and negatively correlated with the pretest FAQ1. The pretest FAQ1 scores showed a weak negative correlation with the posttest AAS scores. The pre- and posttest FAQ1 scores were moderately positively correlated. Lastly, the posttest AAS was moderately correlated with the posttest FSA (positively) and posttest FAQ1 (negatively).

GLM repeated measures analyses were conducted to test the effectiveness of IDP and AP courses over the semester. Between- and within-group factors were education (IDP course and AP course) and time (pre- and posttest), respectively. Results revealed that the main effect of time is statistically significant (Wilks' λ = .866; $F_{(1, 158)}$ = 24.542; p < .001; η^2 = 13). However, this effect is qualified by a significant time X group interaction (Wilks' λ = .957; $F_{(1, 158)}$ = 7.071; p = .009; η^2 = .04). The interaction indicates that the variation in the mean score of FSA over the repeated measurement occasions varies as a function of an education group membership. The main effect of the course group on the mean FSA score across time was statistically significant ($F_{(1, 158)}$ = 8.698; p = .004; η^2 = .05). Accordingly, the FSA scores in the posttest (IDP course group: M = 63.32; AP course group: M = 57.30) were lower than those

Table 2. Correlation Matrix for AP Group

		1	2	3	4	5	6	7	8	9	10
	1.Age	1									
	2.Social Contact	.35**	1								
Pretest	3.FSA	-.01	-.09	1							
	4.FAQ1	-.03	.08	-.34**	1						
	5.AAS	.19	.09	.67**	-.42**	1					
	6.IWOA	-.01	-.14	.17	-.17	.17	1				
Posttest	7. FSA	-.02	-.17	.44**	-.44**	.22	.26	1			
	8.FAQ1	.02	.02	.07	.44**	.14	-.17	-.35*	1		
	9.AAS	.09	.01	.14	-.05	.23	.19	.18	-.01	1	
	10.IWOA	-.01	-.20	-.12	.07	-.02	.10	-.18	-.03	.00	1

Not 1. *p < .05, **p < .001

Not 2. FSA: Fraboni Scale of Ageism, FAQ1: The Facts on Aging Quiz, ASS: Anxiety about Aging Scale, IWOA: Interest İn Working With Older Adult

Not 3. AP group Aging Psychology course group

Table 3. Correlation Matrix for IDP Group

		1	2	3	4	5	6	7	8	9	10
	1.Age	1									
	2.Social Contact	-.01	1								
Pretest	3.FSA	-.06	-.30	1							
	4.FAQ1	.07	.22*	-.32**	1						
	5.AAS	-.07	-.08	.21*	-.16	1					
	6.IWOA	-.23*	.10	.06	-.08	-.10	1				
Posttest	7.FSA	-.10	-.02	.59**	-.12	.32*	-.01	1			
	8.FAQ1	.16	-.10	-.17	.37**	-.15	-.23	-.33	1		
	9.AAS	-.14	-.18	.20	-.28*	.65**	-.09	.34**	-.30*	1	
	10.IWOA	-.02	.12	.29*	-.02	-.01	.25*	.25	-.05	-.09	1

Not 1. *p < .05, **p < .001

Not 2. FSA: Fraboni Scale of Ageism, FAQ1: The Facts on Aging Quiz, ASS: Anxiety about Aging Scale, IWOA: Interest İn Working With Older Adult

Not 3. IDP group Introduction to Developmental Psyhology II course group

in the pretest for both groups (IDP course group: M = 65.26; AP course group: M = 63.73). However, the difference between the pre- and posttest FSA scores was more evident in the AP course group (Table 4).

Regarding the effect of education on the FAQ1 scores, the main effect of time (Wilks' λ = .901; $F_{(1, 158)}$ = 17.379; p <. 001; η^2 = .10) and the time X group interaction (Wilks' λ = .949; $F_{(1, 158)}$ = 8.421; p = .004; η^2 = .05) were significant. The main effect of the course group on the mean FAQ1 scores across time was statistically significant ($F_{(1, 158)}$ = 10.928; p = .001; η^2 = .07). The results revealed a significant increase in the knowledge of aging over the repeated measure. The level of knowledge reported by AP course students in the posttest (M = 15.44) was higher than that in the pretest (M = 13.71), whereas the FAQ1 scores of the IDP group students in the pretest (M = 13.33) and posttest (M = 13.64) did not differ.

The results of the statistical analysis examining the effect of education on AAS scores showed no significant effect of time X group interaction ($F_{(1, 158)}$ = .163; p = .687). Moreover, taking a course did not significantly affect individual interest in working with older people ($F_{(1, 114)}$ = .427; p = .482).

Following these analyses, a two-way analysis of covariance was performed to investigate the main effects of education condition (IDP and AP) and gender on the FSA scores controlling the effects of prior FSA scores. This statistical procedure also tested the interaction between the two education conditions and gender. The main effect of gender was not significant ($F_{(1, 156)}$ = 1.57; p = .212). The interaction between education condition and gender was also not statistically significant ($F_{(1, 156)}$ = 0.417; p = .519). Therefore, the effectiveness of education on FSA scores did not differ by participants' gender.

Table 4. 2x2 Repeated Measures ANOVA Results

Variable	AP		IDP				ANOVA
	M	SD	M	SD	Effect	F ratio	η2
FSA							
Time 1	63.73	10.81	65.26	9.11	T	24.04**	.13
Time 2	57.31	9.59	63.32	8.78	T x E	7.07*	.04
FAQ1							
Time 1	13.71	2.63	13.33	2.62	T	17.38**	.10
Time 2	15.44	2.256	13.64	2.57	T x E	8.42*	.05
AAS							
Time 1	56.16	9.60	56.43	10.70	T	8.37**	.05
Time 2	53.48	10.18	54.40	8.60	T x E	.163	.00
IWOA							
Time 1	3.64	5.35	2.95	1.01	T	.497	.00
Time 2	3.16	1.18	2.95	.95	T x E	.497	.00

Not 1. N = 160. AP, Aging Psychology; IDP, Introduction to Developmental Psyhology II course group; ANOVA= analysis of variance; T= time, E =Education; *p < .05, **p < .001

Not 2. FSA: Fraboni Scale of Ageism, FAQ1: The Facts on Aging Quiz, ASS: Anxiety about Aging Scale, IWOA: Interest İn Working With Older Adult

DISCUSSION

This study investigated the effects of aging-related two different courses (during a semester-long) on the participants' knowledge, attitudes, and anxiety about aging and on their interest in working with older adults. As expected, each of the predictors was correlated with ageism in both the IDP course group and the AP course group. Consistent with many other studies, a higher level of aging anxiety was associated with higher levels of ageist attitudes (15, 16), a finding that substantiates the terror management theory of ageism, and a lower level of knowledge about aging was associated with higher levels of ageist attitudes (16).

It was hypothesized that the ageist attitudes of participants would decline throughout their respective courses. Studies have found mixed results regarding the effects of education on ageism. Although some have indicated that education has a positive effect on ageist attitudes (17, 19), others have found no effect (26). In the present study, neither IDP course group nor AP course group reported significantly less ageism at the end of the semester, but a decrease in ageist attitudes was more evident in those who had taken the AP course. The findings suggest that AP education may be an effective intervention for reducing the ageist attitudes of health professionals. This conclusion can be opened up by a more detailed consideration of the concepts of old age and aging in the AP course compared to the IDP course. While the physical, cognitive and socio-emotional dimensions of old age are discussed with a three-week curriculum in the IDP; in AP course besides the individual processes of aging (physical, emotional and cognitive

changes) social dimensions of aging (such as the transition to retirement, the regulation of family relations and the place of the elderly in the society) to be addressed through whole semester that may have influenced the ageist attitudes of individuals.

It was also hypothesized that the aging-related knowledge of participants would increase as a result of the courses. Only the results for the AP course group supported this hypothesis; these participants reported significantly greater knowledge about aging at the end of the semester. In the case of the IDP group, though, knowledge about aging had not increased by the end of the semester. The results are consistent with the findings of other studies, which show that taking courses specifically focused on aging or on the health of older adults increases knowledge about this period of life (17, 19).

In light of the possibility that gender is relevant to one's knowledge of aging and ageism, the present study investigated whether there was a gender difference in the effects of the courses. Although the ageism scores in the pre-test of the male students were higher than those of the female students, the effectiveness of the courses on ageism and on knowledge of aging did not vary in relation to the gender of the participants. Educational interventions in this subject are thus an appropriate and effective method for both women and men.

Contrary to our hypothesis, we found no significant difference between pre-test and posttest scores of aging anxiety in the two groups. Nor did the interest of the participants in working with the elderly differ by the end of the semester. These findings are contrary to those of other studies, which have suggested that interventions designed to improve knowledge of aging also reduce ageism and aging anxiety and increase interest in working with the elderly (2). However, these studies have also been inconsistent in what they show about the relationship between aging anxiety and level of knowledge. Allan and Johnson (14) found that greater knowledge about aging was significantly associated with a decrease in aging anxiety. But Harris and Dollinger (17) found that education about gerontology produced no significant changes in aging anxiety. These mixed results highlight the need for further research to elucidate the factors that affect aging anxiety. Another study found that participation in education programs about gerontology is associated with greater interest in aging-related careers (4), an association not confirmed by our own study. One explanation may be that courses with field practice that naturally increase students' interactions with the elderly are more effective than purely theoretical coursework in reducing anxiety about aging and increasing the desire to work with the elderly.

This study has several limitations. One is the lack of gender diversity in the sample, likely due to the convenience-based nature of the sampling. Most participants were female, and all were psychology undergraduates. In future studies, it would be beneficial to include students from a variety of departments, including nursing, physiotherapy, and social services, who may be working with the elderly after they graduate. If theoretical instruction is supplemented by field practice, students' interactions with the elderly will increase a change that may also increase the effectiveness of the intervention. The courses were given by a single faculty member. Therefore, the results are affected by the professional skills of the lecturer teaching the course as well as the course syllabus. This limits the generalizability of the results. Other limitation of the study that draws attention is related to measurement tools. Working interest with old people was measured with a single item indicator and may not have been sensitive to the subtleties of working interest. More extensive measurement strategies should be utilized in future studies. Measurement of a broad range of working interests with old people could shed light on how different factors may be more salient in the career plans of university students. Since there is no psychometric information about the Turkish adaptation of the FAQ measurement, these results therefore

need to be interpreted with caution. In future studies, measurement tools with psychometric information should be preferred.

Despite such limitations, this study suggests that educational interventions to change student attitudes and knowledge are working, and it confirms the potential value of increasing knowledge of aging as a means of reducing negative attitudes about the elderly. The findings are consistent with those of other research (3, 16, 17). Although taking a course on aging fostered more positive attitudes toward older adults, doing so did not reduce aging anxiety or increase interest in working with the elderly. More research is needed to understand how ageism and aging anxiety are correlated and what influences them. Enhanced educational interventions may improve the attitudes about aging and aging-related subjects of students preparing for a career working with the elderly.

Conflict of Interest: We have no conflicts of interests to disclose.

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RESEARCH

OBSTRUCTIVE SLEEP APNEA IN ELDERLY

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Abstract

Introduction: This study's purpose is to compare obstructive sleep apnea (OSA) patients over 65 with those under 65 using polysomnography tests.

Materials and Method: The polysomnography tests performed on 108 patients (54 study and 54 control group) from January 1, 2018 to January 1, 2022 were examined retrospectively at the ear, nose and throat clinic in the Adana City Training and Research Hospital.

Results: The study group and the control group shared the same body mass index (BMI) median, apnea-hypopnea index (AHI) median value, the mean oxygen saturation median value, the minimum oxygen saturation median value, the oxygen saturation < 90% (SAT90) median value, the oxygen desaturation index (ODI) median value, the average apnea duration value and the arousal index value. (p>0.01)

Conclusion: In conclusion, being a male above 65 years of age may be a risk factor for obstructive sleep apnea. However, getting older does not increase obstructive sleep apnea.

Keywords: Sleep Apnea Syndrome; Polysomnography; Aged; Oxygen.

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INTRODUCTION

Obstructive sleep apnea(OSA) syndrome is characterized by recurrent complete or partial obstructions of the upper airway during sleep, often accompanied by a decrease in blood oxygen saturation as is arousal. OSA syndrome is common in older adults (1). If left untreated, it can reduce one's quality of life and lead to adverse health outcomes. Effective treatment is possible, so all physicians treating the elderly should be familiar with the clinical manifestations, diagnostic methods, and treatment options for OSA (2).

Most sleep apnea patients are middle-aged men. At least 1% of the global population experiences sleep apnea. Some studies have shown that 18-73% of elderly people suffer from sleep apnea. However, for various reasons, such as a lack of standard criteria, differences in recording techniques, and sleep patterns that may vary from night to night, it is better to avoid making generalizations about the impacts of sleep apnea on the elderly (3).

Experimental and clinical data show that OSA can cause both cellular and molecular changes that accelerate health problems related to aging. Nonetheless, the pathways in which OSA may evoke or speed up aging have not yet been widely researched. (4)

Few studies in the medical literature contain the polysomnography parameters of OSA patients aged 65 and over. This study's purpose is to compare OSA patients over 65 with those under 65 using polysomnography tests.

MATERIALS AND METHODS

Ethics

The University of Medical Sciences, Adana City Training and Research Hospital Ethics Committee approved the study (decision date: 08.08.2022, number: 2059) and it was conducted in compliance with the Helsinki Declaration. Before being included in the study, all the participants including the control group provided written consent. The "good medical practice guidelines and "good laboratories practice guidelines" were followed throughout the study.

Data Collection

The patients' polysomnography test records from January 1, 2018, to January 1, 2022, were examined retrospectively at the ear, nose and throat clinic in the Adana City Training and Research Hospital. The polysomnography tests were performed on 108 patients, with 54 belonging to the study group and 54 belonging to the control group. Patients were divided into groups based on the severity of their OSA according to WHO classification standards: there were individual groups for those with mild, moderate, and severe obstructive sleep apnea; as well as a control group. The polysomnography tests of OSA patients over 65 and the control group under the age of 65 were compared. Exclusion criteria included CPAP use, substance abuse (smoking, alcohol, etc.), chronic illnesses, allergies, and pregnancy.

Polysomnography is the gold standard for diagnosing sleep apnea. While patients were asleep their apnea-hypopnea index (AHI) resulting from respiratory arrest increased. The WHO classifies AHI values of 0-5 as normal, 5-15 as mild OSA, 15-30 as moderate OSA, and >30 as severe OSA.

Statistical analysis

IBM SPSS V23 was used for the statistical analysis. The Kolmogorov-Smirnov test was used to determine whether the variables were distributed normally. A chi-square test was used to compare the gender and OSA severity of the groups. A Mann-Whitney U test was used to compare the study group and the control group. An independent sample t-test was used to compare two independent groups whether there was a statistically significant difference. The results of the analysis for a single categorical variable were described in the

form of frequency (percentage). A standard deviation and a median (minimum–maximum) were used to summarize and describe continuous variables. The significance level was set as $p < 0.01$.

RESULTS

A difference in the gender distribution existed between the two groups ($p = 0.015$). Only 70.4% of the study group was male. On the other hand, 90.7% of the control group was male. There was no statistically significant difference between the median distributions of groups ($p = 0.345$). While 59.3% of the study group was severe, 44.4% of the control group was severe. (Table 1)

A difference in the median ages also existed between the two groups ($p < 0.001$). The study group's median age was 66, while the control group's median age was 45. However, the two groups shared the same BMI median ($p = 0.601$), AHI median value ($p=0.511$), mean oxygen saturation median value ($p=0.219$), minimum oxygen saturation median value ($p=0.453$), SAT90 median value ($p=0.773$), the ODI median value ($p=0.499$) and the average apnea duration value. (Table 2)

DISCUSSION

Obstructive sleep apnea is a common disease in the general population however studies on the elderly are few and the results are discordant. When we look at the literature studies show an increased prevalence of OSA with age but despite high prevalence, it remains underdiagnosed due to a lack of knowledge of the geriatric feature of the disease and the frequency of comorbidities that may worsen it.

The results of this study revealed that although males of all ages may be more at risk of developing OSA but fortunately being over 65 does not inherently result in OSA worsening. The polysomnography variables and oxygen parameters of OSA patients over 65 did not differ from those of OSA patients under 65.

The prevalence of OSA in people over 65 is estimated to be 30% or higher. (5) This increased prevalence is about factors pertaining to age-related physiological changes in older patients such as sleep onset, respiratory chemosensitivity, increase pharyngeal resistance due to airway lengthening and descent of hyoid bone, and the presence of comorbid diseases (5).

The knowledge gaps in research on sleep apnea include etiopathogenesis and its implications. Chowduri et al. (6) revealed that SDB is common in older adults and is associated with significant negative effects. Predominantly central apneas are common in the elderly due to increased breathing instability during non-REM sleep, as suggested by a lower carbon dioxide reserve and a higher controller gain (6). Despite the pharyngeal muscle function and the size of the airway lumen being reduced in elderly people, an increase in arousal frequency due to aging causes hyperventilation and hypocapnia, which promote respiratory instability (7). These two studies of Chowduri et al. were both contrary to our study while in our study oxygen saturation values of the elderly were not significantly different from the younger OSA patients.

According to Hongyo et al., gender (being male), body mass index, and age are risk factors for severe OSA in the elderly (8). Age and body mass index were significantly greater in severe OSA patients in the age cohort than in mild-to-moderate OSA patients. Their research indicates that even in older people who are physically active and neuropsychiatrically healthy, aging worsens OSA symptoms (8). In our study gender, body mass index and, age were not expected to be risk factors for OSA. This may be due to our small sample size.

In Russel et al.'s study, being overweight, male, and elderly and having a genetic predisposition toward sleep apnea and craniofacial aberrations are all possible causes of OSA. However, being over-

Table 1. The comparison of categorical variables by groups.

	Study group	Control	Total	Test ist.	p
Gender					
Male	38 (70.4)	49 (90.7)	87 (80.6)	5.911	**0.015**
Female	16 (29.6)	5 (9.3)	21 (19.4)		
AHI groups					
Normal	7 (13)	6 (11.1)	13 (12)	3.32	0.345
Mild	9 (16.7)	15 (27.8)	24 (22.2)		
Moderate	6 (11.1)	9 (16.7)	15 (13.9)		
Severe	32 (59.3)	24 (44.4)	56 (51.9)		

*Chi-square test, frequency (percent)

Table 2. The comparison of quantitative data by groups.

	Study Group		Control		Total		Test ist.	p
	Mean ± SD	Median (min.-max.)	Mean ± SD	Median (min.-max.)	Mean ± SD	Median (min.-max.)		
Age	67.72 ± 3.83	66.00 (65.00 - 80.00)	45.74 ± 8.46	45.00 (20.00 - 62.00)	56.73 ± 12.83	63.50 (20.00 - 80.00)	0.000	**<0.001***
BMI	30.44 ± 5.58	29.00 (22.00 - 50.00)	30.41 ± 4.02	30.00 (21.00 - 40.00)	30.43 ± 4.84	30.00 (21.00 - 50.00)	1373.000	0.601*
AHI	34.41 ± 22.95	34.95 (1.30 - 90.80)	32.54 ± 26.01	25.05 (0.20 - 95.50)	33.47 ± 24.43	32.30 (0.20 - 95.50)	1351.000	0.511*
SaO2	92.48 ± 1.85	92.80 (86.90 - 95.70)	92.61 ± 2.59	93.45 (83.40 - 96.30)	92.54 ± 2.24	93.00 (83.40 - 96.30)	1258.000	0.219*
minimum SaO2	76.69 ± 8.55	78.00 (52.00 - 90.00)	77.31 ± 10.35	79.00 (51.00 - 93.00)	77.00 ± 9.45	78.00 (51.00 - 93.00)	1336.000	0.453*
ODI	18.40 ± 21.97	9.65 (0.10 - 85.90)	14.18 ± 14.45	9.95 (0.00 - 60.90)	16.29 ± 18.63	9.70 (0.00 - 85.90)	1411.000	0.773*
SAT90	19.33 ± 21.50	13.40 (0.00 - 98.20)	19.17 ± 24.43	7.05 (0.00 - 92.40)	19.25 ± 22.90	8.85 (0.00 - 98.20)	1348.000	0.499*
Apnea duration	23.52 ± 6.12	23.35 (13.50 - 36.10)	24.46 ± 9.56	23.20 (0.00 - 60.00)	23.99 ± 8.00	23.30 (0.00 - 60.00)	-0.611	0.542**
Arousal index	4.35 ± 14.38	0.00 (0.00 - 78.20)	1.01 ± 2.93	0.00 (0.00 - 20.30)	2.68 ± 10.46	0.00 (0.00 - 78.20)	1344.000	0.434*

*Mann-Whitney U test, **Independant Samples T-test, median (minimum – maximum)

weight is not as significant a contributing factor in the geriatric population. (2) Our study did not include craniofacial aberrations.

The relationship between obesity and being an elderly person is less transparent. They have a lower BMI and lesser neck circumference than younger OSA patients. (9) Furthermore, risk stratification models are employed if the patient is male and depending on their BMI. However, these models have been demonstrated to provide incorrect analyses for those who are not obese and the elderly. (10)

According to Morley et al.'s investigation, younger people may exhibit a distinct phenotype of OSA from older people. (11) Although the architecture of younger people with OSA is generally healthy, their stronger respiratory capacity and increased loop gain make them likelier to develop the condition. Worsening anatomy with aging should counteract any reduction in the susceptibility toward OSA, even though the decrease in ventilatory effort and loop gain with age should act as protection against OSA. We think that the study that was mentioned may help to explain why OSA was not worsening in the elderly.

Pinilla et al. (4) examined the link between OSA and aging and found that OSA is connected to an increase in specific aging markers in a dosimetric manner. When the core group was subdivided by age group, they found that OSA was linked to a rise in specific age markers in patients younger than 50, independent of many defined potential confounders. Our study did not include specific age markers.

The sleep patterns of different age groups can vary greatly. Older people complain that they have trouble falling asleep and staying asleep and frequently wake up during the night and in the morning. With age, sleep becomes more fragmented, independent of sleep apnea. (12) In our study the sleep patterns of the patients were not included.

In older adults, some unidentified factors affect these interrelations. Also, due to the sheer anatomical and physiological proclivity for the progression of sleep apnea with advancing age, aged patients could be diverse. It is acknowledged that older people have a range of health issues and functionalities that are not always associated with their biological age. Some people age without developing chronic diseases. As a result, more cohort studies are needed to better understand these interactions.

One of the limitations of our study was the small sample size; not all age groups were included. Another limitation could be that we did not follow the OSA patients from the onset of OSA. Therefore, we could not contribute to the causal relation.

In conclusion, being a male above 65 years of age may be a risk factor for OSA. Hence, early evaluation can reduce risk. However, getting older does not increase OSA. The condition becomes aggravated due to individual differences and well-being. Further studies with large sample sizes are needed.

Conflict of interest: There is no conflict of interest.

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RESEARCH

EVALUATION OF PENTRAXIN 3 UTILITY IN PREDICTING MORTALITY IN GERIATRIC PATIENTS WITH COVID-19: A PROSPECTIVE STUDY

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Abstract

Introduction: The clinical spectrum of coronavirus disease (COVID-19) ranges from mild upper respiratory tract infections to fulminant pneumonia. Nevertheless, it is associated with high rates of morbidity and mortality in elderly individuals. The present study aimed to investigate the levels of pentraxin 3 in geriatric patients with COVID-19 and to determine whether it could serve as a marker for predicting mortality.

Materials and Method: This study included patients aged ≥ 65 years who were diagnosed with COVID-19 infection and admitted to the pandemic ward between October 2021 and march 2022. The patients were classified into two groups: survivors and nonsurvivors.

Results: Of the 95 geriatric patients included in this study, 20 (21%) died and 75 (79%) were discharged upon full recovery. There was a significant difference between male and female patients in terms of mortality. Shortness of breath was noted in 19 nonsurvivors and 9 survivors ($p < 0.05$). The median pentraxin 3 level was 5.8 ng/mL (1–20) for all patients, 3.92 ng/mL (1–19.6) for survivors, and 6.3 ng/mL (4.1–20) for nonsurvivors ($p < 0.001$). The area under the curve in the receiver operating characteristic curve analysis for pentraxin 3 was 0.596 ($p = 0.04$) to predict mortality. The likelihood ratio test revealed a cutoff value of 4.43 ng/mL (sensitivity: 57.1% and specificity: 70.5%) for pentraxin 3.

Conclusion: Pentraxin 3 was found to be a novel biomarker for predicting mortality in geriatric patients with COVID-19, and it was investigated for the first time in this special population.

Keywords: COVID-19; Geriatrics; Mortality; Acute-Phase Proteins.

INTRODUCTION

In December 2019, the World Health Organization reported pneumonia cases of unknown etiology in Wuhan, Hubei Province, China. The causative agent was identified as a new coronavirus (2019-nCoV), and the pneumonia caused by it was termed COVID-19 (1). COVID-19 has affected countries worldwide, giving rise to a pandemic associated with significant morbidity and mortality (2). Disease severity has ranged from asymptomatic clinical forms to severe clinical forms, with signs and symptoms of pulmonary parenchymal involvement (3).

Respiratory infections are among the major causes of morbidity, hospitalization, and mortality throughout the world, especially in elderly individuals. Elderly patients with infectious diseases exhibit atypical prognoses owing to chronic alterations, along with genetic and environmental factors (4). Furthermore, delayed diagnosis and a worsened prognosis are highly prevalent in this population because current symptoms may be considered a natural consequence of aging (5). Nevertheless, early diagnosis and assessment of disease severity are essential for the optimal treatment of respiratory infections (6).

While the lack of reliable means available to diagnose respiratory infections continues to be a major problem, many biomarkers, such as C-reactive protein (CRP), procalcitonin (PCT), erythrocyte sedimentation rate (ESR), plasminogen activation inhibitor-1, and pentraxin 3 (PTX3), have been introduced to improve diagnostic accuracy (6–8). PTXs are a family of acute-phase reactants characterized by a cyclic multimeric structure. The PTX family is classified into two subgroups—short and long—depending on the primary structure of the protein. CRP and serum amyloid-P belong to the short pentraxin subgroup, whereas PTX3 is included in the long pentraxin subgroup. It has been established that increased levels of PTX3 serve as an independent marker associated with the risk of developing certain diseases, including atherosclerosis, cancer, respiratory diseases, and central nervous system diseases (9,10).

The role of PTX3 is not yet clearly understood in the geriatric population with COVID-19. To our knowledge, this is the first study in which a new biomarker was investigated to predict mortality in geriatric patients with COVID-19. The present study aimed to investigate the levels of PTX3 in geriatric patients with COVID-19 and to determine whether it could serve as a marker for predicting mortality.

MATERIALS AND METHOD

This prospective study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of Firat University with the number 3801 dated September 16, 2019. The participants were briefed about the study and their respective written consents were obtained prior to the collection of clinical information and blood samples.

Study design

Patients and Controls: This study included patients diagnosed with SARS-CoV-2 infection and admitted to the pandemic ward between October 2021 and March 2022. According to the inclusion criteria, patients aged ≥ 65 years in whom COVID-19 diagnosis was confirmed via real-time polymerase chain reaction were included in the study. Patients aged < 65 years who were suspected to have another infection and received antimicrobial therapy during the last 1 month were excluded from the study. The patients were classified into two groups—survivors and nonsurvivors.

Data collection

Clinical data: Patient data, including demographic characteristics, medical history, and the status of receiving other COVID-19 therapies (such

as anticytokine treatment), were retrieved from the hospital's electronic registration system. All the patients underwent pulmonary computed tomography at admission. Furthermore, the need for ventilators, length of hospital stay, and rate of mortality were recorded during the study.

Determination of plasma levels of pentraxin 3: At admission, venous blood (5 mL) was collected from the patients and stored in ethylenediaminetetraacetic acid-containing tubes. The blood samples were centrifuged within 40 min of their collection at 3500 rpm for 10 min. The plasma samples were kept at −80°C until examination. Serum PTX3 levels were analyzed using an enzyme-linked immunosorbent assay (ELISA) kit (human PTX3; catalog no.: 201-12-1939; Biological Technology Co., Ltd, Shanghai, China) in accordance to the manufacturer's instructions. The measurement range of the human PTX3 ELISA kit was 0.08–20 ng/mL, and the intra-assay and interassay CV values were <10% and <12%, respectively. The test results were expressed in ng/mL.

Routine biochemistry and hematology: Standard blood assays were performed as a part of the routine analyses for many parameters, including CRP levels, white blood cell count (WBC), ESR, and PCT and D-dimer levels.

Statistical analysis: SPSS v.22 package program (SPSS, Inc., Chicago, IL, USA) was used for data analysis. Visual (histograms and probability plots) and analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk test) were used to test the variables' normality of distribution. Continuous variables with normal distribution were expressed as mean (±standard deviation), whereas data with non-normal distribution were presented as median (minimum–maximum). Categorical variables were expressed as frequency and percentage. Mann–Whitney U test or Student's *t*-test was used to compare continuous variables based on their normality of distribution. The cutoff value for PTX3 to predict mortality was calculated using ROC analysis. A p-value of <0.05 was considered statistically significant.

RESULTS

Of the 95 geriatric patients included in this study, 42 (44%) were females and 53 (56%) were males ($p > 0.05$). The median ages of the female and male patients were 65 (65–85) and 65 (65–89) years, respectively ($p > 0.05$). Additionally, 20 (21%) patients died, and 75 (79%) were discharged upon full recovery. Of the nonsurvivors, 7 (35%) were females and 13 (65%) were males. There was a significant difference between the male and female patients in terms of mortality ($p < 0.05$). The median ages of the survivors and nonsurvivors were 65 (65–82) and 65 (65–89) years, respectively ($p > 0.05$). Shortness of breath was observed in 19 (95%) nonsurvivors and 9 (12%) survivors ($p < 0.05$).

Laboratory values in the general population were 32 (5–334) for CRP, 0.12 (0.03–93) for PCT, 554 for D-dimer (441–1620), 0.71 (0.62–1.6) for creatinine, 4.5 (1.2–16) for high-sensitivity troponin, 40 for ESR (21–123), 6,850 for WBC (2,400–24,900), 4,560 for neutrophils (1,390–22,420), 1,410 (660–6,520) for lymphocytes, 264.2 ± 137 for platelets, 265 ± 364 for ferritin, 38 ± 11 for aspartate aminotransferase, 34 ± 23 for alanine aminotransferase, 293 ± 156 for lactate dehydrogenase (LDH), and 590 ± 297 for fibrinogen. The biochemical parameters of the nonsurvivors and survivors and their relationships are provided in Table 1.

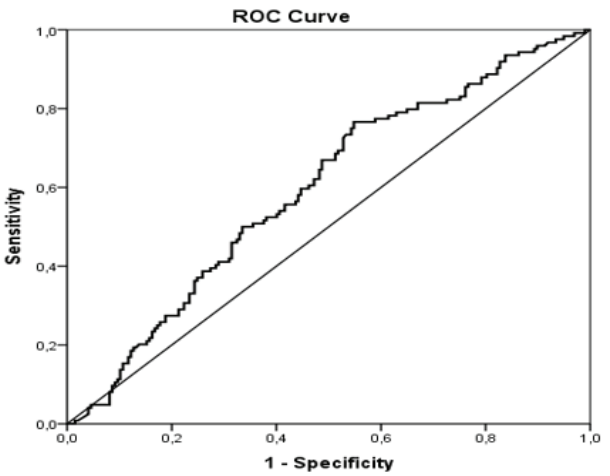
Median PTX3 levels were 5.8 (1–20) ng/mL for all the patients. The survivors and nonsurvivors had median PTX3 levels of 3.92 (1–19.6) ng/mL and 6.3 ng/mL (4.1–20) ng/mL, respectively ($p < 0.001$). The AUC for the ROC curve analysis of PTX3 was 0.596 ($p = 0.04$) to predict mortality (Figure1). When performing the LR test, the cut-off value for PTX 3 was 4.43 ng/mL (sensitivity: 57.1% and specificity: 70.5%).

Table 1. Laboratory parameters of the patients

Characteristics	Nonsurvivors (n:20)	Survivors (n:75)	P value
WBC, K/uL	1200±11700	6230±5700	0.584
Neutrophil, K/uL	1000±1190	4210±510	0.290
Lymphocyte, K/uL	810±500	2260±3360	**0.036**
Platelet count, K/uL	184.2±103.0	323.2±167.5	0.134
CRP, mg/L	75 (34-334)	21 (3-133)	0.046
Procalcitonin, ng/mL	1.15 (0.1-95)	0.10 (0.02-0.28)	0.07
ESR (>20mm/saat)	34±14	63±74	0.606
AST, U/L	48±32	40±14	0.037
ALT, U/L	35±12	42±32	0.233
LDH, U/L	312±186	310±152	0.028
Serum albumin, g/L	3.5±0.7	3.9±0.5	0.002
Kreatinin, mg/dL	0.91 (0.62-1.6)	0.72 (0.63-1.31)	0.187
Ferritin, ug/L	416±262	334±274	0.010
D-dimer, ugFEU/L	723 (441-6970)	675 (458-1620)	0.033
hsTn I, ng/L	4.9 (1.2-13.5)	4.6 (2.9-16)	0.082

CRP: C reactive protein, ESR: Erythrocyte sedimentation rate, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, LDH: Lactate dehydrogenase

Figure 1. ROC curves of pentraxin-3 on differentiating survive patients from nonsurvives with COVID-19



DISCUSSION

SARS-CoV-2 infection may occur in various clinical forms, ranging from mild upper respiratory tract infections to fulminant pneumonia (11), and some affected patients may experience progression to life-threatening acute respiratory distress syndrome, coagulopathy, and septic shock (12). In patients with COVID-19, the risk of progression to severe disease is 26%–32%. An increased risk of mortality is expected, especially in elderly patients, due to an increased risk of a worsening prognosis (13).

The overall rate of COVID-19-related mortality ranges from 2.3% to 14.8% depending on the demographic characteristics of the country or region, age, disease severity, and comorbidities (14). Increased

mortality was directly related to the demographic factors, including advanced age and male sex in the cohorts of the patients with COVID-19(15). The present study on the geriatric patient population supported all the foregoing results, and the overall mortality rate was found to be 21%. Furthermore, the mortality risk was higher in the male patients in our study. The most common symptoms reported by patients with COVID-19 were fever, fatigue, and dry cough (16). Nevertheless, the fever response is generally weak, especially in elderly individuals. Pulmonary involvement with shortness of breath is frequently seen in the critical patient group (17). In the present study, the incidence of shortness of breath was significantly higher in the nonsurvivors than in the survivors.

It was found that increased levels of laboratory parameters, especially CRP, ferritin, LDH, D-dimer levels, and lymphopenia were directly associated with the progression of COVID-19 (18). Critical patients exhibited leukopenia, lymphopenia, increased liver enzyme, ferritin, lactate dehydrogenase, and D-dimer levels, and increased prothrombin time (16). The mortality rate was higher in patients with high D-dimer levels and severe lymphopenia (19). In this study, significantly increased CRP, PCT, D-dimer, LDH, ferritin levels, and lymphopenia were observed in the nonsurvivors. The laboratory results reported in our study were consistent with those reported in the relevant literature.

The serum PTX3 levels are typically very low in healthy individuals (<2 ng/mL) and rapidly and highly increase in patients with various infectious and inflammatory conditions (20). The plasma PTX3 level has a diagnostic and prognostic role in many diseases, as it reaches peak concentration 6–8 h after an inflammatory stimulus (21, 22). It is well established that significantly higher PTX3 levels are observed in association with viral and bacterial diseases (23). Moreover, PTX3 has been proven to be a prognostic marker in community-acquired pneumonia (24), ventilator-associated pneumonia (25), and sepsis (23).

Genç et al. (21) reported a PTX3 level of 3.91 (1.9–23.2) in nonsurvivors, which was statistically significantly higher compared to that of the survivors in a study of 88 patients with COVID-19 aged 67 (23–95) years. In the present study, there was a significant correlation between the inflammation indicator serum PTX3 level and COVID-19-related mortality, and the cutoff value to predict mortality was 4.43 ng/mL. Also, it was suggested that increased PTX3 levels could predict increased mortality risk in geriatric patients with COVID-19, which would enable early intervention in the management of patients included in this high-risk population.

This is the first study to demonstrate the utility of plasma PTX3 levels in geriatric patients with COVID-19. However, there are certain limitations to this study. The relatively limited number of patients, examination of PTX3 levels only at admission, and lack of a healthy control group are also some limitations of the study.

In conclusion, given the increased risk of worse prognosis and mortality rate associated with COVID-19 in the high-risk geriatric patient group, early prognostic information should be obtained by the determination of PTX3 levels along with the evaluation of conventional mortality predictors, thereby improving clinical prognosis and enabling the provision of rapid individualized treatment.

Conflict of Interest: There is no conflict of interest.

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RESEARCH

RHINO-ORBITAL MUCORMYCOSIS IN THE ELDERLY POPULATION AFTER COVID-19

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Abstract

Introduction: In this study, we aimed to retrospectively evaluate the characteristics of mucormycosis cases seen in our clinic during the COVID-19 pandemic, the management of their treatment and the SARS-CoV-2 variants that were dominant at that time.

Methods: The medical records of patients diagnosed with rhino-orbital mucormycosis between March 2020 and July 2022 were retrospectively evaluated.

Results: Nine patients were diagnosed with rhino-orbital mucormycosis. Of these patients, six were male and three were female, and the patients were between the ages of 65-75 (mean 69.2). After the diagnosis of mucormycosis, antifungal treatment was initiated with liposomal amphotericin-B. Eight patients underwent surgery within 48 hours, only one patient refused to undergo surgery.

Conclussions: Mucormycosis is a rapidly progressing opportunistic fungal infection. Therefore, the most basic criteria determining mortality is the early detection of about mucormycosis infection and to diagnose it as soon as possible, especially in patients with an underlying immunosuppressive condition. Once a diagnosis of mucormucosis has been established, risk factors, especially blood sugar regulation, should be corrected. Furthermore, systemic and local antifungal therapy shuold be initiated, and urgent debridement should be performed.

Keywords: COVID-19; Mucormycosis; Aged.

INTRODUCTION

On the 7th of January 2020, the WHO defined a new coronavirus (2019-nCoV) that had not been detected in humans previously. On the 11th of February 2020, the disease was named coronavirus disease-19 (COVID-19) and the virus Severe Acute Respiratory Syndrome Coronavirus -2 (SARS-CoV-2) (1,2).

Since it was detected, SARS-CoV-2, which caused the death of millions, has constantly mutated like any other RNA virus. Although many variants were detected after index virus identification in the first cases in December 2019, five were classified as variants of concern (VOC). On the 18th of December 2020, Alpha (B.1.1.7. United Kingdom), December 2020 Beta (B.1.351, South Africa), 11 th of January 2021 Gamma (S.1, Brazil), 11th of May 2021, Delta (B.1.617.2, India) and on the 26th of November 2021 Omicron (B1.1.529, in multiple countries) have been declared VOCs (3).

Mucormucosis is a rare opportunistic fungal infection (0.005 to 1.7 per million) that progresses rapidly (4). It is often caused by Rhizomucor, Mucor, and Lichthimia spp. Fungi that cause mucor infection can be found in soil and mold or suspended in air (5,6). Deterioration of the immune system, such as Diabetes Mellitus (DM), transplantation, haematological malignancies, neutropenia, iron overload, long-term steroid use, human immune defficiency virüs (HIV), skin trauma, chemotherapy or intravenous drug use, and inhaled saprophytic fungi can be found in the paranasal sinuses and colonise the nasal cavity (4,5,7). This affects the pterygopalatine fossa, eroding the paranasal sinus wall, and spreads to the brain and orbit (rhino-orbito cerebral mucormycosis) or is observed as pulmonary, cutaneous, gastrointestinal, or disseminated mucormucosis (5). These fungi cause vascular thrombosis and tissue necrosis owing to their invasive properties, and causes a black scar in the nasal cavity or hard palate, which is typical of mucormucosis (5,6).

Decreased numbers of routine doctor check-ups due to pandemics, the deterioration of the control of comorbid diseases by Covid 19 infection, high-dose steroids used due to severe COVİD-19 infection, and the need for intubation, increases the incidence of not only mucormycosis but also other opportunistic fungal infections such as candidiazis and aspergillozis (4,7). Mucormycosis infection is more dangerous than other opportunistic infections due is its ability to spread rapidly (4,7,8). A delay of even a few hours in the diagnoses of patients may cause the spread of the disease and even death. If the patient is intubated or unconscious, it is very difficult to diagnose this opportunistic infection, which progresses rapidly in the nasal passage.

In this study, we evaluated the characteristics of the mucormycosis cases referred to our clinic and the management of their treatment by evaluating the dominant SARS-CoV-2 variant periods.

METHOD

The medical records of patients diagnosed with rhino-orbital mucormycosis between March 2020 and July 2022 were evaluated retrospectively. Patients diagnosed with COVID-19 by PCR and whose mucormycosis diagnosis was confirmed by histopathological and direct microscopic methods were included in the study.

All patients diagnosed with mucormucosis were followed up by the Infectious Diseases, Ear Nose Throat (ENT), and Eye Diseases departments using a multidisciplinary approach. Demographic characteristics of these patients, initial symptoms and findings, PCR results for SARS-CoV-2, treatments they received, hospital stay duration, presence of DM and blood sugar levels, presence of other comorbid diseases, physical examination findings, imaging methods, and type of surgery were recorded for patients who underwent surgery. Paranasal sinus computed tomography (PNS-CT) and magnetic resonance imaging (MRI) were performed for all patients to evaluate eye involvement.

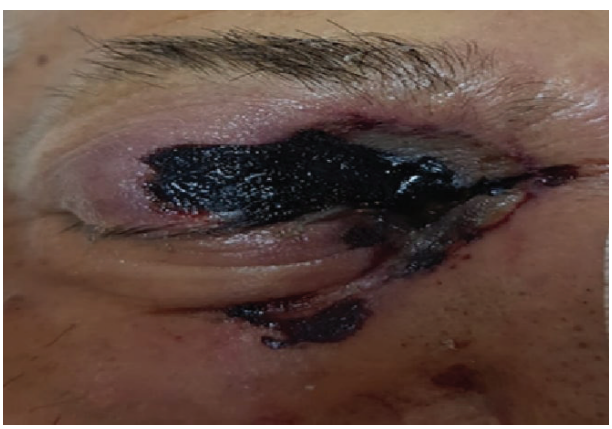
Approval for the study was granted by the University of Health Sciences Antalya Training and Research Hospital Local Ethics Committee (date: 2021, number: 333).

RESULTS:

All patients with mucormycosis were treated between June 2021 and November 2021. All patients were diagnosed with COVID-19 based on nasopharyngeal swab sample examination with SARS-CoV-2 real-time reverse transcription polymerase chain reaction (RTPCR), all of which resulted in delta variants. COVID-19 infection was defined as severe when SpO2 was <90% or the respiratory rate was >30 breaths/min at admisson or during hospitalisation(4). Nine patients were diagnosed with rinoorbital mucormucosis (Figure 1). Of these patients, six were male and three were female, and the patients were between the ages of 65–75 (mean 69.2). The patient information is presented in Table 1.

Seven patients had uncontrolled DM. The mean fasting blood glucose level of the patients was 283.27 mg/dL with a mean glycated haemoglobin (HbA1c) of 10.8% (±1.28). All patients were diagnosed by histopathological and microbiological examination of tissue samples taken from the nasal passage.

Figure 1. Rhinoorbital mucormucosis (orbita, eyelid and facial skin involvement)



The hospitalisation of patients diagnosed with mucormycosis was between 1–85 days. Once mucormycosis diagnosis was confirmed, patients were administered 5–10 mg/kg/day intravenous liposomal amphotericin B. Eight patients underwent surgery within 48 hours. Informed consent was obtained from all patients (first-degree relatives of the intubated patients) before surgery. One patient did not undergo surgery.

Medial maxillectomy and orbital exenteration were performed on the affected side in all the patients who underwent surgery. All patients underwent endoscopic sinus surgery, removal of non-viable tissues, and excision of the septum excised (Figures 2-3). Hard palate excision was performed in four patients. Postoperatively, the patients were followed-up with daily endoscopic examinations. Repeated debridement was performed in all patients during follow-up. The patients were followed up in the hospital for 20–95 days (mean 67.11 days) after the surgical intervention. Three patients were discharged from the hospital. The one patient who refused surgery died because of septic shock, and another five patients died while in the hospital due to cardiac or pulmonary causes. All the patients had unilateral eye involvement. In the patient that did not undergo surgery, the other eye was also involved 6 days after diagnosis (Figure 4).

DISCUSSION

Mucormycosis is a rapidly progressing opportunistic fungal infection (4,8,9). If there is no rapid intervention, it could reach the orbit and brain, causing death.

Although mucormycosis develops after severe COVID-19 infection, it has been reported that people who have mild illness also develop mucormycosis. The average time between COVID-19 infection and the development of mucormycosis is 15 days (6,7). However, mucormycosis infections have also been reported 42–90 days post COVID-19 infection

Table 1. Patients' informations with mucormucosis.

	Age/ Sex	Comorbidity	Vari-ant	Hba1c	Side	Corticosteroid treatment	Anti-fun-gal	Anti viral	ICU	Hos	Surgery	Mor-tality
1	73/M	DM (type 2)	Delta	13,7	Left	Dexamethasone 8 mg for 7 days	L-Amp B	Fav	Entube	62	MM+OE+ESC	Ex
2	68/F	DM (type 2), HT, Obesity	Delta	14,7	Right	Dexamethasone 6 mg for 9 days	L-Amp B	Fav	Entube	75	HPR+M-M+ESC+OE+SE	Alive
3	75/M	DM (type 1)	Delta	10,8	Left	Dexamethasone 6 mg for 10 days	L-Amp B	Fav	None	69	MM+ESC+OE+SE	Ex
4	65/F	CKF, Drug abuse	Delta	5,7	Right	Methylprednisolone 250 mg for 2 days and 80 mg for 5 days	L-Amp B	Fav	None	95	HPR+M-M+ESC+OE+SE	Alive
5	67/M	DM (type 2), HT	Delta	12,6	Right	Dexamethasone 6 mg for 10 days	L-Amp B	Fav	Entube	80	HPR+M-M+ESC+OE+SE	Ex
6	72/M	Pancreas Ca, CT, RT	Delta	4,6	Left	Methylprednisolone 100 mg for 3 days and 60 mg for 7 days	L-Amp B	Fav	None	45	MM+ESC+OE+SE	Alive
7	65/F	DM (type 2), HT	Delta	13,2	Right	Dexamethasone 6 mg for 10 days	L-Amp B	Fav	Entube	20	None	Ex
8	72/M	DM (type 2), HT	Delta	11,8	Right	Dexamethasone 6 mg for 7 days	L-Amp B	Fav	Entube	82	MM+ESC+OE+SE	Ex
9	66/F	DM (type 2), HT	Delta	10,7	Left	Dexamethasone 6 mg for 10	L-Amp B	Fav	Entube	76	HPR+M-M+ESC+OE+SE	Ex

(DM: Diabetes Mellitus, CKF: Chronic Kidney Failure, Hos: hospitalisation time, L-Amp B (Liposomal Amphotericin-B).

Fav (Favipiravir), MM: medial maxillectomy, OE: Orbital exenteration, ESC: Endoscopic Sinus Surgery, HPR: Hard Palate Resection, SE: Septum Excision)

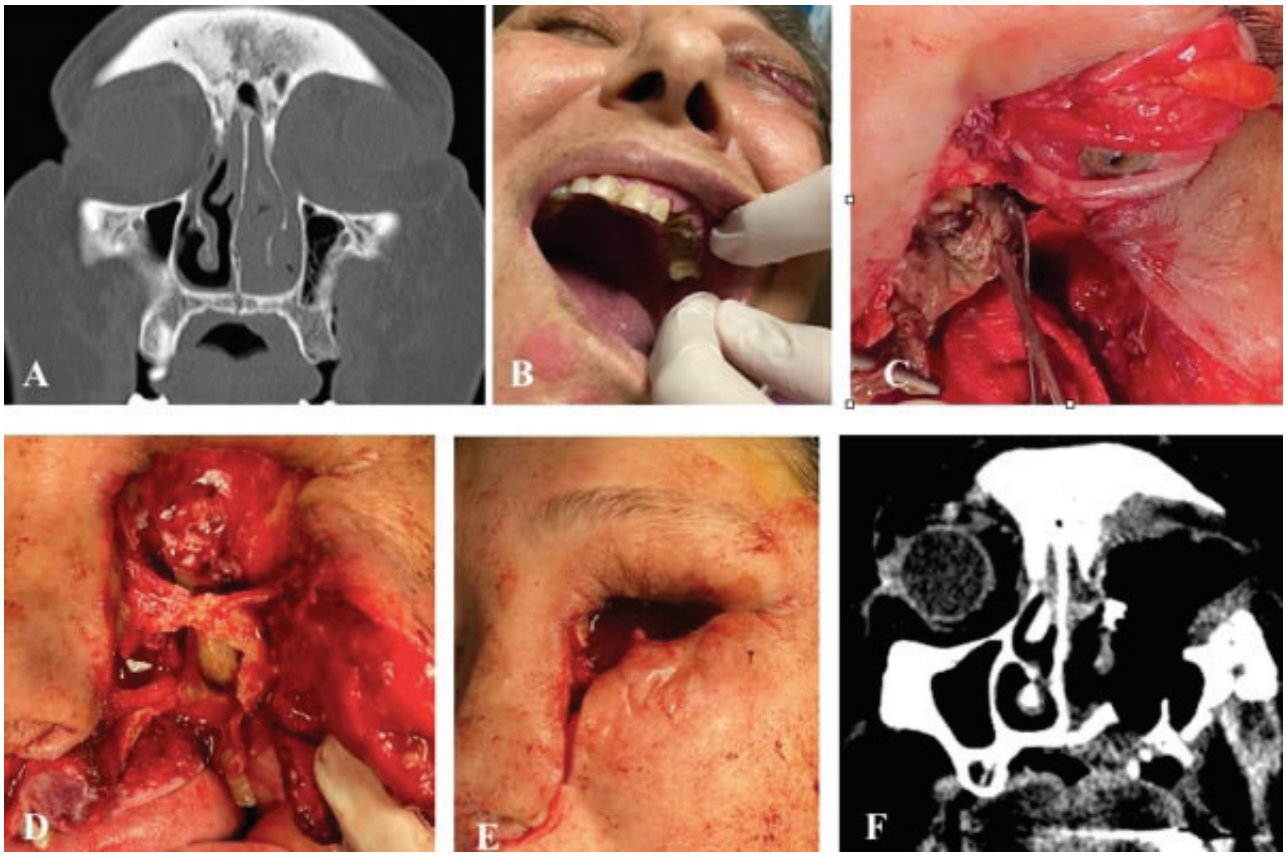
(7). Therefore, if mucormucosis is suspected, a rapid biopsy should be performed, and after histopathological and microbiological diagnoses, treatment should be started as soon as possible. Particular care should be taken in patients who are entubated, are in intensive care units, or have other predisposing factors.

The diagnosis of mucormycosis is typically made by histological and microbiological examination of the biopsy taken from the necrotic focus, with the appearance of strip-like, irregularly circumscribed, non-septate or less divided, wide hyphae, and vertically angled hyphae (4,8,10). However, it should not be forgotten that once biopsied lesions are detected, the disease has already begun. For this reason, studies aiming to detect mucor DNA in the blood and cerebrospinal fluid (CSF) are ongoing, so that diagnosis can be established before lesions occur (5).

Although there are many predisposing factors for the development of mucormycosis, DM is the most important factor determining morbidity and mortality (7,10). The acidic environment created by hyperglycaemia and ketoacidosis disrupts neutrophil chemotaxis, reduces neutrophil effects, and impairs fungal phagocytosis.

Another important risk factor for mucormycosis is steroid use. While steroids were not recommended in the treatment of COVID-19 during the first months of the pandemic, with the publication of many study results reporting the benefit of using corticosteroids to supress the systemic inflamatory over-response in severe COVID-19 patients, the Ministry of Health of our country launched a

Figure 2. A-B: Left rhinoorbital mucormucosis PNS CT and examination findings **C-E:** Subtotal maxillectomy and orbital exenteration intraoperative images **F:** Postoperative paranasal sinus CT



new COVID-19 guideline on the 2nd August 2020, instructing that "For those in need of oxygen, 6 mg/day dexamethasone (or equivalent glucocorticoids, such as 40 mg/day prednisolone or 32 mg/day methylprednisolone) can be used for 10 days" (11). It is believed that dysregulated and exessive cytokine storm may be a major cause of many metabolic problems seriously threatening the lives of COVID-19 patients, causing respiratory distress, multiple organ failure, or thromboembolic disease (12). In terms of recovery, it has been reported that steroid use was effective in reducing mortality in patients that were in need of oxygen (13). However, this high-dose steroid not only raises blood sugar in diabetic COVID-19 patients but also impairs neutrophil functions, which are the most important weapons of the immune system in fungal infections, and paves the way for opportunistic infections, especially mucormycosis (8,12).

Studies have shown that 78% of patients diagnosed with mucormycosis have a history of DM, and 85% have a history of high-dose glucocorticoid use (11). Glycaemic control is difficult to achieve when administering steroid therapy, especially in patients with diabetes and COVID-19.

In our study, only seven patients were diagnosed with DM. As all patients had severe COVID-19, they received corticosteroid therapy in the intensive care unit. There was no blood sugar level deterioration

Figure 3. A-C: Preoperative T2 sequence MRI inages of a patient with rhinoorbital mucormucosis Black arrow: Eye Involvement Star : Necrotic Tissues **D:** Intraoperative view of the patient after orbital exenteration and subtotal maxillectomy **E:** Post-operative image of the patient who was intubated due to COVID-19

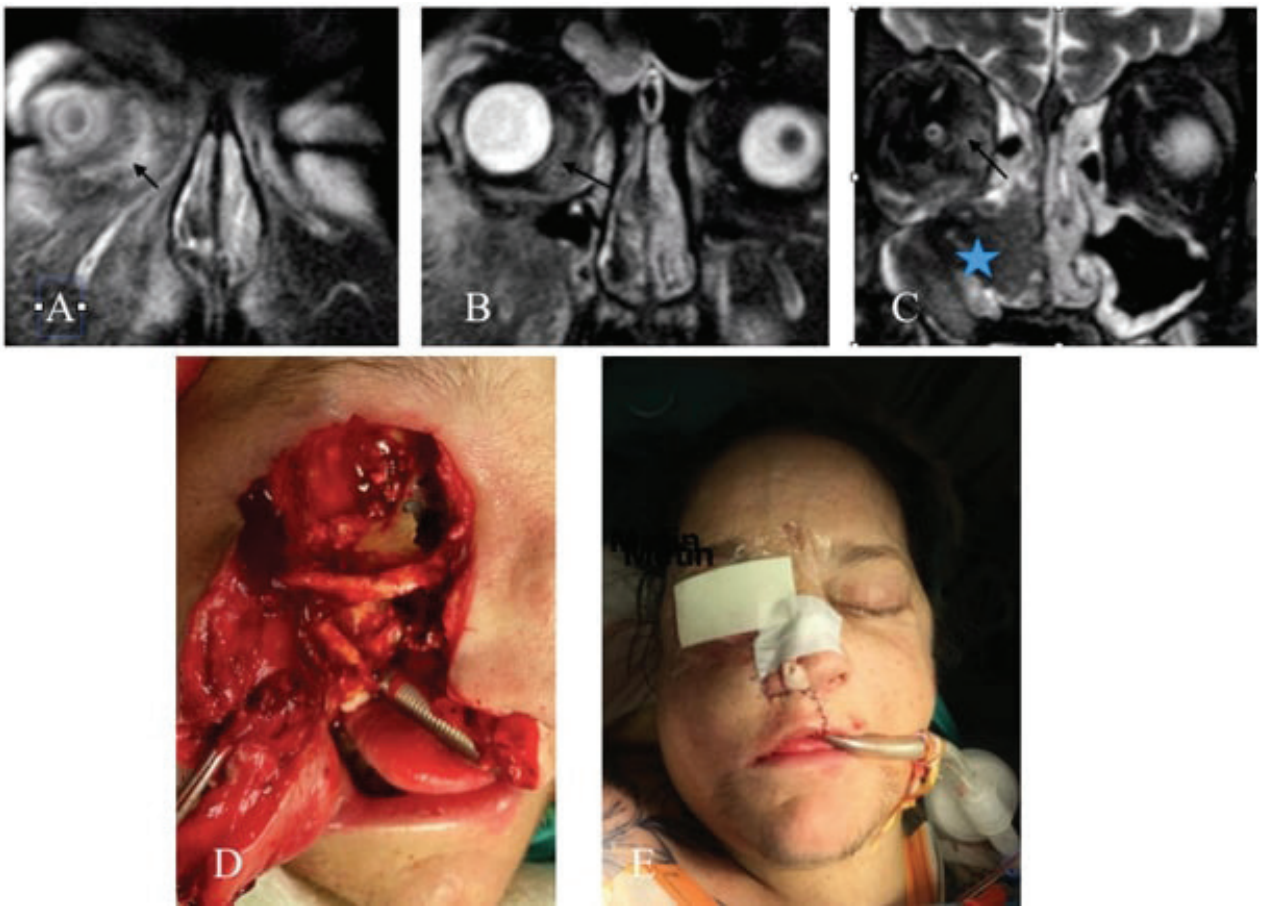


Figure 4. Bilateral eye involvement in the patient who did not accept surgery

in the two patients who did not have DM. However, one of these patients had a history of chronic renal failure and drug abuse, whereas the other had a history of chemoradiotherapy for pancreatic cancer.

In our study, all patients with mucormucosis who were diagnosed with COVID-19 were found to have delta variants. We attribute this situation to the fact that the delta variant causes more severe clinical effects than previous variants and to the increased use of corticosteroids at the intensive care unit. Therefore, opportunistic infections should be carefully considered when initiating corticosteroid treatment in patients with diabetes.

Mucormycosis is a rapidly progressing opportunistic fungal infection. Therefore, the most important criterion determining mortality in treatment is the early suspicion and diagnosis of mucormycosis infection, especially in patients with an underlying immunosuppressive state (4,8). Once mucormycosis has been diagnosed, comorbid risk factors, especially blood sugar regulation, should be corrected, and systemic and local antifungal therapy should begin. Furthermore immediate surgical debridement should also be performed. One year of treatment with posaconazole can be prescribed to patients whose condition stabilises after liposomal amphotericin B administration and surgical debridement.

Debridement should be performed at an early stage, before the infection spreads to the surrounding tissues, especially the skull base. In cases where cerebral involvement occurs, local control cannot be achieved and morbidity increases considerably. It is important to achieve local control of infections with repeated debridement. Washing the cavity with amphotericin B during debridement yielded more successful results in the local control of the infection (5,8). Although nasal and paranasal debridement is safely performed in rhino-orbital mucormycosis, there is no consensus regarding orbital involvement. Orbital orbital exenteration can be performed in collaboration with an ophthalmologist in patients with orbital involvement or permanent vision loss. However, recommending exenteration in patients without total vision loss causes some type of surgical avoidance. However, based on our clinical experience, if the infection extends out of the sinuses and reaches the orbit, exenteration is important for both local disease control and early recurrence detection after surgery.

CONCLUSION

Disease severity in COVID-19 may vary according to the variant. It should be noted that the risk of developing mucormucosis will increase in patients with comorbid diseases, especially in cases of severe COVID-19 or intensive care hospitalisations, which may increase the need for high-dose steroid use. Clinical suspicion plays an important role in the diagnosis of mucormucosis. Treatment should be performed quickly and care should be taken to perform the widest surgical debridement required.

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

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RESEARCH

THE EFFECT OF THE ADHERENCE TO THE MEDITERRANEAN DIET ON FRAILTY IN OLDER PEOPLE WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Abstract

Objective: To examine the adherence of older people diagnosed with chronic obstructive pulmonary disease to the Mediterranean diet and its relationship with frailty.

Methods: This descriptive and cross-sectional study included 446 people aged 65 and over who were hospitalized for chronic obstructive pulmonary disease exacerbations. Disease staging with the Global Initiative for Chronic Obstructive Lung Disease system, Modified Medical Research Council dyspnea intensities, Mediterranean Diet Adherence Screener, and Tilburg Frailty Index.

Results: All older people in the chronic obstructive pulmonary disease exacerbation period were frail. A mild, negative relationship was found between adherence to the Mediterranean diet and frailty levels (r= -0.267; p<0.001). Mediterranean Diet Adherence Screener explained 6.9% of frailty alone (adjusted R^2 = 0.069, p<0.001) and 11.9% of frailty together with disease stage (adjusted R^2 = 0.119, p<0.001).

Conclusions: These findings support the suggestion that a nutrition model based on the Mediterranean diet plays an important role in the management of frailty in older people with chronic obstructive pulmonary disease. High adherence to the Mediterranean diet is associated with lower dyspnea and disease severity in older people with chronic obstructive pulmonary disease and may help reduce frailty.

Keywords: Diet, Mediterranean; Frailty; Geriatrics; Pulmonary Disease, Chronic Obstructive.

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INTRODUCTION

Frailty Syndrome (FS) is generally defined as a decrease in reserves in multiple organ systems and includes physiological, cognitive, and sociocultural aspects. Although several functional definitions exist, FS was defined as "a health syndrome with multiple causes and contributions, characterized by a decrease in physiological function that increases the individual's vulnerability to decreased strength and endurance, increased dependence, and/or death" by a consensus group in 2013 (1). In this context, FS represents a comprehensive syndrome that leads to increased patient disability, healthcare costs, hospitalization rates, morbidity, and mortality, and is associated with chronic disease (2).

Studies have reported evidence that frailty might play an important role in the development of some chronic diseases and vice versa (i.e., chronic diseases may also cause frailty) (3). It is well known that seven of the first ten most common diseases that cause the highest mortality in the world are non-communicable chronic diseases, such as heart disease, stroke, cancer, diabetes, and chronic lung disease, and are responsible for 71% of all deaths (4). Chronic obstructive pulmonary disease (COPD), like other chronic diseases, is a serious public health problem, and its morbidity and mortality rates are increasing globally. COPD is a major global problem, considering the increased prevalence and incidence of COPD and its individual, social, and economic burdens (5).

Although the relationship between frailty and COPD has not been fully elucidated, they share common risk factors (e.g., age, smoking) and physiopathological processes, including systemic inflammation and endocrine dysfunction. Considering the common physiopathological outcomes of frailty and COPD, such as sarcopenia, neuroendocrinal disorders, and chronic malnutrition, diet, and nutrition have become more critical in the management of frailty and COPD. This is because diet and nutrition are modifiable risk factors for the development and progression of chronic diseases, such as COPD, and frailty (6,7).

Excessive consumption of red and processed meat is associated with poorer lung function and an increased risk of COPD (8). It has also been suggested that the current loss of adherence to healthy diets, such as the Mediterranean diet, leads to reduced consumption of fruits, vegetables, whole grains, and fish and increased consumption of processed and refined foods, which contribute to the high prevalence of chronic diseases (9,10). In this context, the Mediterranean diet, an accepted healthy nutrition model, provides effective amounts of fiber, antioxidants, phytosterols, polyphenols, and unsaturated fatty acids. The main foods that provide these nutrients are olive oil, wine, fish, and vegetables, especially tomatoes, onions, garlic, thyme, mint, rosemary, parsley, and dill, which contain significant amounts of omega-3 and vitamins C, E, and A (11,12). The possible beneficial effects of the Mediterranean diet on lung function have been demonstrated in a cross-sectional study with smokers and patients with associated diseases, such as asthma and COPD (13).

In light of previous studies, the hypothesis of our study was that there is a negative association between adherence to a Mediterranean diet and frailty in elderly patients with COPD. This study was conducted in Izmir, the third-most populous city in the Aegean Region in Turkey, a prominent region for agriculture and olive production and thus considered to be the most adaptable to the Mediterranean diet.

MATERIALS AND METHODS

Study Design

This is a descriptive, cross-sectional, and correlational study.

Study Population and Sample

The research population included patients 65 years old and over who were treated for COPD at

the Pulmonary Inpatient Clinic of Dr. Suat Seren Chest Diseases and Thoracic Surgery Training and Research Hospital for Pulmonary Diseases and Surgery. The G*Power 3.1.9.2 program was used to calculate the required sample size, which was found to be 319 given the effect size $\rho = 0.20$, $\alpha = 0.05$, and power (1-β) of 95%. However, to increase the generalizability of the study sample and reduce the margin of error, 446 older people were included in the study.

The inclusion criteria for this study were individuals who were literate, able to speak and understand Turkish, diagnosed with COPD, and hospitalized due to COPD exacerbation, aged 65 and over, agreed to participate in the study, and were not diagnosed with Alzheimer's, dementia, delirium, or any psychiatric disease by a physician. Individuals who did not meet the inclusion criteria and did not agree to participate in the study were excluded.

Data Collection Tools

The data collection tools used in this study were the participant identification form (PIF), Mediterranean Diet Adherence Screener (MEDAS), and Tilburg Frailty Index (TFI).

The PIF was created by the researchers in line with the literature and included a total of 16 questions, seven questions for sociodemographic features (age, gender, educational status, etc.), nine questions for health and disease status (height, weight, smoking and alcohol habits, number of years with COPD, GOLD stage, mMRC dyspnea score, presence of comorbidity, lifestyle health perception). The income levels of the participants were questioned based on the statement. Income levels were evaluated in 3 categories as low, medium and high, and people were asked to choose their perceived income levels. BMI was calculated using the formula body weight (kg)/ body length (2) (m2) and categorized based on the WHO classification. According to this classification, a BMI of 18.5–24.9 kg/m^2 is normal, 25.0–29.9 kg/m^2 is overweight, and ≥30 kg/m^2 is obese (14).

MEDAS, which consisted of 14 questions and had been used in 32 studies (PREDIMED) investigating Mediterranean diet habits, was demonstrated by Schröder et al. to be a valid and reliable tool (15). Two of the items of the scale are related to food consumption habits, and the remaining twelve items are related to food consumption frequency. Scored as 1 or 0 points based on the amount of consumption, the maximum score is 14 total points. A score of seven or above indicates that the individual can be considered adhering to the Mediterranean diet, while a score of nine or above indicates that the individual has a strict adherence to the Mediterranean diet. The validity and reliability study for the Turkish version of MEDAS was performed by Özkan Pehlivanoğlu et al. in 2019 (16).

The TFI was developed by Gobbens et al. (17) in 2010; the validity and reliability study of the Turkish version was performed by Arslan et al. (18) in 2018. The TFI includes a total of 15 questions in three dimensions that constitute frailty (eight items in the physical component, four items in the psychological component, and three items in the social component). Eleven items were answered as "yes" and "no"; four items were answered as "yes", "sometimes", and "no". In items 1, 12, and 15, "no" is coded as "1" and "yes" is coded as "0"; all other items are coded in reverse (yes=1 and no=0). For items with three choices; the "sometimes" option is coded as "0" in item 9 and "1" in items 10, 11, and 14. The score range is 0-15; a score of five or higher is considered as having frailty (17,18).

Data Collection Method

After the approval of the ethics committee and the institution, the data were collected by the researchers through the face-to-face interview technique, which lasted 10-15 minutes, after obtaining verbal consent from the individuals who met the inclusion criteria and made the necessary explanations.

Ethical Aspect of Research

Permission to use the scales was obtained via e-mail from the responsible authors who performed the validity and reliability studies of the Turkish versions of MEDAS and TFI. The ethics committee approval was obtained from the institution (approval number 2021/70); permission was also obtained from the Izmir Provincial Health Directorate to which the hospital is affiliated.

Evaluation of Data

Data analysis was performed with IBM SPSS 23.0 statistical package program. Skewness and kurtosis coefficients were used to evaluate the normal distribution of continuous variables; values between (-1.5) and (+1.5) were considered to indicate normal distribution. The descriptive statistics were presented as number, percentage, mean, and standard deviation. Independent-Samples *t*-test, Kruskal-Wallis *H*-test, Mann-Whitney *U*-test, and one-way analysis of variance (ANOVA) were used for comparisons of descriptive features and scale scores. Pearson analysis was used to evaluate the relationship between continuous data and scale scores; linear logistic regression was performed to determine the effect of independent variables on the dependent variables. The results were evaluated at the 95% confidence interval and the $p<0.05$ significance level.

RESULTS

The mean age of the individuals included in the study was 73.56±4.62 years; 51.8% of them were 75 years or older. Of the participants, 59.4% were male, 87.2% were married, 78.7% had eight years of education or less, 67.5% were retired, 55.2% had low income, and 52% lived in rural areas (Table 1).

Of the participants, 57.2% were overweight, 53.2% had quit smoking, and 65.4% never consumed alcohol. The average years of having COPD was 17.29±4.86; 41.5% of the participants had COPD for more than 20 years; 59% had GOLD stage III; 55.8% had an mMRC dyspnea severity of 3. At least one additional disease other than COPD was present in 98% of the participants. The mean MEDAS score, which shows the level of adherence to the Mediterranean diet, was 8.45±2.28; 49.4% of them adhered to the Mediterranean diet closely. The mean TFI score, which indicates the frailty level, was 10.13±2.17, and all patients (100%) were frail based on the cutoff score of 5 (Table 2).

Table 1. Sociodemographic characteristics of older COPD patients

Variables	n	%
Age (years) (Mean±SD) (Min-Max)	73.56±4.62 (65-88)	
65-74	215	48.2
75 ≤	231	51.8
Gender		
Male	265	59.4
Female	181	40.6
Marital status		
Single	57	12.8
Married	389	87.2
Education status		
≤ 8 years	351	78.7
≥ 9 years	95	21.3
Labor status		
Unemployed	124	27.8
Worker	21	4.7
Retired	301	67.5
Income status		
Low	246	55.2
Medium	191	42.8
High	9	2.0
Residential area		
City	214	48.0
Rural	232	52.0
TOTAL	**446**	**100.0**

The comparison of the participants' adherence to the Mediterranean diet and frailty when they are grouped according to their sociodemographic characteristics is shown in Table 3. Significant differences were found between the groups based on gender and occupational status ($p<0.001$). Men had lower MEDAS scores and higher TFI scores than women. The difference in the occupational groups originated from retirees, who had lower MEDAS

Table 2. Health and disease characteristics and scale scores of the participants

Variables	n	%
	Mean±SD (Min-Max)	
BMI	29.71±2.37 (20.96-35.16)	
BMI Classifications		
Normal (18.50-24.99 kg/m^2)	12	2.7
Over weight (25-29.99 kg/m^2)	255	57.2
Obese (≥30 kg/m^2)	179	40.1
Smoking status		
Smoker	142	31.8
Ex-smoker	237	53.2
Non-smoker	67	15.0
Alcohol Consumption		
Drinking	19	4.3
Withdrawal	135	30.3
Non-drinking	297	65.4
COPD years Mean±SD (Min-Max)	17.29±4.86 (5-30)	
COPD years		
< 11	56	12.5
11-19	205	46.0
19 <	185	41.5
GOLD Stage		
Stage II	73	16.4
Stage III	263	59.0
Stage IV	110	24.6
mMRC Dyspnea Scale		
≤2	73	16.4
3	249	55.8
4	124	27.8
Comorbidity		
Yes	437	98.0
No	9	2.0
MEDAS Mean±SD (Min-Max)	8.45±2.28 (2-13)	
MEDAS		
Low adherence (<7p)	92	20.6
Medium adherence (7p-8p)	134	30.0
High adherence (9p≤)	220	49.4
TFI	10.13±2.17 (5-15)	
TFI Classification		
Frail (≥5p)	446	100.0
TOTAL	**446**	**100.0**

scores and higher TFI scores than the other groups. There was a significant difference between the MEDAS scores of groups based on their area of residence ($p<0.05$, those living in rural areas had higher MEDAS scores); however, there was no significant difference between their TFI scores ($p>0.05$) (Table 3).

The comparison of the participants' adherence to the Mediterranean diet and frailty when they are grouped according to the variables related to health and disease status is shown in Table 4. Significant differences were found between the MEDAS scores of the participants grouped based on their BMI category, smoking status, and alcohol consumption ($p<0.05$); however, no significant difference was found between their TFI scores ($p>0.05$). In the posthoc analyses, the difference between the MEDAS scores was found to be due to the normal BMI group, non-smokers, and alcohol users.

Significant differences were found between the groups when the participants were grouped based on disease-specific variables such as the number of years with COPD, GOLD staging, and mMRC dyspnea severity, and their MEDAS and TFI scores were compared ($p<0.001$). According to the posthoc analyses, the mean MEDAS score was lower and the mean TFI score was higher for those who had COPD for 20 years or more and whose disease severity was GOLD stage IV and dyspnea severity was 4 (Table 4).

The explanatory power of the models developed by multivariate linear regression analysis (Adjust R^2) according to the data obtained from the participants was given in Table 5. Accordingly, the explanatory power of the relationship between adherence to the Mediterranean diet and frailty level was 6.9% (Model 1; $\beta = -0.267$, Adjust $R^2 = 0.069$, $p<0.001$). The explanatory power of the adherence to the Mediterranean diet and GOLD staging together for the frailty level was 11.9% (Model 2; Adjust $R^2 = 0.119$, $p<0.001$) (Table 5).

DISCUSSION

Considering that Fried et al. (19) (2001) established a frailty phenotype that includes weight loss, fatigue, weakness, slowness, and low physical func-

Table 3. Comparison of MEDAS and TFI scores of the participants grouped based on sociodemographic variables

Variables	MEDAS 8.46±2.27		TFI 10.00±2.89	
Age				
65-74 (n=215)	8.49±2.26	t= 0.317	10.26±2.21	t= 1.141
75 ≤ (n=231)	8.42±2.30	p>0.05	10.02±2.11	p>0.05
Gender				
Male (n=265)	7.97±2.34	t= -5.633	10.46±2.22	t= 5.079
Female (n=181)	9.16±1.97	**p<0.001**	9.33±2.46	**p<0.001**
Marital Status				
Single (n=57)	8.24±2.12	t= -0.778	10.26±2.94	t= 0.742
Married (n=389)	8.49±2.29	p>0.05	9.96±2.29	p>0.05
Education status				
≤ 8 years (n=351)	8.38±2.36	t= 4.078	10.04±2.32	t= 0.164
≥ 9 years (n=95)	8.54±1.97	p>0.05	9.82±2.73	p>0.05
Labor status				
Unemployed (n=124)	9.11±2.05	X^2= 18.556	9.49±2.29	X^2= 10.312
Worker (n=21)	9.13±2.28	**p<0.001**	9.39±3.46	**p<0.001**
Retired (n=301) [a]	8.14±2.30		10.25±2.29	
Income status				
Low (n=246)	8.42±2.34	X^2= 0.802	10.15±2.22	X^2= 3.294
Medium (n=191)	8.47±2.21	p>0.05	9.86±2.60	p>0.05
High (n=9)	9.11±1.76		8.89±1.27	
Residential area				
City (n=214)	8.22±2.07	t= 2.216	10.19±2.16	t= 0.490
Rural (n=232)	8.70±2.47	**p<0.05**	10.09±2.18	p>0.05

t: Independent Sample t test; X^2: Kruskal Wallis H; [a] The group causing intergroup significance

tion components, individuals with COPD constitute a vulnerable group of older people who may also exhibit frailty. Based on this information, all older people with COPD participating in our study were frail according to the assessment tool we used (≥5 points), and their frailty levels were quite high based on the mean score (10.13±2.17). Also in Turkey reported that the prevalence of frailty in older people with COPD ranged from 50.2% to 84.7% (20). The difference in this study is thought to be due to the fact that the study sample consisted of individuals who were treated in the hospital due to COPD exacerbation. In our study, advanced age was not a predictor of frailty because frailty levels were quite high in the 65-74 age group as well as in those 75 and over. However, contrary to the common view, there are opinions arguing that chronological age is not the only factor to be taken into account and that some individuals may remain strong and active even at advanced ages (21).

Despite high levels of frailty in both genders, the main finding that caught our attention was that the frailty level of males was significantly higher than that of females in our study. Although it was claimed that women were frailer than men and some studies supported this view (19,20). However, this is the first time a higher level of frailty was reported for men. Such a higher level of frailty can be attributed to the man with COPD exacerbation being more affected by the disease burden or the difference in the assessment tools used in the study. A similar study reported that the unemployed were frailer (20); similarly, our study concluded that the retired had a higher level of frailty. Indeed, it is assumed that this is related to the fact that the male gender in our study had higher frailty. It is thought that the dif-

Table 4. Comparison of MEDAS and TFI scores of the participants grouped based on variables related to health and disease status.

Variables	MEDAS 8.46±2.27		TFI 10.00±2.89	
BMI Classifications				
Normal (n=12) [a]	9.17±1.94	X^2= 7.422 **p<0.05**	8.92±1.78	X^2= 5.468 p>0.05
Over weight (n=255)	8.78±2.12		10.12±2.18	
Obese (n=179)	8.39±2.37		10.24±2.15	
Smoking status				
Smoker (n=142)	8.23±2.20	F= 4.427 **p<0.05**	9.89±2.50	F= 0.746 p>0.05
Ex-smoker (n=237)	8.39±2.28		9.98±2.37	
Non-smoker (n=67) [a]	9.19±2.67		9.81±2.21	
Alcohol Consumption				
Drinking (n=19)	9.05±2.42	X^2= 13.475 **p<0.05**	10.25±2.43	X^2= 4.526 p>0.05
Withdrawal (n=135)	8.99±2.02		9.70±2.37	
Non-drinking (n=297) [a]	8.18±2.33		10.12±2.39	
COPD years				
<11 (n=56)	9.84±1.72	F=17.333 **p<0.001**	9.50±2.06	F=11.411 **p<0.001**
11-19 (n=205)	8.58±2.24		9.80±2.11	
19< (n=185) [a]	7.90±2.27		10.69±2.13	
GOLD Stage				
Stage II (n=73)	9.12±2.00	F=11.534 **p<0.001**	9.40±2.12	F=20.875 **p<0.001**
Stage III (n=263)	8.61±2.19		9.89±2.13	
Stage IV (n=110) [a]	7.63±2.43		11.20±1.92	
mMRC Dyspnea Scale				
≤2 (n=73)	9.12±2.00	F=12.361 **p<0.001**	9.45±2.16	F=27.243 ***p<0.001***
3 (n=249)	8.65±2.17		9.77±2.10	
4 (n=124) [a]	7.65±2.44		11.27±1.87	

X^2: Kruskal Wallis H; F: One Way ANOVA; [a] The group causing intergroup significance

ference may be due to the fact that the retirees are predominantly men since the unemployed group is mostly composed of women and the labor force is generally composed of men in the Turkish population.

Similar to our study, Bozkurt et al. (20) (2021) reported no relationship between smoking and frailty levels; however, in the same study, those who consume alcohol were found to have lower frailty, unlike our study. It is assumed that the difference may be due to the differences in the patient groups involved.

A significant relationship was found between the level of frailty and the number of years with COPD and GOLD disease stage, which indicate the disease burden, and the mMRC scale, which indicates the severity of dyspnea. This difference was due to individuals who have lived with COPD for many years and had the end-stage disease and severe dyspnea. In fact, this did not change the result that all older

Table 5. The relationship between the disease stage of the participants and their adherence to the Mediterranean diet or frailty level according to multiple linear regression analysis

Models	B (95.0%CI for B)	ß	t	*p*	Adjust R^2	Model p
Model 1. TFI						
MEDAS	-0.253 (-0.339, -0.169)	-0.267	-5.832	**0.000**	0.069	**0.000**
Model 2. TFI						
MEDAS	-0.206 (-0.291, -0.121)	-0.216	-4.748	**0.000**	0.119	**0.000**
GOLD Stage	0.791 (0.486, 1.096)	0.232	5.092	**0.000**		

TFI: Tilburg Frailty Index; MEDAS: Mediterranean Diet Adherence Screener; GOLD: Global Initiative for Chronic Obstructive Lung Disease; B: unstandardized coefficients; CI: confidence interval; β: standardized regression coefficient; R^2: coefficient of determination.

COPD patients in our study were frail, but the fact that the participants were being treated for COPD exacerbations may also explain the increased frailty levels. Similarly, the positive correlation of these values with frailty as indicators of disease and dyspnea severity was also in line with the findings of a previous study (20).

Nutritional imbalances in older people lead to morbidity and mortality and emerge as protein-calorie malnutrition in advanced ages. A study have also focused on dietary patterns, such as the Mediterranean diet, to understand the relationship between frailty and diet (22). In our study, the mean MEDAS score, which shows the level of adherence to the Mediterranean diet, was 8.45±2.28; approximately half of the participants were found to follow the Mediterranean diet closely. This was expected because İzmir, where the study was conducted, is one of the provinces where the consumption of olives, olive oil, and vegetable-based foods is among the highest in the country. Being on the coast of the Aegean Sea, fish is consumed regularly in İzmir. Cheese and especially yogurt have an indispensable place in Turkish cuisine and are consumed frequently. It was found that women adhered to the Mediterranean diet more closely than men. Similarly, a recent study with older patients hospitalized in the departments of internal medicine in Italy reported that women had higher adherence to the Mediterranean diet than men (23). In line with their frailty, retirees had a significantly lower level of adherence to the Mediterranean diet compared to other groups. This can be attributed to the fact that the retiree group is mostly composed of men. Dinu et al. (24) observed no relationship between adherence to the Mediterranean diet and area of residence (rural vs. city). In our study, on the contrary, individuals living in rural areas had higher MEDAS scores ($p<0.05$). We think that this difference may be due to the fact that individuals living in rural areas consume more natural foodstuffs. It may also be due to the lack of an equal representation of the different areas of residence in our study.

When the adherence of the older people to the Mediterranean diet was compared with their BMIs, we found that the individuals with normal weight adhered to the Mediterranean diet more closely than the overweight and obese individuals. This was expected, but it may be wrong to make a definitive judgment since the number of participants with normal weight was quite low.

We found that the adherence to the Mediterranean diet decreased as the number of years with COPD, disease stage, and severity of dyspnea in-

creased. In fact, the groups that underlie this significant difference were those with COPD for more than 20 years, GOLD stage IV, and mMRC dyspnea severity of "4"; however, even these groups showed "moderate adherence" to the Mediterranean diet. On the other hand, a cross-sectional study with smokers and asthma and COPD patients have reported possible beneficial effects of the Mediterranean diet on lung function (13). Therefore, it can be concluded that high adherence to the Mediterranean diet might have a slowing effect on the progression of the disease, even if their lung function is impaired due to COPD. As we indicated in Table 5, the disease stage had a negative correlation with the MEDAS score, albeit at a very low level. Although the result of this analysis is not sufficient to make a definitive judgment, it is known that vitamin C and omega-3 fatty acids in the Mediterranean diet are associated with high lung function in individuals with COPD as well as in healthy individuals (25). Similarly, a positive correlation has also been shown between vitamin E found in olives, a staple in the Mediterranean diet, and forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1), which indicates the disease stage (26).

The aim of our study was to examine the relationship between adherence to the Mediterranean diet and the level of frailty in older people with COPD, and to our knowledge, this was the first study conducted in Turkey. In line with the data we obtained, the effect of adherence to the Mediterranean diet on the frailty level was 6.9%. The combined effect of adherence to the Mediterranean diet and disease stage on the frailty level was 11.9%. We think that our sample group is representative of conditions with a high physio pathological burden such as both COPD and old age. Based on these results, that all older people under treatment for COPD exacerbation were frail, even in a region with high adherence to the Mediterranean diet, may indicate that the burden of disease and the level of frailty might be further increased in societies that do not comply with the Mediterranean diet or have adopted other dietary models. Of course, diet alone is not sufficient, but it is an important modifiable factor that is thought to have substantial benefits for both the disease burden and frailty in older people with COPD.

There were several limitations to our study. First, the study has a descriptive and associated pattern; therefore, the results of the study do not suggest causality. We evaluated only the elderly who received inpatient treatment. Finally, the sample was small and findings were limited to the chest clinics of a single hospital in Turkey. These disadvantages, together with our non-random sampling and single-center data collection, limit the generalizability of the findings to all Turkish older people with COPD.

Despite the limitations noted above, this study demonstrated the importance of adherence to MD in geriatric populations with COPD to reduce frailty level. It was observed that frailty levels were lower in the group with high adherence to MD. In addition, the strength of our study is that it is the first study to examine the relationship between adherence to the Mediterranean diet and frailty in the geriatric COPD population in Turkey.

CONCLUSION

Frailty is a syndrome that increases with advanced age and comorbidity. Although it was first thought to be only a physiological phenomenon, over the years it has been established as a biopsychosocial concept and that there are mental and social dimensions to it as well as physical aspects. However, due to the fact that it has been on the agenda for the last 30 years, the focus has been on the physical dimension to prevent or eliminate the development of frailty. In this context, physical activity and healthy nutrition have been emphasized in the literature. Thus, this study consisted of older hospitalized patients, who were diagnosed with COPD, and hence

have many risk factors for frailty. In this context, we think that the Mediterranean diet, which is accepted as one of the most valid healthy nutrition models in line with the data in the literature and in our study, may be beneficial for COPD and frailty syndrome. Thus, it would be appropriate to recommend the Mediterranean diet by health professionals for the management of these physiopathological conditions. This study provides instructions for future longitudinal or experimental studies.

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RESEARCH

COMPARISON OF THE MODIFIED 5-ITEM FRAILTY INDEX WITH THE AMERICAN SOCIETY OF ANESTHESIOLOGISTS CLASSIFICATION AND CHARLSON AGE COMORBIDITY INDEX FOR PREDICTING POSTOPERATIVE OUTCOMES IN GERIATRIC PATIENTS: A PROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Introduction: Frailty scores estimate postoperative outcomes in elderly patients. This study sought to compare the performance of the modified 5-item frailty index (mFI-5) with the other indexes as postoperative outcome predictors, especially for 1-year mortality in geriatric patients.

Materials and Method: Patients aged ≥ 65 years who underwent elective surgery were enrolled. Along with comparisons in scoring systems, demographics, anesthesia method, operation duration, presence of preoperative transfusion, complications, length of hospitalization, intensive care admission, hospital mortality rate, and 1-year mortality were recorded. Pearson's chi-square test, receiver operating characteristic curve analysis, and binary logistic regression analysis were performed.

Results: Overall, 33% of patients experienced complications and 12% were admitted to intensive care units. The hospital mortality rate was 3.3% (n=10), and the 1-year mortality rate was 27.4% (n=82). The Charlson aged comorbidity index was associated with the overall complications (Area Under Curve (AUC): 0.819, $p<0.001$) very well, and patients with a score over 5 have a 16.075 ($p<0.001$) times higher risk of hospital mortality. The American Society of Anesthesiologists (ASA) classification was associated satisfactorily with overall complications, intensive care admission, hospital mortality, and 1-year mortality (Respectively, AUC: 0.698, 0.662, 0.653, 0.629; $p<0.05$ in all). The mFI-5 score was associated well with intensive care admission (AUC: 0.702, $p<0.001$), and patients with a score over 2 have a 2.741 ($p<0.02$) times higher risk of 1-year mortality.

Conclusions: The mFI-5 was associated with intensive unit admission and 1-year mortality and, was not superior to the ASA classification and the Charlson age comorbidity index classification in predicting the overall postoperative outcomes.

Keywords: Intensive Care Units; Hospital Mortality; Aged; Frail Elderly; Risk Factors.

INTRODUCTION

In the second half of the 20th century, improvements in survival after 65 years of age have led to an increase in life expectancy and a decline in mortality rates at an advanced age (1). The global population of the elderly is projected to double between 2019 and 2050, with all regions expected to experience an increase in their elderly population (2). The increasing proportion of older adults in the general population has resulted in an increase in the number of geriatric patients undergoing surgery.

Elderly patients present additional challenges for perioperative management as a result of the increase in comorbidities and a decrease in physiologic reserve; they also require appropriate, effective, and specialized postoperative care and treatment. Therefore, preoperative recommendations and guidelines for elderly patients can provide a useful starting point for evaluating and optimizing preoperative assessment (3). Traditional methods of operative risk assessment include the ASA physical status classification and the Charlson comorbidity index (CCI) (4, 5). The Charlson comorbidity index (CCI) was developed and validated as a measure of 1-year mortality risk and morbidity (6). In one study, the Charlson age comorbidity index (CACI) was considered a more appropriate prognostic indicator for clinical practice (7).

Frailty scores have been used to predict postoperative complications and outcomes in elderly patients undergoing surgery (8). The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) uses 11 variables listed to predict frailty in preoperative settings. However, the effectiveness of the 11-item modified frailty index (mFI-11) has been questioned since 2012 due to the irregular registration of the 11 original variables. In response, researchers developed the modified frailty index-5 (mFI-5), which includes consistently recorded and validated variables in the NSQIP dataset. In a few studies, the mFI-5 was shown to be as good as the mFI-11 for predicting 30-day mortality (9,10).

Our objective was to compare mFI-5, ASA classification, and CACI as independent predictors of postoperative outcomes in geriatric patients. We were interested in the ability of these measures to predict complications, intensive care unit (ICU) admission, hospital mortality, and specifically 1-year mortality as these outcomes have the potential to significantly impact the quality of life of geriatric patients. We hypothesized that mFI is better than ASA classification and CACI in predicting postoperative outcomes in geriatric patients.

MATERIALS AND METHOD

This prospective observational study included patients aged 65 years and older who underwent elective surgical operations in neurosurgery, urology, orthopedics, or general surgery clinics from the Health Sciences University Hamidiye International Faculty of Medicine Kartal Dr. Lutfi Kirdar City Hospital from July 2019 to May 2021. Patient information and consent were obtained from the preoperative services. Patients who were under the age of 65 years, underwent emergency surgery, and had a psychiatric, genetic, or coagulation disorder, were excluded from the study.

Study Design

Detailed baseline clinical and pathological characteristics were extracted for each patient and included sex, age, educational status, medical history, oncological disease, operation type (Table 1), anesthesia method, and duration of the operation. The European Society of Cardiology and European Society of Anesthesiology on Non-Cardiac Surgery (ESC/ESA-NCS) guidelines were used as references for the classification of surgical interventions (11).

Postoperative complications were graded according to the Clavien–Dindo system (12) which classifies complications into five grades: grade

1 (Any deviation from the normal postoperative course without the need for pharmacological treatment or any interventions except wound infections opening at the bedside. Allowed therapeutic regimens are drugs such as antiemetics, antipyretics, analgesics, diuretics and electrolytes, and physiotherapy), grade 2 (Requiring pharmacological treatment with drugs other than such allowed for grade I complications including blood transfusions and total parenteral nutrition), grade 3 (Requiring surgical, endoscopic or radiological intervention which is classified into two subsections: not under general anesthesia (3a) and under general anesthesia (3b)), grade 4 (Life-threatening complication, including CNS complications and requiring IC/ICU-management, is classified into two subsections: single organ dysfunction including dialysis (4a) and multiorgan dysfunction (4b)), and grade 5 (death of a patient).

ASA classification (4) was extracted directly from the NSQIP. One patient was classified as ASA 1 (indicative of a normal healthy patient) and was enrolled with patients classified as ASA 2 (indicative of mild systemic disease) for a combined analysis. The CACI (7) was calculated based on the following ACS-NSQIP variables and the mFI-5 score (9) was created using previously established methods. Assessment and explanations of risk scores with reference sources mentioned before are depicted in Table 2.

After routine discharge, the length of hospital stay, ICU admission, length of ICU stay, and hospital mortality rate were recorded. The length of hospital stay was compared with Turkey's average duration of 4.1 days, and this statistical measurement was used to calculate prolonged LOS. As none of the patients who were admitted to ICUs stayed longer than 14 days, prolonged ICU stay was not recorded in this study. After one year, the patients or their relatives were contacted via telephone, and the status of the patients was determined.

The primary outcomes of our analyses were the finding of the three risk scores' success that may predict overall complications, ICU admission, prolonged LOS, hospital mortality, and 1- year mortality. Secondary outcomes were the finding of all factors that may affect the postoperative outcomes.

This study was approved by the Health Sciences University Hamidiye International Faculty of Medicine Kartal Dr. Lutfi Kirdar City Hospital Ethics Committee (Protocol No:2019/514/158/4-Date:24.07.2019). All authors have acknowledged that there were no conflicts of interest related to this work to declare. This study was conducted in accordance with the ethical principles of the Helsinki Declaration-2013 and followed good clinical practice guidelines.

Statistical Analysis

The conformity of the variables to the normal distribution was examined using visual (histogram and Q-Q plot) and analytical methods (Kolmogorov-Smirnov test). Median and minimum, maximum or percentages, and frequencies were reported for non-normal distributed continuous or categorical variables, respectively. The Mann-Whitney U test was used for ordinal variables, and Pearson's chi-square test and Fisher's exact tests were used for categorical variables.

In this study, mFI-5, CACI, and ASA classes were determined as three different groups, and the effect size was taken to be the same as the medium (medium=0.25), with a confidence interval (CI) level of 80% and an alpha of 5% in power analysis. Each group consisted of 75 patients, and the total number of patients was 225. (G Power 3.1.9.2. Windows 10). All the scoring systems were assessed as ordinal variables. Data were analyzed using the SPSS version 26 (IBM, Chicago, IL, USA). Receiver operator curve (ROC) analysis was used to evaluate the performance of risk scores as continuous variables for predicting complications, ICU admission, hospital mortality, and 1-year mortality prediction. The cut-off values in the study were calculated according to Youden's index; mFI-5 (group1 = mFI-5 < 2, group2= mFI-5 ≥ 2), CACI (group1= CACI < 5, group2= CACI

Table 1. Operation types.

General Surgery	Orthopedics	Neurosurgery	Urology
- Thyroidectomy (Partial / Total) - Parathyroidectomy - Mastectomy (BCT/Radical) - Esophagectomy - Gastrectomy (Partial/Total) - Colectomy (Hemicolectomy/ Total) - Low Anterior Resection - Hepatectomy - Whipple Procedure - Hernia Surgery (Incisional/ Inguinal/ Umbilical) - Cholecystectomy	- Lower/Upper Limb Tumor Excision - Below/Above Knee Amputation - Knee Replacement Surgery - Total Hip Replacement - Lower/Upper Extremity Fracture Fixation	- Tumor Excision (Frontal/Occipital/Posterior Fossa /Temporoparietal/ Extradural) - Thoracal/Lumbal/Lumbosacral Stabilization - Spinal Instrumentation Removal - Spondylolisthesis Surgery - VP Shunt Surgery - Chronic Subdural/Epidural Hematoma Evacuation Surgery	- Nephrectomy (Partial/ Radical) - Cystectomy - Transurethral Resection - Intervention with ureteroscopy - Retrograde Intrarenal Intervention

Table 2. Risk Stratification Methods

ASA classification (4)	**Class**	**CACI*** (7)	**Score**	**mFI-5**** (9)	**Score**
-A normal healthy patient	ASA 1	-Age (for each decade ≥ 50 years)	1	-Impaired functional status prior to surgery (partial or total dependence)	1
-A patient with mild systemic disease	ASA 2	-MI within 6 months prior to surgery	1	-CHF within 30 days before surgery	1
-A patient with severe systemic disease	ASA 3	-CHF	1	-Hypertension requiring medication	1
-A patient with severe systemic disease that is a constant threat to life	ASA 4	-PVD	1	-Severe COPD or current pneumonia	1
-A moribund patient who is not expected to survive without the operation	ASA 5	-Ulcer disease	1	-Diabetes mellitus	1
-A declared brain-dead patient whose organs are being removed for donor purposes	ASA 6	-Dementia	1		
		-Mild liver disease	1		
		-Diabetes mellitus	1		
		-History of TIA or CVA	1		
		-COPD	1		
		-DM with end-organ damage	2		
		-Hemiplegia	2		
		-ESRD	2		
		-Any tumor	2		
		-Leukemia	2		
		-lymphoma	2		
		-Disseminated cancer	6		
		-AIDS	6		

ASA: The American Society of Anesthesiologists Physical Status Classification, mFI-5: Modified 5-item frailty index, CACI: The Charlson age comorbidity index, MI: Myocardial infarction, CHF: Congestive heart failure, PVD: Peripheral vascular disease, TIA: Transient ischemic attack, CVA: Cerebrovascular accident, COPD: Chronic obstructive pulmonary disease, DM: Diabetes mellitus, ESRD: End-stage renal disease.

* Higher CACI results are associated with higher mortality and morbidity risk.

**Higher score of mFI-5 is associated with higher frailty risk.

≥ 5), and ASA class (group1= ASA class < 3, group2= ASA class ≥ 3) were divided into two groups. Covariates were analyzed using the backward stepwise binary logistic regression method to determine associations with postsurgical outcomes, considering factors such as age, sex, presence of oncological disease, surgical-grade classification, anesthesia method, perioperative transfusion, ICU admission, LOS, and mFI-5, CACI, or ASA class categorization. Statistical significance was set at $p < 0.05$.

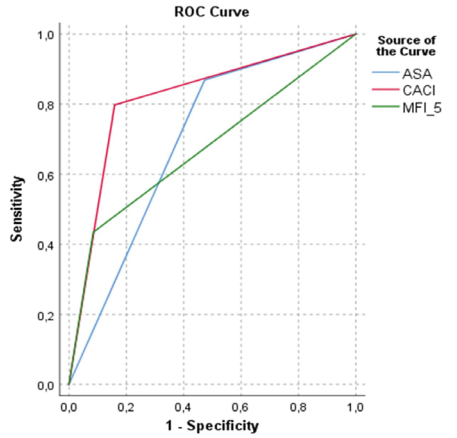
RESULTS

During the study period, 300 patients underwent different types of surgeries at four clinics (neurosurgery, urology, orthopedics, or general surgery). Patient demographics, preoperative characteristics, operative characteristics, and postoperative outcomes are shown in Table 3. The median age was 71 (65-95). Female patients accounted for 47% (n=141) of the study group; one-third of the patients had oncological diseases preoperatively (n=100, 33.3%) and 43% (n=129) of the patients had intermediate surgical risk according to ESC/ESA-NCS guidelines. The median of ASA class values was 3(2- 4), the median of CACI values was 5(2- 13), and the median of mFI-5 scores was 2(0- 5). A total of 175 patients received general anesthesia. Thirty-eight patients (12.7%) required blood product transfusion. Total 33% of the patients (n = 99) experienced a complication; the most common complication grades are grade 1 (n=43, 14.3%) and grade 4 (n=36, 12%) according to Clavien Dindo classification. Only 12% (n= 36) of the patients were admitted to the ICU. The median LOS was 2 days (1–51) and prolonged LOS was observed in 82(27.3%) patients. The overall hospital mortality rate was 3.3% (n=10) and the 1-year mortality rate was 27.4% (n=82).

ROC analysis (Figure1) demonstrated a very good association of CACI (area under the curve [AUC], 0.819; 95% CI, 0.765-0.874), and satisfactory association of mFI-5 (AUC, 0.675; 95% CI, 0.606-0.744) and ASA class (AUC, 0.698; 95% CI, 0.638-0.758) with overall complications. The AUC for mFI-5 and ICU admission were 0.702 (95%CI, 0.601-0.804), 0.669 (95%CI, 0.574-0.763) for CACI, and 0.662 (95%CI, 0.580-0.745) for ASA. As per the AUCs, mFI-5 is a better risk stratification index for ICU admission compared to CACI and ASA classes. The AUC for CACI and hospital mortality was 0.774 (95%CI, 0.653-0.895), for mFI-5 was 0.759 (95%CI, 0.591-0.926), and for ASA class was 0.653 (95%CI, 0.509-0.797). The mFI-5 was not superior to the CACI and ASA classes. All three indices were satisfactory for predicting 1-year mortality.

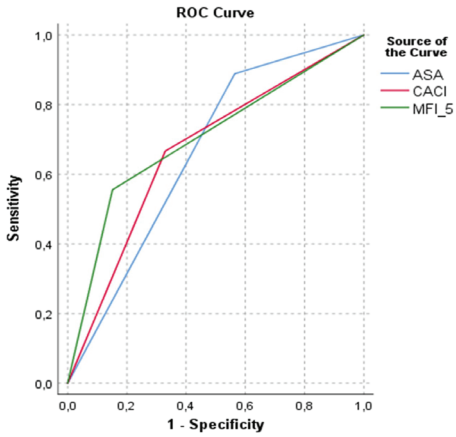
According to the results of binominal logistic regression analysis (Table 4), the risk of complications was 0.215 (95%CI 0.087-0.529, p=0.001) times higher in patients with an mFI-5 score greater than '2', 0.366 (95%CI 0.063-0.300, p=0.025) times higher in patients with an ASA class greater than '3', 0.138 (95%CI 0.152-0.881, p<0.001) times greater in patients with a CACI score greater than '5' and 0.218 (95%CI 0.096-0.492, p<0.001) times greater in patients with oncological diseases. Importantly, patients with an mFI-5 score greater than '2' had 0.165 odds ratio (95%CI 0.061-0.444, p<0.001), male patients had 0.346 odds ratio (95%CI 0.136-0.880, p=0,026), and patients who received transfusion had 0.056 odds ratio (95%CI 0.021-0.152, p<0.001) of ICU admission. Furthermore, patients with a CACI score greater than '5' had a 16.075 odds ratio (95%CI 1.557 -166.006, p=0,020), and patients with oncological diseases had a 0.146 odds ratio (95%CI 0.023-0.935, p=0.042), and patients admitted to ICU had 8.555 odds ratio (95%CI 1.655-44.228, p=0.010) of hospital mortality. Finally, older age had 0.383 odds ratio (95%CI 0.233-0.631, p<0.001), and patients with an mFI-5 score greater than '2' had 2.741 odds ratio (95%CI 1.094-6.869, p= 0.032), prolonged LOS had 9.476 odds ratio 95%CI 4.370-20.549, p<0.001), patients admitted to the ICU had

Figure 1. Receiver operating curve (ROC) analysis is illustrated by comparing risk scores with postoperative complications, ICU admission, hospital mortality, and 12 months mortality. AUC: Area under curve, ASA: The American Society of Anesthesiologists Classification, mFI-5: Modified 5-item frailty index, CACI: The Charlson age comorbidity index, ICU: Intensive care unit, *: p<0.05, **:p<0.001.



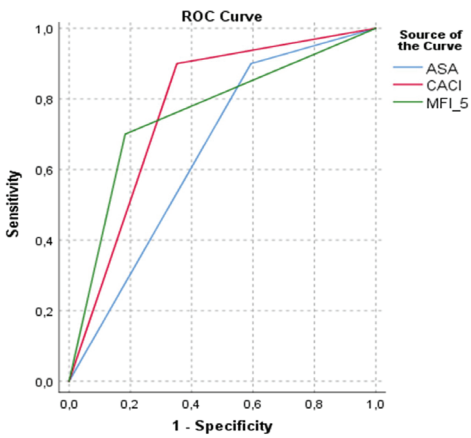
Index	AUC(%95 CI)
CACI	**0.819(0.765-0.874)****
mFI-5	0.675(0.606-0.744)**
ASA class	0.698(0.638-0.758)**

(A)



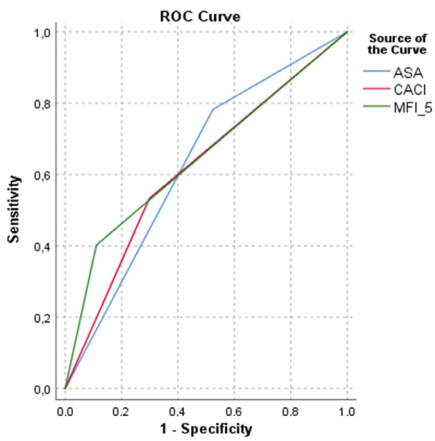
Index	AUC(%95 CI)
CACI	0.669(0.574-0.763)**
mFI-5	**0.702(0.601-0.804)****
ASA class	0.662(0.580-0.745)**

(B)



Index	AUC(%95 CI)
CACI	**0.774(0.653-0.895)****
mFI-5	**0.759(0.591-0.926)***
ASA class	0.653(0.509-0.797)*

(C)



Index	AUC(%95 CI)
CACI	0.617(0.547-0.687)*
mFI-5	0.646(0.574-0.718)**
ASA class	0.629(0.563-0.696)**

(D)

Table 3. Patient demographics, preoperative, operative characteristics, and postoperative outcomes.

Parameter	Frequency (Percentage)	Median (Min-Max)
Age (year)		71(65-95)
Gender (Female/ **Male**)	141(47%)/ **159(53%)**	
Oncologic Disease	100(33, 3%)	
Surgery Classification -Low Risk **-İntermediate Risk** -High Risk	 46(15, 3%) **129(43%)** 125(41, 7%)	
ASA Classification -ASA Class ≥ 3 - ASA Class < 3	 181(60,3%) 119(39,7%)	3(2-4)
Charlson Age Comorbidity Index - CACI ≥ 5 - CACI <5	 182(60,6%) 133((39,4%)	5(2-13)
Modified Frailty Index-5 - mFI-5 ≥ 2 - mFI-5 < 2	 183(61%) 117(39%)	2(0-5)
Anesthesia Method (**General**/ Spinal & Epidural)	175(58, 3%)/ 125(41, 7%)	
Transfusion	38(12, 7%)	
Overall Complications	99(33%)	
Clavien Dindo Classification **-Grade 1** -Grade 2 -Grade 3 Grade 3a/ Grade 3b **-Grade 4** Grade 4a/ Grade 4b	 **43(14,3%)** 17(5,6%) 3(1%) 1(0,3%)/ 2(0,6%) **36(12%)** 32(10,6%)/ 4(1,3%)	
ICU Admission	36(12%)	
LOS -Prolonged LOS	 82(27, 3%)	2(1-51)
Hospital Mortality	10(3, 3%)	
1-Year Mortality	82(27, 4%)	

Values are presented as the number of patients, frequency (percentage), or median(minimum-maximum). ASA: The American Society of Anesthesiologists Physical Status Classification, mFI-5: Modified 5-item frailty index, CACI: The Charlson age comorbidity index, ICU: Intensive Care Unit, LOS: Length of Hospital Stay

Table 4. Binomial logistic regression analysis for postoperative outcomes.

	p	OR(Odds Ratio)	%95 CI(Confidence Interval)
Complications			
ASA class ≥ 3	**0,025**	0,366	0,063-0,300
mFI-5 ≥ 2	**0,001**	0,215	0,087-0,529
CACI≥ 5	**<0,001**	0,138	0,152-0,881
Oncological Disease	**<0,001**	0,218	0,096-0,492
ICU Admission			
mFI-5≥ 2	**<0,001**	0,165	0,061-0,444
Sex(Male)	**0,026**	0,346	0,136-0,880
Transfusion	**<0,001**	0,056	0,021-0,152
Hospital Mortality			
CACI≥ 5	**0,020**	16,075	1,557-166,006
Oncological Disease	**0,042**	0,146	0,023-0,935
ICU Admission	**0,010**	8,555	1,655-44,228
1-Year Mortality			
Age	**<0,001**	0,383	0,233-0,631
mFI-5≥ 2	**0,032**	2,741	1,094-6,869
LOS	**<0,001**	9,476	4,370-20,549
ICU Admission	**0,012**	17,719	1,862-168,651
Transfusion	**0,005**	5,152	1,632-16,264
Complications	**0,013**	3,625	1,310-10,033

Binomial logistic regression analysis was used for the evaluation of variables affecting complications.

$p < 0.05$ was used to indicate statistical significance. ASA: The American Society of Anesthesiologists Physical Status Classification, mFI-5: Modified 5-item frailty index, CACI: The Charlson age comorbidity index

17.719 odds ratio (95%CI 1.862-168.651, p=0.012), patients who received transfusion had 5,152 odds ratio (95%CI 1.632-16.264, p=0.005), and complications had 3.625 odds ratio (95%CI 1.310-10.033, p=0.013) of 1-year mortality.

DISCUSSION

In our study, 33% of patients experienced complications, the hospital mortality rate was 3.3%, and the 1-year mortality rate was 27.4%. ROC analysis demonstrated a very good association of CACI with overall complications and a good association of mFI-5 with ICU admission and hospital mortality. All three indices were satisfactory predictors of prolonged LOS and 1-year mortality. The patients with higher mFI-5 scores had a greater risk of ICU admission, and 1-year mortality; in addition, patients with higher CACI scores had a greater risk of hospital mortality.

The functional status and preferences of geriatric patients should guide the surgical decisions as most elderly patients value the quality of life rather than the length of life for the remaining time they are alive (13). In this study, 27.4% of patients who underwent surgery died within a year. Therefore, the importance of examining 1-year mortality in our study was once again reinforced. Complications affect the functional results of surgery. Good

evaluation of the patient's physiological state in the preoperative period, knowledge, and early recognition of possible complications reduce the risk of disability and/or death reduce significantly (14). In our study, grade 4 (life-threatening) complications were seen in 12% of the patients, and overall complications which include all grades were also found to be associated with increased 1-year mortality.

It is yet to be determined whether ASA class is an independent predictor of medical complications in a wide variety of surgical patients from different institutions. There is also a need to justify the use of ASA as a consistently reliable predictor of outcomes (15). Hackett et al. (16) reported that the ASA classification of physical conditions had strong, independent associations with postoperative medical complications and mortality. In addition, another survey (17) showed that ASA was superior to CCI and CACI in predicting mortality. In contrast, "Rosa et al." (18) reported that in gastric cancer patients, ASA evaluation alone is insufficient to predict postoperative complications and long-term mortality. In our study, the ASA classification was a satisfactory predictor of ICU admission, overall complications, hospital mortality, and 1-year mortality. Although the risk of developing complications was higher in patients with ASA ≥ 3, in the same patient group, no significant relationship was found between ICU admission and hospital mortality.

In recent years, surveys by different surgical clinics (19, 20) have shown that CCI is a good predictor of postoperative mortality and complications. However, as CCI is insufficient in geriatric patients, CCI with age added (CACI) is considered a more appropriate prognostic indicator for clinical use and practice (7). In another study (21), patients with CCI scores greater than 5 had a higher risk of mortality than those in the other group (OR: 4.6[2,4-9.0]). It was observed that patients with systemic complications had a higher mean CCI (p=0.001) compared to the other group. In our study, CACI demonstrated a very good association with the overall complications and was equal to the mFI-5 in predicting hospital mortality. Furthermore, it was determined that the hospital mortality rate increased approximately 16 times in patients with CACI≥ 5.

Compared to an adult, a fragile elderly person is at a higher risk for conditions such as disability, morbidity, and death. Frailty scores have been used to estimate postoperative complications and outcomes in elderly patients undergoing surgery (8). Weaver et al. (22) reported that increased mFI-5 scores were significant in predicting 30-day mortality and morbidity. Another study (23) reported that mFI-5 was as successful as CACI and mFI-11 in predicting postoperative 90-day mortality. In our study, mFI-5 demonstrated a good association between ICU admission and hospital mortality. Higher mFI-5 levels increased the risk of complications, ICU admission, and 1-year mortality.

Ondeck et al. (24) evaluated the predictive power of mFI, mCCI, and ASA for complications, serious complications, mild complications, infectious complications, prolonged hospitalization, and intensive care admission. ASA combined with age was found to be the most useful index for predicting comorbidities. The combination of a demographic parameter and a comorbidity index was found to be the best index for predicting at least five of the six complications.

Different types of surgeries and comorbidities in the same age group provided an advantage in terms of evaluating the indices in different patients simultaneously. This study had some limitations that should be addressed. Adding cardiovascular surgery and thoracic surgery clinics to the study could have made the selected patient group more similar to society. We believe that a study with a larger sample size will better reflect this population. We had to terminate data collection to avoid false results due to the Covid-19 pandemic.

Due to a global increase in the elderly population, the proportion of the geriatric population among those applying to health services is increas-

ing rapidly. According to the results of this study, mFI-5 was associated with ICU admission and 1-year mortality, and CACI was associated with complications and hospital mortality in geriatric patients. Furthermore, mFI-5 was not better than ASA class and CACI in predicting the overall postoperative outcomes. We suggest that the validity and reliability of mFI-5 should be increased by its common usage in multiple centers. Furthermore, creating different evaluation scale combinations with other evaluation indices or parameters is likely to be beneficial.

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RESEARCH

COMPARISON OF CLINICAL OUTCOMES OF CORONAVAC VACCINATED AND UNVACCINATED OLDER ADULTS WITH HOSPITALIZED COVID-19

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Abstract

Introduction: We aimed to compare the COVID-19 outcomes in unvaccinated and CoronaVac vaccinated older adults.

Materials and Method: In this single-center study, patients aged ≥65 years who were hospitalized for COVID-19 were retrospectively analyzed in two groups: unvaccinated and vaccinated.

Results: A total of 742 patients were included. The mean age was 76.6±7.6 years. Of these, 46.1% (n=342) were male, 76.0% (n=564) were vaccinated. Among patients who were transferred to the intensive care unit (n=217), 206 (27.8%) received invasive mechanical ventilation support and 194 (26.1%) were died. In the multivariate analysis, advanced age (OR=1.03, 95%CI=1.01-1.06, p<0.01) and a high Charlson Comorbidity Index (OR=1.24, 95%CI=1.12-1.38, p<0.01) were predictors of mortality, while being vaccinated (OR=0.75, 95%CI=0.62-0.91, p<0.01) was associated with survival. Vaccination reduced the need for intensive care by 26.5% and mortality by 24.9 %. When the vaccinated group was evaluated, high Charlson Comorbidity Index (OR=1.428, 95%CI=1.14-1.64, p<0.01) was an independent predictor for mortality. However, booster vaccination in the last 130 days was the only protective factor that reduced mortality (p=0.04, 95%CI=0.43-0.99, OR=0.66) in multivariate analysis. Booster dose vaccination in the last 130 days reduced mortality by 33.8%.

Conclusion: CoronaVac vaccination improved survival in hospitalized older adult patients (≥65 years old) with COVID-19. However, delaying the booster dose for more than 130 days were significantly associated with decreased survival. Therefore, older adults who completed their primary vaccination series with CoronaVac should not delay their booster dose to reduce the risk of death.

Keywords: COVID-19; Aged; Death; Vaccination.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was unexpectedly resulted in a global pandemic with significant disruption and many loss of life. In response, an extraordinary effort has been made to develop vaccines against SARS-CoV-2 (1). Mass vaccination programs with newly approved COVID-19 vaccines have been implemented all around the world, giving priority to high-risk individuals to induce protective immunity and control the spread of SARS-CoV-2 (2).

CoronaVac (Sinovac Biotech), an inactivated whole virus vaccine, is the first vaccine approved in Turkey. The vaccination campaign for CoronaVac started on January 14, 2021. For this reason, most healthcare workers and older adults in the high-risk group in our country were vaccinated with CoronaVac (3). The World Health Organization's Emergency Use Listing (WHO EUL) procedure approved the use of the CoronaVac vaccine in early June 2021, but stated that new evidence-based information is needed on its efficacy and safety in adults aged ≥ 60 years (4). However, in an observational study in Chile, referred by WHO EUL, adjusted vaccine efficacy in people aged ≥ 60 years was 66.6% for the prevention of COVID-19, 85.3% for the prevention of hospitalization, 89.2% for the prevention of admission to the intensive care unit, and 86.5% for prevention of COVID-19 related death (5).

Our 1000-bed hospital was built as a pandemic epicenter where only COVID-19 patients were hospitalized in Istanbul, which is the most populated city of Turkey. In this study, we aimed to compare CoronaVac vaccinated and unvaccinated patients aged ≥ 65 years who were hospitalized with COVID-19 in the delta (B.1.617.2) variant dominant period in terms of disease severity, need for admission to the intensive care unit (ICU), and death. In addition, we determined the factors affecting the severity of COVID-19 in vaccinated patients and evaluated the effect of booster vaccine doses on survival.

MATERIALS AND METHOD

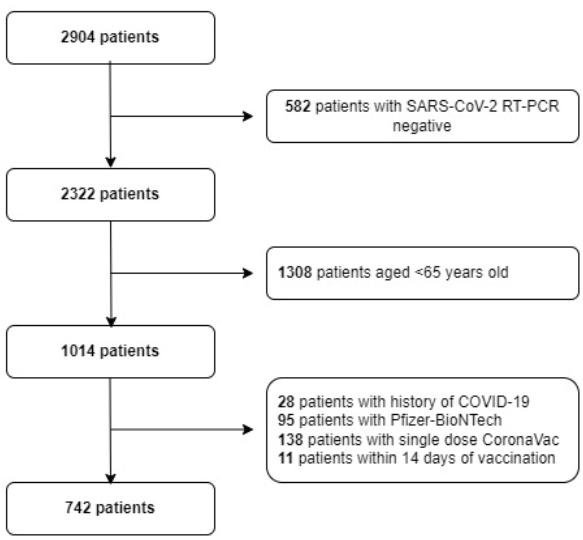
Study Design

This was an analytical, cross-sectional, epidemiological study. Patients aged ≥ 65 years who were hospitalized for COVID-19 in a tertiary care hospital between September 1, 2021 and December 15, 2021, were included. Patients who had at least two doses of CoronaVac vaccine were defined as "vaccinated", and patients who did not receive any vaccine were defined as "unvaccinated".

Inclusion criteria were as follows: (1) patients aged ≥ 65 years; (2) positive testing for SARS-CoV-2 by real-time polymerase chain reaction (RT-PCR); and (3) hospitalization for COVID-19. Exclusion criteria were as follows: (1) previous history of confirmed COVID-19; (2) patients vaccinated with a single dose of CoronaVac; (3) patients who received Pfizer-BioNTech as the primary vaccination; and (4) patients who had COVID-19 14 days after the 2nd dose.

A total of 2162 of the 2904 patients were excluded (Figure 1). Demographic characteristics includ-

Figure 1. Flow diagram demonstrating patient enrollment



ing age, sex, underlying diseases, clinical features, laboratory findings, vaccination status, admission to the intensive care unit, need for mechanical ventilation, and clinical outcomes were retrospectively collected from medical charts and electronic medical records.

The primary outcomes were the need for ICU admission and death in hospitalized patients with COVID-19. The secondary outcome was death in vaccinated patients with COVID-19.

The following criteria were used according to WHO definitions to determine disease severity (6).

• Critical COVID-19: Sepsis, septic shock, acute respiratory distress syndrome (ARDS), or conditions that cause necessary treatments for survival, such as mechanical ventilation (invasive or non-invasive) or vasopressor therapy

• Severe COVID-19: SpO2 <90% on room air; or respiratory rate>30 breaths/min; or signs of severe respiratory distress

• Non-severe COVID-19: Absence of any criteria for severe or critical COVID-19.

According to the Republic of Turkey Ministry of Health COVID-19 Guideline, favipravir (2 x 1600 mg loading on the first day, 2 x 600 mg in the next four days) was started in all patients with COVID-19 and decord 6 mg or prednol 40 mg was started in those with a room air oxygen saturation <92% (7).

The Charlson Comorbidity Index (CCI) was used to evaluate the comorbidity status of the patients. Mortality was defined as the in-hospital death.

Statistical analysis

Continuous variables were expressed as mean and standard deviation, while categorical variables were expressed as percentages (%) and frequencies (n). The normal distribution of the data questioning the necessity of using the parametric test was evaluated using Kolmogorov-Smirnov test, Kurtosis and Skewness tests. According to the normality of the distribution, appropriate parametric or non-parametric tests were applied.

Univariate logistic regression analysis was performed to identify the factors causing death in COVID-19 and to detect poor prognostic predictors in vaccinated patients. All factors with $p<0.05$ were included in the multivariate logistic regression analysis. Kaplan Meier analysis was applied to compare the expected survival status in vaccinated and unvaccinated patients with COVID-19.

The results were evaluated using a 95% confidence interval (CI) with a p-value < 0.05. IBM SPSS-21 (Statistical Package for Social Sciences, Armonk, NY, USA) was used for statistical analyses.

Ethical Approval

This study was approved by local ethics committee (Decision No: 2022-14-10, Date: 18.07.2022). Written informed consent was waived, given the retrospective nature of this study.

RESULTS

In total, 742 patients were included in the study. There were 342 male patients (46.1%), and the mean age was 76.6 ± 7.6 years. Regarding the immunization status, 564 (76.0%) patients were vaccinated and 178 (24.0%) were unvaccinated. Among those vaccianted, 281 patients received a third booster dose. Of these patients, 71.5% (n = 201) received the CoronaVac and 28.5% (n = 80) received the Pfizer-BioNTech vaccine. The mean ages of vaccinated and unvaccinated patients were similar (76.8 ± 7.5 years versus 76.2 ± 7.9 years, p = 0.32). The mean length of hospital stay was 13.9 ± 10.8 days. Ferritin (551 ± 749 µg/L versus 714 ± 817 µg/L, p < 0.01), alanine aminotransferase (ALT) (24 ± 24 IU/L versus 30 ± 27 IU/L, p < 0.01), and aspartate transaminase (AST) levels (35 ± 39 IU/L versus. 42 ± 41 IU/L, p < 0.01) were lower in vaccinated patients than in unvaccinated patients. Leukocyte count (p = 0.95), procalcitonin (p = 0.89), C-reactive protein (CRP) (p

= 0.09), creatinine (p = 0.06), and D-dimer levels (p = 0.12) did not significantly differ between groups. A comparison of demographic features, clinical characteristics, and biochemical parameters of the patients with vaccinated and unvaccinated is shown in Table 1.

The mean CCI in the vaccinated group was higher than in the unvaccinated group (5.6±1.6 vs. 5.1±1.8, p<0.01). Comorbidities, of at least one present, were more frequent in vaccinated patients (n = 487, 86.3%) than in unvaccinated patients (n = 138, 77.5%) (p < 0.01). The most frequent comorbidities were hypertension (n = 491, 66.1%), diabetes mellitus (n = 284, 38.2%), coronary artery disease (n = 173, 23.3%), and asthma/*chronic obstructive pulmonary disease (COPD)* (n = 94, 12.7%). Hypertension (68.3% versus 59.5%, p = 0.03), diabetes mellitus (41.5% versus 28.1%, p < 0.01), and coronary artery disease (26.7% versus. 12.4%, p < 0.01) were higher in vaccinated patients than in unvaccinated patients (Table 1). In the subgroup analysis, there was no significant difference in mortality between the vaccinated and unvaccinated patients according to comorbidities (Table 2). There was no comorbidity in 13.7% (n = 77/564) of the vaccinated patients and 22.5% (n = 40/178) of the unvaccinated patients (p < 0.01). In the subgroup analysis, the need for ICU admission was 22.1% in the vaccinated patients (n = 17/77) and 42.5% in the unvaccinated patients (n = 17/40) (p=0.02). In hospital death was higher in the unvaccinated patients (n= 14, 35.0%) compared to vaccinated patients (n = 13, 16.8%) (p = 0.03).

Of the 742 patients with COVID-19, 29.8% had mild disease (n = 221), 38.3% had severe disease (n = 284), and 31.9% had critical disease (n = 237). While non-severe and severe diseases were more common in vaccinated patients, critical diseases were more common in unvaccinated patients (p = 0.03). Among the total, 217 (29.2%) patients were followed up in the ICU, 206 (27.8%) patients required invasive mechanical ventilation, and 194 (26.1%) patients died. The need for ICU admission (n = 66, 37.1%, versus n = 151, 26.8%, p = 0.01), invasive mechanical ventilation support (n = 63, 35.4%, versus n = 143, 25.4%, p = 0.01), and mortality (n = 58, 32.6%, versus n= 136, 24.1%, p = 0.03) were higher in the unvaccinated group than in the vaccinated group.

In the multivariate analysis, advanced age (OR = 1.03, 95% CI = 1.00–1.05, p = 0.01) and high CCI (OR = 1.21, 95% CI = 1.09–1.34, p < 0.01) were associated with increased need for ICU admission while being vaccinated (OR = 0.73, 95% CI = 0.61–0.89, p < 0.01) was found to be the protective factor. Similarly, advanced age (OR = 1.03, 95% CI = 1.01–1.06, p < 0.01) and high CCI (OR = 1.24, 95% CI = 1.12–1.38, p < 0.01) were predictors of mortality. However, being vaccinated (OR = 0.75, 95% CI = 0.62–0.91, p < 0.01) was associated with survival in the multivariate analysis. Vaccination reduced the need for ICU admission by 26.5% (95% CI = 11–39) and mortality by 24.9 % (95% CI = 9–38).

Among the vaccinated patients, death was more common in patients with advanced age (p = 0.01), high CCI (p < 0.01) and chronic kidney disease (p = 0.03). Mortality was lower in patients who received a booster dose during the last 130 days (20.0% versus 27.4%, p = 0.04) (Table 3). There was no significant difference between patients who had booster dose of CoronaVac and Pfizer-BioNTech in terms of the need for ICU admission (21.4% versus 28.7%, p = 0.19) or death (18.4% versus 26.2%, p = 0.14). We found that high CCI was an independent predictor of ICU admission (OR = 1.25, 95% CI = 1.11–1.41, p < 0.01) and death (OR = 1.428, 95% CI = 1.14–1.64, p < 0.01), while booster vaccination in the last 130 days was the only protective factor that reduced mortality (p = 0.04, 95% CI = 0.43–0.99, OR = 0.66) among vaccinated patients (Table 4). Booster dose vaccination in the last 130 days reduced mortality by 33.8% (95% CI = 1–57) in vaccinated patients.

Table 1. Demographic characteristics and outcomes of patients hospitalized for COVID-19

	Total (n=742)		Vaccinated (n=564)		Unvaccinated (n=178)		P
	N	%	N	%	N	%	
Gender (Male)	342	46.1	267	47.3	75	42.1	0.22
Age (Mean±SD)	76.6±7.6		76.8±7.5		76.2±7.9		0.32
Disease Severity Non-Severe Severe Critically	 221 284 237	 29.8 38.3 31.9	 173 226 166	 30.6 40.0 29.4	 48 59 71	 27.0 33.1 39.9	**0.03**
CCI (Mean±SD)	5.5±1.7		5.6±1.6		5.1±1.8		**<0.01**
Hypertension	491	66.1	385	68.3	106	59.5	**0.03**
Diabetes Mellitus	284	38.3	234	41.5	50	28.1	**<0.01**
CAD	173	23.3	151	26.7	22	12.4	**<0.01**
Asthma/COPD	94	12.7	75	13.3	19	10.7	0.36
CKD	87	11.7	70	12.4	17	9.5	0.30
CHF	77	10.4	61	10.8	16	9.0	0.69
Others	60	8.1	45	8.0	15	8.4	
Wbc (10^3/uL) (Mean±SD)	7.54±5.01		7.56±5.25		7.47±4.17		0.95
Ferritin (µg/L) (Mean±SD)	590±768		551±749		714±817		**<0.01**
CRP (mg/L) (Mean±SD)	103±79		106±79		96±80		0.09
Procalcitonin (ng/mL) (Mean±SD)	0.89±5.25		0.83±4.73		1.07±6.66		0.89
Creatinine (mg/dl) (Mean±SD)	1.35±1.23		1.40±1.34		1.19±0.77		0.06
ALT (IU/L) (Mean±SD)	26±25		24±24		30±27		**<0.01**
AST (IU/L) (Mean±SD)	37±39		35±39		42±41		**<0.01**
D-dimer (µg FEU/mL) Mean±SD)	1.12±1.65		1.09±1.65		1.20±1.63		0.12
Length of (Mean±SD) hospital stay (days)	13.9±10.8		13.6±10.6		14.9±11.5		0.13
ICU admission	217	29.2	151	26.8	66	37.1	**0.01**
Invasive mechanical ventilation	206	27.8	143	25.4	63	35.4	**0.01**
Mortality	194	26.1	136	24.1	58	32.6	**0.03**

CCI: Charlson Comorbidity Index, CAD: Coronary artery disease, COPD: *Chronic obstructive pulmonary disease, CKD: Chronic Kidney Disease, CHF:* Chronic heart failure, *ICU: Intensive care unit*

Table 2. Mortality rates of COVID-19 patients by comorbidity and vaccination status

		Total		Vaccinated		Unvaccinated		p	OR
	Death	N	%	N	%	N	%		
Hypertension	No	371	76.6	297	77.1	74	69.8	0.12	0.69
(n=491)	Yes	120	24.4	88	22.9	32	30.2		
DM	No	215	75.7	180	76.9	35	70.0	0.30	0.70
(n=284)	Yes	69	24.3	54	23.1	15	30.0		
CAD	No	124	71.7	108	71.5	16	72.7	0.91	1.06
(n=173)	Yes	49	28.3	43	28.5	6	27.3		
Asthma/COPD	No	70	84.3	57	87.5	13	82.6	0.50	0.68
(n=94)	Yes	24	15.7	18	12.5	6	17.4		
CKD	Yes	55	63.2	46	65.7	9	52.9	0.33	0.59
(n=87)	No	32	36.8	24	34.3	8	47.1		
CHF	No	54	70.1	44	71.0	10	66.7	0.75	0.82
(n=77)	Yes	23	29.9	18	29.0	5	33.3		

DM: Diabetes Mellitus, CAD: Coronary artery disease, COPD: *Chronic obstructive pulmonary disease, CKD: Chronic Kidney Disease, CHF:* Chronic heart failure,

Table 3. Comparison of characteristics of survived anddeceased in vaccinated patients

		Survivors (n=428)		Non-Survivors (n=136)		p	OR
	N	N	%	N	%		
Gender (Male)	267	197	46.0	70	51.5	0.27	1.25
Age (Mean±ss)	564	76±7		79±8		**0.01**	
Number of Vaccines 2 dose 3 dose	 283 281	 205 223	 47.9 52.1	 78 58	 57.4 42.6	0.05	0.68
Post-vaccine Duration ≤130 days >130 days	 250 314	 200 228	 46.7 53.3	 50 86	 36.7 63.3	**0.04**	0.66
CCI (Mean±ss)	564	5.4±1.5		6.2±1.8		**<0.01**	
Hypertension	385	297	69.4	88	64.7	0.31	0.81
Diabetes Mellitus	234	180	42.0	54	39.7	0.63	0.91
CAD	151	108	25.2	43	31.6	0.14	1.37
Asthma/COPD	75	57	13.3	18	13.2	0.98	0.99
CKD	70	46	10.7	24	17.6	**0.03**	1.78
CHF	62	44	10.3	18	13.2	0.34	1.33

CCI: Charlson Comorbidity Index, CAD: Coronary artery disease, COPD: *Chronic obstructive pulmonary disease, CKD: Chronic Kidney Disease, CHF:* Chronic heart failure,

Table 4. Multivariate analysis of factors that cause need ICU admission and death in vaccinated patients

	Multivariate Analysis for ICU Admission			Multivariate Analysis for Mortality		
	OR	95 %CI	P	OR	95 %CI	P
Age	1.02	0.99-1.05	0.13	1.03	0.99-1.05	0.07
Charlson Comorbidity Index	1.25	1.11-1.41	**<0.01**	1.28	1.14-1.46	**<0.01**
Post-vaccine Duration (≤130 days)	0.69	0.46-1.02	0.06	0.66	0.43-1.00	**0.04**

DISCUSSION

Older adults, who are most vulnerable to the devastating impact of the COVID-19 pandemic, comprise of a significant proportion of COVID-19-related deaths during the pre-vaccine period (8). In this study, we presented a detailed analysis of the demographic characteristics, clinical findings, and outcomes of 564 vaccinated and 178 unvaccinated patients aged ≥ 65 years hospitalized for COVID-19 in a pandemic epicenter. We found that 26% of older patients with COVID-19 died. Vaccination with at least a double dose of CoronaVac reduced the need for intensive care and mortality by approximately 25%. In addition, delaying booster vaccination for > 130 days increased mortality by 52%.

The main purpose of vaccination in older adults is to protect against serious COVID-19 and its fatal consequences. Immune senescence, general fragility, mental and psychosocial health problems, underlying diseases, and nutritional disorders are important problems that reduce vaccine efficacy in older populations (1). Compared to the Pfizer-BioNTech and Oxford-AstraZeneca vaccines, fewer population-based analyses have studied the efficacy of the CoronaVac vaccination in older adults (9-11) In studies evaluating the antibody levels induced by the CoronaVac, it was shown that post-vaccine seropositivity rates were similar to young adults, and neutralizing antibody titers were lower in elderly people (4,12). In addition, neutralizing antibody levels against SARS-CoV-2 variants in the CoronaVac vaccine have also been reduced (13,14).

In the population-based ESPERANZA cohort, which included people ≥ 60 years of age, approximately 2,830,000 individuals were evaluated over a seven-month period. In the ESPERANZA study, the effectiveness of CoronaVac was found to be lower than that of the Pfizer-BioNTech and Oxford-AstraZeneca. In addition, researchers showed that with increasing age, the effectiveness of CoronaVac decreased more than that of other vaccines. CoronaVac was found to reduce hospitalization without death by 47.3% and with death by 72.1% in people aged ≥ 60 years (9). Ranzani et al. reported that CoronaVac was 46.8% effective against symptomatic COVID-19, 55.5% effective against COVID-19-related hospitalization, and 61.2% effective against COVID-19-related deaths during the gamma variant predominant period. In addition, they found that the effectiveness of CoronaVac decreased to 30–40% in people aged > 80 years (10). In another population-based study, CoronaVac was reported to reduce mortality in older adults during the gamma variant dominant period (11). In our hospital, we did not routinely perform SARS-CoV-2 genotyping, but more than 90% of the SARS-CoV-2 variants determined in COVID-19 patients in our country were delta during the study period and the omicron variant had not yet been detected. In the present study, CoronaVac reduced mortality by 25%, and this rate was lower than the results of other studies (9-11).

However, since we evaluated patients who required hospital admission, we found that the effectiveness of CoronaVac on mortality was relatively low. In addition, the decreased effectiveness can probably be explained by the fact that the study was conducted in the more deadly delta variant-dominant period and the time elapsed after vaccination was prolonged. Therefore, we evaluated the impact of delayed booster doses and found that in-hospital mortality was lower in recently vaccinated patients.

Many studies have revealed that COVID-19 patients with underlying diseases have increased risk of poor prognosis (15-18). In the study of Yavuz et al., chronic pulmonary disease, malignancy, chronic kidney disease, and cardiovascular diseases were reported as independent risk factors for mortality (17). In the study by of Sezen et al., mortality was found to be significantly higher in patients with CCI ≥ 1 (18); however, there is a limited number of studies evaluating the effect of comorbid diseases on prognosis in patients with CoronaVac. In our study, increased CCI was an independent risk factor for mortality in patients aged ≥ 65 years regardless of vaccination status. Among vaccinated patients, those patients with chronic kidney disease had an approximately two-fold increased risk of death.

There is no consensus regarding when the booster dose of CoronaVac vaccine should be administered. However, studies evaluating neutralizing antibody titer levels have reported that the optimal timing for a booster dose is 6–8 months (19-20). WHO stated that a booster dose can be administered to high-risk groups 4–6 months after completion of the primary CoronaVac vaccination series (21). In our study, delaying the booster dose for > 130 days in patients aged ≥ 65 years was associated with a 1.5-fold increase in mortality. Therefore, we deduced that patients aged ≥ 65 years with primary vaccination with CoronaVac should receive booster doses earlier because of decreased cellular immune response against SARS-CoV-2 variants and increased mortality.

Many studies have compared heterologous vaccines (a different vaccine product from CoronaVac) and homologous vaccines as a booster vaccine (22-23). In a population-based study conducted by Jara et al., the homologous CoronaVac vaccine was less effective than heterologous vaccination (booster dose Pfizer-BioNtech or Oxford-AstraZeneca) in preventing symptomatic COVID-19, COVID-19-related hospitalization, need for ICU admission, and death (22). In the study conducted during the delta variant dominant period by Suah et al., homologous CoronaVac vaccination was less effective in preventing COVID-19 than heterologous (booster dose Pfizer-BioNTech or Oxford-AstraZeneca) vaccination (23). In our study, mortality was similar in patients who received a booster dose of CoronaVac and those with a booster dose of Pfizer-BioNTech.

This study had several strengths. First, only older patients (≥ 65 years old) were included in the study. Thus, we ensured patient homogenization by reducing age-related confounding conditions. Second, to our knowledge, this is the first study to determine the predictors of mortality in vaccinated older adults with COVID-19 in our country. Third, we adjusted the independent covariates including age and comorbidty index by the multivariate analysis. However, our study had some limitations. First, this cross-sectional study was conducted at a single center. Second, only hospitalized patients with confirmed COVID-19 were included in this study. Therefore, the effectiveness of vaccination with CoronaVac against COVID-19 development and against COVID-19-related hospitalization could not be evaluated.

CONCLUSION

In conclusion, CoronaVac vaccination improved survival in hospitalized older adult patients (≥ 65 years old) with COVID-19. However, delaying the booster dose for more than 130 days were significantly associated with decreased survival. Therefore, older adults who completed their primary vaccination se-

ries with CoronaVac should not delay their booster dose to reduce the risk of death.

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Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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RESEARCH

EVALUATION OF PREOPERATIVE NUTRITION WITH THREE DIFFERENT TOOLS IN ELDERLY PATIENTS

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Abstract

Introduction: This study was conducted to evaluate the preoperative nutritional status of patients over 65 years of age, determine the factors affecting nutrition, and compare the effectiveness of the three screening tools that were used to evaluate nutritional status.

Materials and Method: The research was cross-sectional and correlational. Two hundred elderly patients in the preoperative period of the surgical service were interviewed. The Mini Nutritional Assessment short form (MNA-SF), Nutritional Risk Screening form (NRS-2002), and Geriatric Nutritional Risk Index (GNRI) were used.

Results: Elderly patients—35.0% according to the MNA-SF, 35% according to NRS-2002, and 39.5% according to GNRI —were found to have a higher risk of preoperative malnutrition. A significant correlation was found between dysphagia and loss of appetite in elderly patients and the risks of malnutrition. Based on Receiver operating characteristic analysis, GNRI and MNA-SF were found to have high diagnostic value for preoperatively diagnosing malnutrition in elderly patients (area under the curve 0.95 and 0.90, respectively). The highest sensitivity (93.7%) belongs to Geriatric Nutritional Risk Index.

Conclusion: The use of the Geriatric Nutritional Risk Index tool is appropriate in evaluating the preoperative nutritional status in elderly patients.

Keywords: Aged; Malnutrition; Nutritional Status; Preoperative Care.

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INTRODUCTION

According to the World Health Organization, aging is defined as a progressive decrease in vital functions and the adaptation process in the environment (1). Physiological changes occur in elderly patients as the result of cellular damage caused by aging. Physiological changes, psychological problems, loneliness, chronic diseases, and multiple drug use affect the elderly's nutritional status (2). In a study of 425 geriatric patients in China, the rate of malnutrition was found to be 40.9% with the *Nutritional Risk* Screening 2002 (NRS 2002) tool and 58.6% with the Nutritional *Assessment* Short *Form* (MNA-SF) tool (3). In a study conducted with 284 geriatric patients in Italy, 24.6% of the elderly were diagnosed for malnutrition, and 28.2% of the patients were found to be at high risk of malnutrition (4). Malnutrition is a serious problem that increases the development of complications and mortality in elderly patients who will undergo surgery. The European Association for Parenteral and Enteral Nutrition (ESPEN) emphasizes that the nutritional status of every elderly patient should be evaluated (5). If malnutrition is present in the patient during the preoperative period and necessary nutritional support is provided, then wound healing is accelerated, the risk of developing complications is reduced, and the duration of the patient's hospital stay is shortened (6-8). The literature provides limited studies on the factors affecting the preoperative malnutrition rates and nutritional status of elderly patients (3,4,9).

Several screening tools are used to determine the nutritional status of elderly patients (10). In a study conducted in China, 425 patients over the age of 70 years were evaluated, and the NRS 2002 and MNA-SF screening tools were compared. The NRS 2002 and MNA-SF were considered appropriate tools for assessing nutritional deficiency in geriatric patients (3). In a study conducted on 131 patients over 60 years of age, the Geriatric *Nutritional Risk Index* (GNRI) and MNA-SF assessment tools were compared, and GNRI was found to be a more appropriate tool for evaluating nutrition in the elderly (9). ESPEN recommends the use of MNA-SF to diagnose nutritional status in the elderly (5). In Turkey, NRS 2002 is used to evaluate the nutritional status of elderly in hospitals. In the literature, there is no study about which tool is more meaningful for evaluating the nutritional status in the preoperative period in patients aged 65 years and over.

This study was conducted to evaluate the preoperative nutritional status of patients over 65 years of age and to compare the MNA-SF, NRS 2002, and GNRI screening tools, which are used to define the preoperative nutritional status of the patient.

MATERIALS AND METHODS

Study Design

The study was conducted on patients aged 65 years and over in the preoperative period who applied to the General Surgery, Orthopedics, Cardiovascular Surgery, Urology, and Ear Nose and Throat Clinics of Research Hospital in the Aegean region between October 2020 and June 2021. The sample size was calculated as 15% malnutrition rate in elderly patients, 95% confidence interval and significance level of 0.05. The sample size was 185 people. In this study the stratified sampling method was applied. A total of 200 patients were interviewed, including 79 from orthopedics, 34 from general surgery, 39 from urology, 28 from otolaryngology and 20 from cardiovascular surgery services.

The study sample included patients aged 65 years and older who were in the pre-operative period, fed orally, had occasional person orientation, had no cognitive problems, and were admitted to the clinic for 24 h. The sample excluded those who were intubated, parenterally and enterally fed, immobile, or had hip fractures.

Data Collection

The patient descriptive information form was created by reviewing the literature (3, 4, 6) and com-

posed of two parts. In the first part, there were questions regarding the patient's sociodemographic characteristics and anthropometric measurements were determined and BMI was calculated. The second part included questions about the problems affecting nutrition. In our study, Mini-Nutritional *Assessment* Short *Form* (MNA-SF), *Nutritional Risk* Screening 2002 (NRS 2002) and Geriatric *Nutritional Risk Index* (GNRI) are used to evaluate the nutritional status of the elderly in hospitals.

Rubenstein et al. in 2001 developed the MNA-SF form (11). In the validity and reliability study conducted in Turkey, the kappa compliance score of MNA-SF was found to be 0.66, while the sensitivity and specificity were 94% and 81%, respectively (12). The MNA-SF consists of six items to evaluate the patient's nutritional status. Those who were normally fed received between 12 and 14 points, at risk patients received between 8 and 11 points, and patients who were markedly malnourished received seven points or less.

NRS-2002 was developed by Kondrup et al. (13). The scale was examined in two stages. In the first stage, the patient's BMI, weight loss, decrease in food intake, and presence of risky disease were evaluated. If one of these items was yes, the main evaluation was initiated. The second stage is evaluated as deterioration in nutritional status and disease severity and scored. In addition to this score, if the patient was 70 years or older, one point was added. If the total score was three or more, it was determined that there was a risk and a nutrition plan was applied (13). The Turkish version of the NRS 2002 showed the following results: kappa compliance score of 0.804; sensitivity of 88%; and specificity of 92% (14).

The GNRI is a nutritional formula developed specifically for the elderly to identify and predict nutrition-related complications rather than diagnose malnutrition (15). The sensitivity and specificity of the GNRI was 45% and 81.7%, respectively. A score below 82 on the index indicates a severe risk. A score between 82 and 92 is interpreted as medium risk, a score between 92 and 98 is interpreted as low risk, and an index above 98 points is interpreted as no risk (15).

This index calculated using the following equation:

GNRI = [1.489 × albumin (g/L)] + [41.7 × (weight/WLo*)]

*WLo = the ideal weight calculated from the Lorentz formula as follows:

For men: height (cm) – 100 – [(height in cm – 150)/4]

For women: height (cm) – 100 – [(height in cm – 150)/2.5]

Patients were interviewed at least 24 h after hospitalization. The researcher collected data of our study. The patient's height measurements were made by placing the patient's feet together and placing the head in the horizontal Frankfort plane while standing. The patients' weight was measured using the Tefal PP1061V0 coded scale. In order to measure the weight accurately, the patients were dressed thinly and shoes were taken off before measurement. The BMI value was calculated. The albumin value was taken from the patients' records.

Statistical analysis

Statistical Package for Social Sciences (SPSS) version 22.0 version was used for the data analysis. Number, percentage, and mean were used in evaluating the data. Correlation analysis was applied to the relationship between malnutrition and the variables affecting nutrition. Kappa analysis was used to evaluate the agreement between the scales. Receiver operating characteristic (ROC) curves of the three scanning tools were also used to assess the ability to accurately distinguish between the malnourished patients. The ROC analysis was based on the fact that ESPEN took a BMI threshold value of 22 kg/m^2 for elderly patients who lost 5% weight in the last 2 months (5). All statistical analyses were conducted

at the 95% confidence level and at a significant level of 0.05. Ethics approval of our study was granted by the local non-interventional clinical research ethics committee (protocol number 2020/05-20).

RESULTS

In our study, 54.5% of the patients were male, mean age was 69.62±3.7 years, 41.0% were secondary school graduates, 83.0% were married, 66.5% were living with their spouses. It was determined that 43.5% had income equal to expenditure, 58% had a BMI between 18.5 - 24.9 kg/m^2, and 92% had at least one chronic disease.

It was determined that 58.5% of the patients had oral and dental problems, 38.5% had difficulty in swallowing, and 45% had a loss of appetite. Looking at the daily diets, it was determined that 14.5% of the patients were on a diet due to their chronic disease, 83.5% were consuming their main meals regularly, 57.5% had snacks, and 56.5% had snacks than the main meal. It was determined that 36% of the patients were smoking cigarettes and 16.5% were consuming alcohol.

It was determined that 35.0% of the patients, according to MNA-SF and NRS-2002, and 39.5% according to GNRI, were at high risk in malnutrition (Table 1). According to the MNA-SF, 6.5% (n:13) of the patients were malnourished.

A significant correlation was found between dysphagia and loss of appetite in patients according to NRS 2002, MNA-SF, and GNRI scores ($p < .001$). In our study, there was a weak correlation between patients' dysphagia and the risk of malnutrition, and a high relationship between loss of appetite and malnutrition risk. There was not significant correlation between oral and dental problems in patients according to MNA-SF, NRS 2002, and GNRI scores ($p >. 05$) (Table 2).

Table 1. Classification of The Risk of Malnutrition with MNA-SF, NRS 2002, and GNRI Tools (n: 200)

Risk of malnutrition	MNA-SF		NRS 2002		GNRI	
	n	%	n	%	n	%
No	117	58.5	130	65	121	60.5
Risk	70	35.0	70	35	79	39.5
Malnutrition	13	6.5	-	-	-	-
Total	200	100	200	100	200	100

MNA-SF, Short Form of Mini Nutritional Assessment; NRS 2002, Nutritional Risk Screening 2002; GNRI, Geriatrics Nutritional Risk Index

Table 2. Pearson Correlation Coefficients of Factors Affecting Nutrition and Tools

Factors Affecting Nutrition	NRS 2002		MNA-SF		GNRI	
	r	p	r	p	r	p
Oral and dental problems	0.104	0.143	-0.068	0.338	-0.055	0.456
Dysphagia	0.335**	0.000	-0.340**	0.000	-0.294**	0.000
Loss of appetite	0.625**	0.000	-0.722**	0.000	-0.649**	0.000

MNA-SF, Short Form of Mini Nutritional Assessment; NRS 2002, Nutritional Risk Screening 2002; GNRI, Geriatrics Nutritional Risk Index. Correlation analysis **$p < 0.01$.

The agreement between the three tools was examined. There was a good agreement between NRS 2002 and MNA-SF (κ =.668, p<0.001), moderate agreement between NRS 2002 and GNRI (κ =.409, p<0.001), and moderate agreement between MNA-SF and GNRI (κ = .561, p<0.001) (Table 3).

It was found that GNRI had the highest sensitivity (93.7%) and NRS 2002 had the lowest sensitivity (66.7%). The specificity was the same for all three tools (88.9%) (Figure 1). According to AUC, the GNRI and MNA-SF had high diagnostic values and NRS 2002 had a moderate diagnostic value for diagnosing malnutrition preoperatively in elderly patients (Table 4).

DISCUSSION

Nutritional tools can aid healthcare professionals in assessing the nutritional status of patients. However, suitability and applicability of these tools is need to evaluate for specific populations. The nutritional health of older inpatients before surgery was assessed using NRS2002, MNA and GNRI in this study. The results of the current study showed the differences in nutritional risk detected by different screening tools.

The prevalence of malnutrition risk for the older patients before surgery ranged from 35.0% to 39.5%. According to the GNRI, MNA-SF and NRS-2002, 39.5%, 35.0%, and 35.0% of the patients were

Table 3. The Agreement Among NRS 2002, MNA-SF and GNRI

		NRS 2002	MNA-SF	GNRI
NRS 2002	κ		.668	.409
	p		.000	.000
MNA-SF	κ	.668		.561
	p	.000		.000
GNRI	κ	.409	.561	
	p	.000	.000	

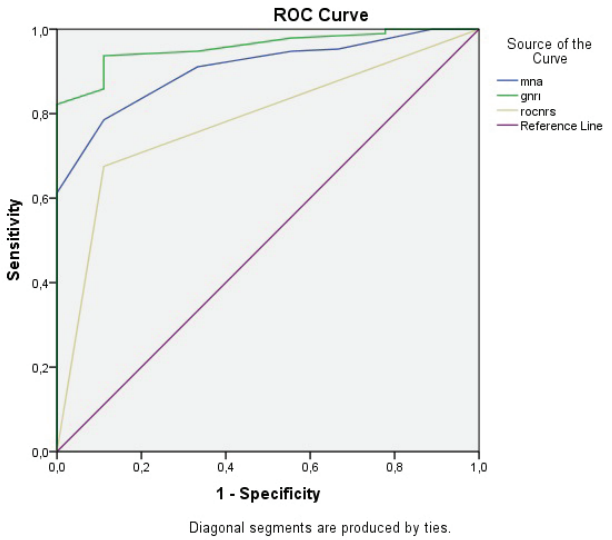
MNA-SF, Short Form of Mini Nutritional Assessment; NRS 2002, Nutritional Risk Screening 2002; GNRI, Geriatrics Nutritional Risk Index, **κ,** Kappa analysis

Table 4. Statistical Evaluation of Nutrition Screening Tools Compared with BMI

	NRS 2002	MNA-SF	GNRI
Sensitivity %	67.5	78.5	93.7
Specificity %	88.9	88.9	88.9
p value	.004	.000	.000
(AUC 95 %)	0.78 (0.650–0.914)	0.90 (0.839–0.973)	0.95 (0.921–0.994)
Cut-off value	2.5	10.5	93.5

AUC, area under the curve from ROC; MNA-SF, Short Form of Mini Nutritional Assessment
NRS 2002, Nutritional Risk Screening 2002; GNRI, Geriatrics Nutritional Risk Index

Figure 1. Receiver operating characteristics of predicted probabilities for nutritional risk incorporating the Mini Nutritional Assessment-Short Form (MNA-SF), Geriatric Nutritional Risk Index (GNRI), and Nutritional Risk Screening 2002 (NRS2002) tools.



malnourished, respectively. According to the MNA-SF tool, 6.5% (n:13) of the patients were malnourished. In a study conducted with 425 geriatric patients hospitalized in China, the risk of malnutrition was 40.9% with the NRS 2002 tool and 58.6% with the MNA-SF tool (3). In a study conducted with 284 geriatric patients hospitalized in Italy, 24.6% of the elderly were diagnosed with malnutrition and 28.2% of the patients were at high risk of malnutrition (4). It was found that 4.3% of the elderly patients who will undergo surgery in the USA are malnourished, and 18.2% of the patients have a risk of malnutrition (16). Our study showed that the rate of malnutrition risk seen in elderly patients who will undergo surgery is higher than the rate of malnutrition risk in Italy and USA. Food intake of elderly patients may be decreased due to reasons such as loss of appetite and low retired pay. Additionally, malnutrition is observed in patients due to the catabolism created by stress in the preoperative period (17). For these reasons, it is thought that the risk of malnutrition is higher in elderly patients who will undergo surgery.

In this study it was found that 58.5% of the elderly patients had oral and dental problems. There was found no significant relationship between the presence of oral and dental problems and the three tools' scores (p >. 05). In studies, a statistically significant difference was found between dental problems and malnutrition in the elderly (18,19). In systematic review, there was found an extensive interrelation between oral health and malnutrition; however, it remains unclear whether poor oral health increases the risk of being malnourished (20). Oral and dental problems of our patients may not have caused malnutrition.

We were found that 38.5% of the elderly had dysphagia. A weakly significant correlation was found between the patients' dysphagia and the nutritional status of the MNA-SF, NRS 2002, and GNRI tools (p < .001). Approximately 53.2% of patients with dysphagia have a risk of malnutrition, according to NRS 2002, and 55.8% of these patients have a risk of malnutrition according to GNRI. According to MNA-SF, 11.7% of patients with dysphagia are malnourished. A study conducted on 73 elderly people living in nursing homes found that 24.7% of the elderly had dysphagia and 85% of patients with dysphagia were at risk of malnutrition (21). Patients with dysphagia experience discomfort while eating, so their food intake is reduced, and leading to malnutrition. Therefore, the risk of malnutrition is high in our patients with swallowing difficulties who will undergo surgery.

In our research, 45% of the elderly patients had a loss of appetite. A moderately correlation was found between the loss of appetite and the nutritional status of the MNA-SF, NRS 2002, and GNRI tools (p < .001). In studies investigating the appetite status of the elderly, loss of appetite was found in 31-32.5% of the patients (22,23) and a correlation was found between the loss of appetite and malnutrition (23). A good appetite is necessary to maintain adequate food and nutrient intake. When there is a decrease

in the appetite of elderly patients, adequate and balanced nutrition will not be available and oral intake will decrease. For this reason, patients with loss of appetite may have a high risk of malnutrition.

It was found that there was good agreement between NRS 2002 and MNA-SF tools, moderate agreement between NRS 2002 and GNRI tools, and moderate agreement between MNA-SF and GNRI tools. In a study evaluating the agreement of MNA-SF and NRS 2002 in elderly patients, moderate agreement was found between these tools (3). In our study, ROC analysis was used to determine which of the three nutritional assessment tools was more effective with BMI values. The AUC values were 0.78 (0.650–0.914) for NRS 2002, 0.90 (0.839–0.973) for MNA-SF, and 0.95 (0.921–0.994) for GNRI. The AUC = 0.5 indicates that a tool has no diagnostic value, AUC = 0.5–0.7 indicates a tool has a low diagnostic value, AUC = 0.7–0.9 indicates that a tool has moderate diagnostic value, and AUC = 0.9–1 means that a tool has a high diagnostic value (24). In studies evaluating the nutritional status of elderly patients with MNA-SF and NRS 2002, these tools were moderate diagnostic value according to their AUC values (3,25). In another study in which MNA-SF and GNRI were compared in 134 hospitalized elderly patients, it was emphasized that both tools had a moderate diagnostic value in geriatric patients according to AUC values, but GNRI was simpler and more efficient (9). In our study, when the nutritional status of elderly patients was evaluated according to the AUC value, MNA-SF and GNRI had a high diagnostic value, and when the sensitivity of the scales was evaluated, the highest value belonged to the GNRI scale (93.7%). For this reason, the use of GNRI is appropriate in evaluating the preoperative nutritional status in elderly patients.

CONCLUSION

Our research found that the risk of malnutrition was between 35% and 39.5% in elderly patients in the preoperative period. There was a relationship between the loss of appetite and dysphagia of elderly patients and the risks of malnutrition. The GNRI tool was found more effective in diagnosing the preoperative nutritional status of elderly patients

It is recommended that patients aged 65 and over be should be evaluated in terms of nutritional deficiency when they are hospitalized for surgery, a detailed evaluation of the nutrition of patients with loss of appetite and swallowing difficulties.

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RESEARCH

AGING EFFECT IN PROSPECTIVE MEMORY MONITORING: AN EYE-TRACKING STUDY

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Abstract

Introduction: Prospective memory is a robust predictor of functional capacity among older adults. Studies examining prospective memory and aging have suggested that prospective memory deficits are associated with aging. Although the impairment of prospective memory processes is mostly attributed to the impairment of the monitoring process, contradictory findings have been reported in the literature. This study aimed to determine the main factors underlying the negative effects of aging on prospective memory. To this end, we compared the monitoring performances of older and younger adults in time- and event-based prospective memory tasks using the eye-tracking method.

Materials and Method: A total of 88 healthy and voluntary participants participated in the experiment. The time- and event-based prospective memory tasks were presented on a computer-screen. Participants were instructed to count the living/non-living objects, and when they saw the prospective memory target on the right corner of the screen, they were asked to press the spacebar on the keyboard.

Results: A 2×2 analysis of variance was conducted. We found an age-related decline in event-and time-based prospective memory. In addition, the aging effect was greater in the time-based prospective Memory task, which requires more executive function than the event-based prospective memory task. The eye-tracking findings suggest that there is no monitoring deficit among older adults in either prospective memory task.

Conclusion: We conclude that aging deficits in prospective memory tasks may not be due to monitoring deficits. Instead, executive functions other than monitoring are discussed as possible mechanisms underlying older adults' reduced prospective memory performance.

Keywords: Memory; Aged; Young Adult; Executive Function; Eye-Tracking Technology.

INTRODUCTION

Prospective memory (PM) is to remember to perform a planned action at the necessary time or place (1,2). Remembering a dentist appointment at 14.00 on Saturday is an example of a PM task. Existing literature suggests that there are two types of PM tasks: time-based and event-based PM (1). Time-based PM involves performing a pre-planned action at the appropriate time by retrieving that actual action, whereas event-based PM refers to performing a pre-planned action after detecting an environmental cue and retrieving that action. Recently, with changing age demographics worldwide, more attention has focused on the effect of aging on PM (3). One reason for this is that PM is a vital cognitive function for older adults in terms of health needs (e.g., remembering medication). Moreover, PM deficit is an early marker of Alzheimer's disease (4).

Among older adults, PM is a robust predictor of functional capacity (5). Most laboratory studies examining PM and aging have revealed aging-related deficits (3). However, contradictory results exist in the studies focusing on PM task types (Event-based PM or Time-based PM) that have demonstrated that the elderly perform poorer in time-based PM tasks compared to event-based PM tasks. (6). Compared to event-based PM tasks, time-based PM tasks involve self-initiated processes and are based more on executive functions, especially strategic monitoring processes (7,8). These results suggest that the poorer performance of older adults compared with younger adults in time-based PM tasks is due to their limited strategic monitoring resources (7). According to the executive framework of PM, several core executive functions (including inhibition, working memory, set-shifting, and strategic monitoring) play a crucial role during certain PM stages (9). In particular, strategic monitoring, which is defined as shifting attention from the ongoing task to the PM task at the appropriate moment, is essential for PM (10). One reason for this is that individuals monitor the external environment for the appearance of PM cues. Given the essential role of executive functions attributed to PM, this framework predicts that age-related differences in executive functions mediate age-related differences in PM performance (9).

Although the age-related impairment of PM processes is mostly attributed to the impairment of the strategic monitoring process (10), more recent literature has emerged that offers contradictory findings on the effect of aging on strategic monitoring (11,12). These studies suggest that strategic monitoring is not affected by aging (11,12). These controversial results may be related to methodological limitations, however. A commonly used behavioral indicator for strategic monitoring is the so-called "ongoing task cost". Ongoing task cost is the decrease in the performance of an ongoing task while performing a PM task (13). However, it has been suggested that the ongoing task cost is associated with short-term relief experienced, rather than strategic monitoring after completing a PM task (12). Studies that compare older adults and younger adults in terms of ongoing task cost have shown that regarding the balance between speed and accuracy, older adults take a lot longer to deliver an accurate PM reaction (14,15). In this respect, the need to measure strategic monitoring using a direct method rather than an indirect one, such as ongoing task cost, is a contentious issue (13).

Strategic monitoring can be measured directly, especially by providing a target outside the ongoing task area and taking eye-tracking records. Physiological data based on eye-tracking records provide detailed information to understand and explain the mechanisms underlying many complex cognitive processes such as attention (16), visual perception (17), and memory (11,13). For this reason, it is frequently used in the fields of "Psychology" and "Neuroscience". In the PM research area, although only a few studies have investigated strategic monitoring using the eye-tracking method (11,13), these studies have shown that eye-tracking methods are

ideal instruments to measure strategic monitoring directly. One study compared the strategic monitoring performances of older and younger participants in event-based PM tasks using the eye-tracking method and demonstrated that there was no difference between older and younger participants in terms of strategic monitoring, unlike behavioral measurements (11). In this study, the researchers did not utilize the time-based PM task. Although strategic monitoring has mostly been investigated in event-based PM tasks, it is well-known that there is a greater need for strategic monitoring in time-based PM tasks (18). In this context, the effect of aging on strategic monitoring in time-based PM tasks should be investigated using an eye-tracking method.

The main aim of this study was to compare the strategic monitoring performance of older and younger adults in time-based PM and event-based PM tasks using the eye-tracking method. To our knowledge, this study is the first study to compare event and time-based PM monitoring in older adults. If older adults have poorer strategic monitoring abilities, then their strategic monitoring performance will be lower in both PM tasks than that of younger individuals. In this case, we can conclude that older adults' reduced PM performance may stem from impaired monitoring. Furthermore, considering that time-based PM requires higher strategic monitoring processes, participants would perform more strategic monitoring on a time-based PM task than on an event-based PM task. On the other hand, if there is no difference between younger and older adults regarding their strategic monitoring abilities, we can conclude that the poor PM performance of older adults might not be directly linked to the strategic monitoring process. In either case, this study will contribute to exploring how strategic monitoring affects the decline in PM among older adults. This study examines the effect of aging on strategic monitoring in event-based PM and time-based PM tasks using eye-tracking and provides new insights into aging and PM research.

METHOD

Participants

A total of 88 healthy individuals, comprising 46 younger adults (32 females; M_{age}= 20.74; SD=1.23) and 42 older adults (14 females; M_{age}= 68.82; SD= 4.17) voluntarily participated in the study. The younger adult participants were studying at Hacettepe University, while the older adult participants were living in Ankara, Turkey. All participants had normal or corrected-to-normal vision, no history of neuropsychological or psychiatric disorders, and had not been taking medications that affected the nervous system in the past six months. Table 1 presents the demographic characteristics.

To select "healthy" participants, the Montreal Cognitive Assessment (19) and the Geriatric Depression Scale (20) was used for older adult participants, whereas the Beck Depression Inventory (21) was used for younger adult participants. Nine individuals' data of those who took the above score from the cut-off score in Depression Inventories were excluded from the behavioral analyses. Thus, we conducted behavioral analyses with 79 participants. Also, the eye-tracking data of 13 participants, whose eye-tracking data quality was lower than 70% were excluded from the eye-tracking data analyses. Thus, we conducted eye-tracking analyses with 66 participants. Table 1 lists the test results. Informed consent was obtained from all the participants.

MATERIALS

Prospective Memory Tasks

In this study, we used the eye-tracking method to obtain a more objective and direct measurement of strategic monitoring in PM tasks. In light of this, we used a slightly modified version of the PM task developed by Shelton and Cristopher (13).

Event-based PM and time-based PM tasks included an ongoing task and a PM task that was presented simultaneously. In both PM tasks, the

Table 1. Demographic characteristics and screening test scores of participants

	Event-Based PM		Time-Based PM	
	Younger Adults	Older Adults	Younger Adults	Older Adults
Age (M*± SD*)	20.90 ± 1.55	68.67 ± 3.62	20.56 ± 0.70	69.00 ± 4.81
Sex (%)	Male (%28.6) / Female (%71.4)	Male (%23.8) Female (%76.2)	Male (%27.8) Female (%72.2)	Male (%31.6) Female (%68.4)
Education (M ± SD)	13.33± .26	14.66 ± .45	13.55± .28	13.79± .44
Depression Scales** Score (M ± SD)	5.26±3.92	3.39±.42	4.96±3.91	3.45±.45
Working Memory Score***	10.14± 1.24	6.71±1.35	10.01±1.05	6.26±1.45
MoCA* Score (M ± SD)		24.5±0.42		25.4±0.3

Note:*M: Mean, SD: Standard deviation, MoCA: Montreal Cognitive Assessment. ** Depression scales represent the Beck Depression Inventory for young adults and Geriatric Depression Scale for older adults. *** Working Memory Scores represent the Wechsler Adult Intelligence Scale-Revised (WAIS-R) Backward Digit Span subtest.

PM target and ongoing task area were positioned at different locations on the screen. The ongoing task region was located at the center of the screen, whereas the PM target region was located in the top right-hand corner (Figure 1 A and B).

In the ongoing task trials for both event-based PM and time-based PM, there were a total of 12 black and white images at the center of the screen, including living objects and non-living objects in every trial. In the event-based PM condition, the ongoing task of the participants was to count the living objects presented as black and white image collages, whereas in the time-based PM condition, they were asked to count non-living objects.

In PM tasks, hand-drawn black and white images (fruit and vegetables in event-based PM and a digital clock starting at 8 a.m. and running until 9.59 a.m. in time-based PM) were shown in the PM target

Figure 1. Example of sub-trail in event-based PM (A) and time-based PM (B) tasks.

area in the top right corner of the screen. In the PM task, participants were asked to press the space bar on the keyboard whenever they saw the PM target stimuli (when they see an "apple" for instance, or every 25 minutes according to the "digital clock") while performing the ongoing task. The PM target in event-based PM was an "apple" whereas in time-based PM the PM targets were "08.25," "08.50," "09.15," and "09.40". The screen time for each PM trial was 2 s. The PM targets were displayed in only four trials in random order.

The images used in each trial were different. To select the images to be used in the ongoing task, we used the Google search engine to search for non-commercial and royalty-free images that could be reused. The collages comprised images that had high external validity and that were neutral living and non-living objects.

Both PM tasks consisted of 40 ongoing task trials. The screen time for each ongoing task (living/non-living object task) trial was 6 s, and the screen time for each PM task trial was 2 s (see Appendix 1). The purpose of changing images in the PM target region was to encourage overt strategic monitoring for targets, which is often required in more dynamic real-world visual scenes (13). Each task (event-based PM and time-based PM tasks) lasted approximately 5 min.

Eye Movement Recording

Tobii T120 eye tracker was used to collect the eye movement data of participants in the study. Tobii T120 is equipped with a buried eye-tracking server and a 17" TFT monitor with a resolution of 1280 × 1024.

Eye movements were recorded throughout the experiment, and the PM task area was defined in Tobii Studio for each task trial as the area of interest (AOI).

Procedure

Participants who voluntarily responded to the (study) announcement were given individual appointments. Before the experiment commenced, participants were given detailed information about the study. Written informed consent was obtained from all participants for voluntary participation. Younger adults completed the Demographic Information Form and Beck Depression Inventory, and the Geriatric Depression Scale and Montreal Cognitive Assessment were administered to older adult participants. After the screening tests, the younger and older participants were randomly assigned to the event-based PM and time-based PM task groups. The task type (event-based PM and time-based PM task) variables of this study were designed as "between-group," which differed between these two groups. Participants were requested to count the living objects on the screen in event-based PM or the non-living objects in time-based PM (an ongoing task) and to say the number out loud. Ongoing task responses were recorded by the researcher on a scoring form. While performing the ongoing task, participants were asked to press the space bar on the keyboard whenever they saw the PM target stimuli (when they see an "apple", for instance, or every 25 minutes according to the "digital clock"). After the instructions were issued, participants were positioned 55–65 cm away from the screen of the eye-tracking device, and a practice session consisting of five ongoing task trials was conducted. After the practice trials, a 2 min distractor phase, which included listing the male or female names starting with the letter A, was applied. The main experimental session was conducted after the distractor phase. After completion of the experimental phase, the Wechsler Adult Intelligence Scale-Revised (WAIS-R) Digit Span subtest (22) was administered to all participants to measure their working memory performance. The experiment lasted approximately 20 min.

This study was approved by the Hacettepe University Ethics Committee (letter no. 12908312-300).

Statistical Analysis

Behavioral analyses were conducted with 79 participants (39 younger and 40 older adults) and eye-tracking analyses with 66 participants (34

younger and 32 older adults). All analyses were performed using Statistical Package for the Social Sciences (IBM®, SPSS 22). The data were analyzed using a 2 (age: younger and older adult) × 2 (task type: event-based PM and time-based PM) analysis of variance (ANOVA). Both the independent variables "age" and "task type" were manipulated between groups.

RESULTS

Strategic Monitoring

Strategic monitoring was measured with both ongoing task accuracy rate (behavioral data) and the number of PM target checks, which were "apple" check-in event-based PM tasks and "clock" check-in time-based PM tasks (eye-tracking data).

Ongoing Task Accuracy Rate

Ongoing task accuracy, which is the behavioral measurement of strategic monitoring, was measured by the number of correct living (event-based PM) or non-living (time-based PM) stimuli specified by the participants in each trial. The ongoing task accuracy rate was calculated by dividing the total number of accurate responses by the number of trials. In line with previous studies (14), ongoing task trials involving the PM target were removed from the ongoing task analysis to avoid any limitation resulting from only the performance of the PM task.

According to the results of the 2 (age: older adult vs. younger adult) × 2 (task type: event-based PM vs. time-based PM) ANOVA, the main effect of age group on the ongoing task accuracy rate was significant ($F_{(1,75)}$=78.721, p <.000, η_p^2= .512). Younger adults (M = .81, SE = .01) performed better in the ongoing task than older adults (M = .69, SE=.01). The main effect of task type ($F_{(1,75)}$= .209, p= .649, η_p^2= .003) and the interaction effect of age group and task type ($F_{(1,75)}$=.156, p = .694, η_p^2= .002) were not significant.

Number of PM Target Checks

The number of PM target checks was the total number of participants fixated on the PM target area (top right-hand corner of the screen) to detect PM targets ("apple" and "clocks") across all task trials.

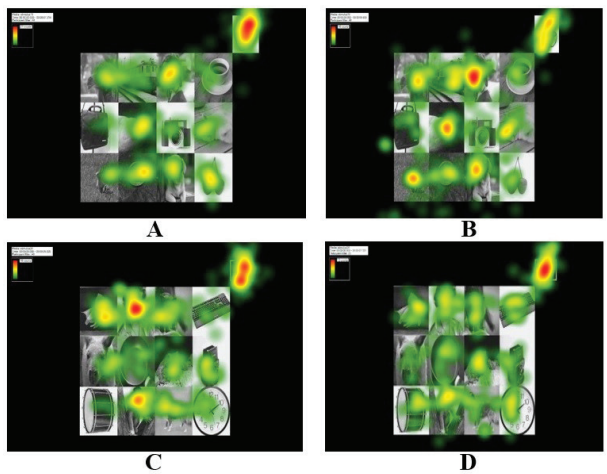
According to the results of the 2 (age: older and younger adults) × 2 (task type: event-based PM and time-based PM) ANOVA, the main effect of age group ($F_{(1,62)}$=2.3, p =.134, η_p^2= .036), task type ($F_{(1,62)}$= 2.2, p= .143, η_p^2= 003.) and the interaction effect of age group and task type ($F_{(1,62)}$=.002, p = .96, η_p^2= .000) were not significant (see Figure 2).

Prospective Memory Performance

PM Accuracy Rate

Regarding PM performance, this was operationalized as the rate at which participants hit the space bar after a PM target appeared. According to the results of the 2 (age: old vs. young) × 2 (task type:

Figure 2. Heatmaps of event-based PM and time-based PM tasks.



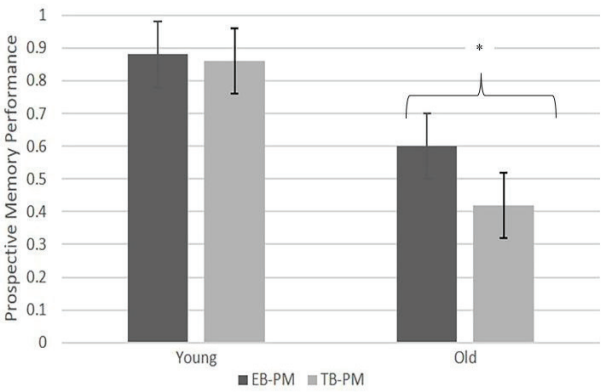
Note: Figure A represents the younger participants' event-based PM task, Figure B represents the older participant's event-based PM task, Figure C represents the younger participant's time-based PM task, and Figure D represents the older participants' time-based PM task.

event-based PM vs. time-based PM) ANOVA, the main effects of age ($F_{(1,75)}$=72.04, p <.001, η_p^2= .491) and task type($F_{(1,75)}$=4.27, p<.05, η_p^2= .054) were significant. Younger adults (M = .88, SE = .03) were more successful in PM accuracy than older adults (M = .51, SE=.03). On the other hand, both age groups were more successful in the event-based PM task (M = .74, SE = .03) than in the time-based PM task (M = .65, SE = .03). In addition, the interaction effect of age and task type ($F_{(1,75)}$=3.73, *p*<.05, η_p^2= .047) was significant; the simple effect test was examined and the results were as expected, indicating that older adult participants were more successful in the event-based PM task (M=.59, SE= .04) than in the time-based PM task (M=.42, SE= .04) ($F_{(1, 75)}$ = 8.11, p<.01, η_p^2 = .61). However, in terms of PM accuracy in younger adult participants, there was no difference between event-based PM (M=.88, SE= .04) and time-based PM (M=.86, SE= .05) tasks ($F_{(1, 75)}$ = .000, *p*=.924, η_p^2 = .000) (see Figure 3). Descriptive analysis of results is summarized in Table 2.

Further Correlation Analysis

The PM accuracy rate was found to be positively correlated to working memory performance in both young and older adults (respectively, r = .42, p < .05; r = .61, p < .001) (Table 1).

Figure 3. PM accuracy rate as a function of task type and age group.



Note: Error bars represent standard errors per conditions

DISCUSSION

This study examined the effect of aging on the monitoring process in event-based and time-based PM tasks. We hypothesized that the main reason for the decline in PM tasks that require more attentional control in older adults is impaired monitoring. In this context, we compared older and younger adult participants in different PM tasks (time-based PM event-based PM tasks). Apart from the behavioral measures of monitoring, we utilized the eye-tracking task used by Shelton and Cristopher (13) to measure monitoring directly.

Table 2. Descriptive statistics for ongoing task accuracy, PM check number, and prospective memory performance

	Young Aduts				Older Adults			
Task Type	EB-PM*		TB-PM*		EB-PM		TB-PM	
	M*	SD*	M	SD	M	SD	M	SD
OTAR*	.80	.06	.81	.04	.68	.06	.69	.06
PMAR*	.88	.15	.86	.18	.59	.27	.42	.15
NPMC*	196.16	34.72	186.62	24.35	186.41	18.51	176.31	26.82

Note: *EB-PM: Event-based PM, TB-PM: Time-based PM, M: Mean, SD: Standard Deviation, OTAR: Ongoing task accuracy rate, PMAR: Prospective memory accuracy rate, NPMC: Number of PM checks.

The findings of the PM performance showed that there was an age-related decline in both PM tasks. Furthermore, we found greater age differences in time-based PM than in event-based PM, as expected (23,24). This finding supports studies suggesting that time-based PM is more affected by aging because of its greater reliance on self-initiated processes and executive functions (25,26). The observed increased age-related decline in time-based PM can be explained by the multi-process framework, which states that older adults are less able to perform resource-demanding tasks that involve preparatory attentional processes required to detect prospective cues.

The main purpose of this study was to determine whether there is an age-related decline in strategic monitoring in different PM tasks (event-based PM and time-based PM) to find out how monitoring patterns might be related to differences in PM performance. Therefore, we operationalized strategic monitoring as the number of PM target checks (eye-tracking measurement) and ongoing task accuracy rate. We found no age-related decline in the number of PM checks; however, an age-related decline in the ongoing task accuracy rate was observed. How do we explain the discrepancy between the behavioral and eye-tracking measures of strategic monitoring? As mentioned in the introduction section, the behavioral indicator of monitoring is the decrease in ongoing task accuracy while performing a PM task (ongoing task cost). That cost may represent short-term relief experienced, rather than strategic monitoring after completing a PM task. Therefore, one can argue that the eye-tracking measurement of strategic monitoring measures the monitoring process directly and is more accurate than behavioral measurement. In this context, the findings of the current study are significant in revealing the importance of direct measurements in the measurement of strategic monitoring.

The results of the number of PM target checks indicate that the decline in PM performance of older adults cannot solely be attributed to their monitoring processes. Similarly, Ballhausen, Lauffs, Herzog, and Kliegel (11) examined the event-based PM task and found no age-related decline in strategic monitoring. These findings suggested that older participants may not realize the importance of the PM cues when they appear in the PM target area, even when participants follow PM cues. Furthermore, these findings can be explained by the executive framework, which suggests that monitoring, as well as several core EFs (including, *working memory*, *inhibition*, and *set-shifting*), play crucial roles during certain PM stages. For example, *working memory* serves to maintain or refresh the prospective intention that needs to be recalled each time a prospective cue appears. *Inhibition* is needed to end the ongoing task (the prepotent response) and activate the novel PM response. *Set shifting* is also required in PM because participants need to switch continuously between ongoing and PM tasks as a function of the presence of the PM cue (9,26). Supporting this conclusion, we found a moderate positive correlation between working memory measurement (WAIS-R Digit Span test performance) and PM accuracy rate both in young and older adults. To clarify this issue, future studies should examine whether other executive functions, such as inhibition, set-switching, and working memory contribute to PM performance in older adult participants.

It is essential to note that, the present study compared directly event-based and time-based PM monitoring behavior using eye-tracking methods, for the first time, in older adults. From this point, we consider the results of this study to be very valuable and believe future studies should focus on designing new eye-tracking paradigms to shed light on the above topics and inform theoretical discussions in the PM literature.

The limitation of the present study includes the clock in the time-based PM task, which did not work in real-time. Previous studies have shown a positive relationship between time perception and

time-based PM performance (27). Even though the participants were informed that the clock was not working in real-time, this may have created an inconsistency in their time perception, which in turn may have led to a decrease in strategic monitoring performance in time-based PM performance. Clock manipulation in the time-based PM is another limitation of this study that should be addressed in future research.

In conclusion, the current study suggests that older adults showed lower PM performance in time-based PM tasks than in event-based PM tasks. The results suggest that the strategic monitoring process supports but is not sufficient for successful PM performance. It is important to determine the mechanism underlying the age-related decline in PM to find appropriate solutions that will increase PM performance among older adults. Based on this, it is suggested that future studies should examine the contribution of inhibition, set-shifting, and working memory to PM to identify the underlying mechanism of age-related decline in PM.

Declaration of Conflicting Interests

We declare that there is no conflict of interest.

Appendix 1. Pilot Study

We have conducted a pilot study separately in age groups (10 young, M_{age} = 21.35, SD= .7; 10 old, M_{age}= 63.12, SD=1.1) to determine screen time of ongoing and PM tasks. In the pilot study, participants conducted 5 trials of the ongoing task. For each trial, the reaction time was measured. As a result of the pilot study, the mean of the counting task (ongoing task) time of the young participants in each trial was 5.87 s (SD=.63), and the mean of the counting task time of the older participants was 6.79 s (SD=.57). As a result of the independent t-test analysis, it was shown that there was no statistically significant difference between the young and older adults in terms of counting task time (t (18) =.03, p >.05). The descriptive analysis results of the pilot study are shown in Table A1. Based on the results of this analysis, the screen time of ongoing tasks was determined as 6 s for both age groups.

Based on the 1/3 ratio (PM task trial/Ongoing task trial= 1/3) in Shelton and Cristopher's study (13), the screen time of the PM trials for young participants was 2.10 s (5.87/3); it was calculated as 2.37 s (6.79/3) for the older participants. Therefore, for both young and older participants, the screen time of the PM trial was 2 s in each trial, while the screen time for the ongoing task was 6 s.

Table A1. Descriptive Statistics of Pilot Study

N=20	The shortest reaction time	The longest reaction time	Mean (M)	Standart Deviation (SD)	t-test value
Younger Adults	4.83	8.76	5.87	.63	.03
Older Adults	5.05	9.49	6.79	.57	

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RESEARCH

THE RELATIONSHIP BETWEEN GLYCAEMIC INDEX, DAILY ENERGY INTAKE, METABOLIC PARAMETERS, AND BODY COMPOSITION IN THE ELDERLY: A CROSS-SECTIONAL STUDY

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Abstract

Introduction: This study aimed to evaluate the relationship between dietary glycaemic index, daily energy intake, metabolic parameters and body composition in elderly individuals.

Materials and Methods: This is a cross-sectional study that included 198 elderly individuals who applied to the endocrinology outpatient clinic. Participants were asked to record the foods they consumed on three-day diet forms, which would be collected the following week at the time when also the metabolic parameters would be measured and body composition analyses performed at the polyclinic. Nutrient content was recorded with the BeBIS software. The body composition was analysed by using the bioelectrical impedance method.

Results: The mean age of 198 people included in the study was 67.78±2.76 (65–78). HbA_{1c}, insulin and HOMA-IR, visceral adiposity rates, body fat mass and metabolic age were found to be higher in participants with a dietary glycaemic index ≥70, and the effect of the glycaemic index on these parameters was statistically small. The daily energy intake showed a positive correlation with fasting blood glucose, triglyceride and triglyceride-glucose (TyG) index. Both the daily energy intake and glycaemic index showed a weakly positive correlation with visceral adiposity, metabolic age, body fat mass and body mass index. A dietary glycaemic index ≥70 was observed to increase the risk of obesity OR=3.7 times (95% CI=1.72 – 7.94), and the risk of HbA_1C higher than 8 to increase OR=3.13 times (95% CI=1.0 – 9.74).

Conclusion: An increase in the dietary glycaemic index and the daily energy intake in the elderly results in poor glycaemic control.

Keywords: Aged; Glycaemic Index; Obesity.

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INTRODUCTION

Nutrition is a complex issue involving many factors and variables that affect health. Adverse health effects of low-quality, carbohydrate-containing foods and beverages have resulted in an increase in the scientific popularity of so-called low-carb diets (1). The glycemic index (GI) is a rating system for foods that contain carbohydrates. It indicates how quickly each food alters blood sugar level when eaten on its own and ranks carbohydrate-containing foods by the amount of increase in blood glucose levels after consumption, compared to reference foods with a GI ≤ 55 (pure glucose or white bread). The values between 56 and 69 are classified as "moderate GI" and those ≥ 70 as "high GI" on the glucose scale (1). Clinical practice guidelines recommend dietary and lifestyle changes as the basis of treatment strategies to prevent and manage diseases. Approaches that target postprandial glycaemic changes through changes in dietary carbohydrate quality and quantity may have some advantages (2). In addition to the glycemic index of foods, the amount of energy consumed daily can also have an impact on health and disease. An adequate caloric intake is an important determinant of health status, especially when degenerative conditions and difficult-to-treat diseases become dominant with age (3). In general, large variations in daily energy intake may be associated with poor diet quality (4). Since the risk of disease increases with age, adequate caloric intake and low glycaemic index diets are important to maintain a balanced health status, especially during older ages. Maintaining adequate nutritional balance is the best preventative measure to eliminate nutritional risk. This study aimed to examine the relationship between dietary content, glycaemic index, and daily energy intake with metabolic parameters and body composition in a group of elderly individuals.

MATERIALS AND METHODS

This cross-sectional study included individuals aged ≥ 65 years who applied to the endocrinology outpatient clinic at Turgut Özal University Training and Research Hospital, Malatya, Türkiye in 2022. The permission to conduct the study was obtained from the ethics committee of Turgut Özal University's Non-interventional Clinical Research Ethics Committee. The sample size calculation (with 99% of power, 1% of confidence interval, and r = 0.381) revealed a minimum sample size of 152 (5), and 198 people were included in the study. From those who wanted to participate, individuals who met the inclusion criteria were included in the study, after obtaining written consent. The study exclusion criteria were individuals younger than 65 years of age, having any organic eating disorder, recent surgery, psychiatric illness, dementia, chronic kidney disease, heart failure, and those with a specific diet.

Measurements

Dietary content analysis

After a sociodemographic questionnaire was administered to people who applied to the outpatient clinic, they were asked to record a nutrition information form (NIF) for three days (two weekdays and one day over the weekend). NIFs were provided using the 3-day, 24-hour recall method to assess nutrient intake at home. The method of keeping the records and the days on which they should be filled out were explained in detail. The completed food registration forms were directly received. The 3-day nutritional values were calculated using the BeBIS (Nutritional Information System), which is a software designed to analyse nutrient content. BeBIS calculates the average carbohydrate, fat, and protein amounts (in %), glycaemic index, and the daily energy amount (in kcal) of the diet content. In the glycaemic index classification, GI ≤ 55 was accepted as "low GI", GI = 56 – 69 as "moderate

GI", and GI ≥ 70 as "high GI" (6). Measurement of metabolic parameters and the analysis of body composition were performed at the time of submission of NIFs at the clinic.

Metabolic parameters

Blood samples (for detecting the metabolic parameters) were collected from the participants when they came to submit the filled NIFs. Fasting blood glucose (FBG), HbA_{1c}, total cholesterol, triglyceride, low-density lipoprotein (LDL), high-density lipoprotein (HDL), insulin, and homeostatic model assessment of insulin resistance (HOMA-IR) were measured. The triglyceride and glucose index (TyG index) was calculated as follows:

Ln (Fasting triglyceride(mg/dl) x Fasting glucose(mg/dl)/2)

Bioelectrical impedance analysis

Body composition analyses of the participants were performed using the Body Composition Analyser BC-420MA device along with the metabolic measurements at the time of submission of the filled NIFs. The device works by measuring bioimpedance after the administration of an electric current of 50 kHz into the body through the feet (via electrodes). The analysis included visceral fat rating, basal metabolic rate, metabolic age, bone mass, skeletal muscle mass, free fat mass, body fat mass, body fat, and body mass index (BMI) measurements.

Statistical analysis

The SPSS 22 software was used for data analysis. Student's t-test, Mann-Whitney U test, Spearman and Pearson correlation analyses, chi-square test, and binary logistic regression analysis were used. Statistical significance was set at $p < 0.05$.

RESULTS

The mean age of 198 elderly participants included in the study was 67.78 ± 2.76 years (range, 65–78). Among patients with GI ≥ 70, the proportion of obese patients and those with HbA_{1c}>8 was significantly higher. The sociodemographic characteristics of patients according to the GI group are shown in Table 1.

HbA_{1c}, insulin, HOMA-IR, visceral adiposity rates, body fat mass, and metabolic age were significantly higher in patients with a dietary mean GI ≥ 70, while the effect size of the GI on these parameters was small (Table 2).

The average daily energy intake showed a weak positive correlation with diet, fasting blood glucose, triglyceride, and TyG index. The average daily energy intake showed a weak positive correlation between diet, glycaemic index, visceral adiposity, metabolic age, body fat mass, and BMI (Table 3).

Logistic regression models created to predict the risk of obesity (BMI ≥ 30) and high HbA1C levels (> 8) were found to be significant. Every 0.003 unit (kcal) increase in daily energy intake increased the risk of obesity 1.003 times (3 per thousand), and every 0.001 unit rise, increased the risk of high HbA1C 1.001 times (1 per thousand). A mean dietary glycaemic index > 70 increased the risk of obesity 3.7 times and the risk of HbA1C (>8) 3.13 times (Table 4).

DISCUSSION

An appropriate dietary intake is essential for the elderly population. Although proper dietary intake can increase longevity, ageing itself can increase the risk of malnutrition. Adequate and balanced nutritional intake throughout life helps maintain health by protecting tissues or providing defence against infections. Maintaining proper nutrition (especially high in protein and calorie balance) may improve the degeneration processes accompanying ageing and the development and control of diseases (7).

In this study, the effects of dietary content, glycaemic index, and daily energy intake on metabolic and anthropometric parameters in the elderly were

Table 1. Sociodemographic characteristics

Characteristics	Glysemic Index (mean±SD) or n(%)		p
	<70 (n=55)	≥70 (n=141)	
Age	68.00±2.94	67.69±2.70	0.480
Sex (Male/Female)	23 (41.8)/32(58.2)	60(42.6)/81(57.4)	0.925
Chronic disease (Yes/No)	55(100.0) / 0(0.0)	139(98.6) / 2(1.4)	1.000
Hypertension (Yes/No)	36(65.5)/19(34.5)	91(64.5)/50(35.5)	1.000
Diabetes mellitus (Yes/No)	35(63.6)/20(36.4)	103(73.0)/38(27.0)	0.261
Cardiovascular disease (Yes/No)	9(16.4)/46(83.6)	15(10.6)/126(89.4)	0.392
Chronic obstructive pulmonary disease or asthma (Yes/No)	3(5.5)/52(94.5)	17(12.1)/124(87.9)	0.267
Cancer (Yes/No)	2(3.6)/53(96.4)	2(1.4)/139(98.6)	0.314
Rheumatological disease (Yes/No)	3(5.5)/52(94.5)	10(7.1)/131(92.9)	1.000
Obesity (Yes/No)	18(32.7)/37(67.3)	80(56.7)/61(43.3)	**0.003**
HbA_{1c} (<8/≥8)	51(92.7)/4(7.3)	113(80.1)/28(19.9)	**0.027**

Table 2. Comparison of metabolic and anthropometric parameters

	Glycemic index					
	<70		≥70			
Metabolic parameters	Mean±SD	Median	Mean±SD	Median	p	Effect Size
FBG (mg/dl)	132.80±45.86	120	135.94±52.11	118	0.445	0.012
HbA_{1c}	6.73±1.00	6.60	7.09±1.35	6.70	**0.039**	**0.130**
Total cholesterol	188.91±35.14	191.00	187.38±42.787	185.00	0.642	0.033
Triglyceride	156.60±62.20	142.00	167.50±107.34	145.00	0.469	0.007
LDL	118.78±48.453	112.00	113.41±33.45	111.00	0.627	0.029
HDL	52.21±10.93	50.00	53.84±12.85	53.00	0.219	0.071
Insulin	10.33±6.14	10.00	13.05±18.06	10.00	**0.034**	**0.168**
HOMA-IR	3.15±2.04	2.90	3.74±2.31	3.10	**0.039**	**0.162**
TyG index	9.12±0.581	9.14	9.15±0.641	9.12	0.450	0.010
Body composition analyse						
Viceral fat rating (%)	12.95±4.03	12.0	14.57±4.90	14.0	**0.007**	**0.227**
Basal metabolic rate	1606.69±287.73	1523.0	1651.46±282.45	1623.0	0.113	0.111
Metabolic age	61.44±11.13	60.00	66.86±11.57	69.00	**0.001**	**0.281**
Bone mass (kg)	3.00±0.52	3.00	3.30±2.57	3.10	0.145	0.097
Skeletal muscle mass (kg)	49.10±11.72	50.00	51.94±9.44	51.00	0.083	0.127
Free fat mass (kg)	53.10±9.58	52.80	58.51±44.64	53.90	0.099	0.118
Body fat mass (kg)	26.96±12.00	26.00	32.82±12.14	31.80	**<0.001**	**0.294**
Body fat (%)	32.80±10.56	33.00	36.31±9.56	36.00	**0.016**	**0.198**
BMI (kg/m^2)	29.77±6.84	28.00	33.11±7.00	32.00	<0.001	0.316

Table 3. Correlations between daily energy intake, glycaemic index, and metabolic and anthropometric measurements

Metabolic parameters	Energy (kcal)	Glycemic index	Body composition analysis	Energy (kcal)	Glycemic index
FBG	0.154*	-0.053	Viceral fat rating (kg)	0.140*	0.170*
HbA_{1c}	0.105	0.079	Basal metabolic rate	0.125	0.143*
Total cholesterol	0.106	-0.049	Metabolic age	0.229**	0.192**
HDL	-0.051	0.028	Bone mass (kg)	0.111	0.030
LDL	0.130	-0.083	Skeletal muscle mass (kg)	0.043	0.132
Triglyceride	0.164*	-0.022	Free fat mass	0.027	0.120
Insulin	0.032	0.094	Body fat mass (kg)	0.192**	0.213**
HOMA-IR	0.117	0.118	Body fat (%)	0.159*	0.138
TyG index	0.175*	-0.051	BMI (kg/m^2)	0.220**	0.235***

***p<0.05, **p<0.01, ***p<0.001**

Table 4. Logistic regression model

Obesity risk model	β	p	OR (CI 95%)
Daily Energy Intake (kcal)	0.003	**<0.001**	**1.003** (1.002-1005)
Protein (%)	-0.042	0.306	0.958(0.883-1.040)
Fat (%)	0.003	0.885	1.003(0.957-1.052)
Carbohydrate (%)	0.005	0.756	1.005(0.973-1.038)
Glycemic Index (≥70-<70)	1.309	**<0.001**	**3.702** (1.725-7.946)
HbA_{1c} elevation model			
Daily Energy Intake (kcal)	0.001	**0.022**	**1.001** (1.00011-1.00015)
Protein (%)	-0.019	0.710	0.981(0.887-1.090)
Fat (%)	-0.012	0.651	0.987(0.987-0.936)
Carbohydrate (%)	-0.007	0.677	0.992(0.959-1.030)
Glycemic Index (≥70-<70)	1.143	0.048	**1.010-9.740**)

investigated. There was no significant relationship between fat, carbohydrate, and protein proportions in the diet, and obesity and glycaemic control. The daily energy intake and glycaemic index were correlated with obesity (body fat ratio, visceral fat ratio, and BMI) and poor glycaemic control (HbA_{1C}, HOMA-IR, and insulin).

A meta-analysis by Chiavaroli et al. revealed that low GI diet ingredients reduced HbA_{1C} more than high GI diets in 1617 participants with type 1 and 2 diabetes, who were predominantly middle-aged, overweighted or obese, with moderately controlled type 2 diabetes. In addition, a low GI diet was found to reduce fasting glucose, LDL-C, non-HDL-C, apoB,

triglycerides, body weight, and BMI (8). In a systematic review by Ojo et al., a low GI diet was shown to be more effective in controlling HbA_{1C} and fasting blood sugar levels in patients with type 2 diabetes than a high GI diet (9). Another meta-analysis by Livesey et al., found that the risk of type 2 diabetes mellitus increased 1.27 times for every 10 units increase of GI in the diet, and 1.26 times for every 80 units of GI in a 2000 kcal diet (10). Sacks et al. compared a low glycaemic index - low carbohydrate diet with a high glycaemic index - high carbohydrate diet and found that insulin sensitivity, systolic blood pressure, LDL cholesterol, and HDL cholesterol were not affected, but triglycerides were reduced by 23% (11). Argiana et al. reported that consumption of a dessert with a low glycaemic index or low glycaemic load improved glucose and insulin responses in patients with type 2 diabetes compared to a conventional dessert with similar carbohydrate content, but with different sugar and fibre contents (12). In our study, it was found that a high glycaemic index was associated with poor glycaemic control; the risk of elevated HbA_{1C} increased 3.13 times, and insulin and HOMA-IR values were higher in patients consuming a high GI diet (i.e. GI ≥ 70). A low GI diet appears to have a positive effect on glycaemic control. TyG index, a new marker, is an important predictor of insulin resistance. In our study, a weak positive correlation was found between daily energy intake and the TyG index. Selvi et al. found that TyG index showed a significant positive correlation with HbA_{1C} and HOMA-IR (13). The TyG index is a potential risk factor for diabetes mellitus (DM) and cardiovascular diseases (CVD) (13). The increase in daily energy intake contributes to an increase in this index. A higher GI diet causes a higher glucose response and increases the risk of CVD and DM. Sieri et al. reported that a high glucose load (GL) was associated with a higher risk of CVD (Hazard ratio (HR) = 1.16). Every 50 g/day GL was found to increase CVD risk (HR = 1.18) (14). It would not be wrong to say that increased daily energy intake and a high dietary glycaemic index are potential risk factors for DM and CVD. Vega et al. found a relationship between GI and disease outcomes such as DM and CVD in their analysis of intervention studies on diet content (15). Another finding of our study was that a high glycaemic index and daily energy intake increased the risk of obesity, body fat ratio, and visceral adiposity. Being overweight and obese are risk factors for CVDs, such as heart diseases, stroke, DM, and various cancers, which are the leading causes of death worldwide. The International Carbohydrate Quality Consortium agreed that diets low in GI are relevant for the prevention of diabetes, coronary heart disease, and possibly obesity. It is accepted that low GI diets are especially important in individuals with insulin resistance (16). In a study by Hameed et al., a high visceral adiposity index was found to be associated with poor glycaemic control, dyslipidaemia, and an increased TyG index, and it was reported that as visceral adiposity quartile increased, the rates of poor glycaemic control also increased (17). An increase in the dietary glycaemic index and daily energy intake will lead to negative consequences for both metabolic parameters (insulin, HOMA-IR, and fasting blood glucose) and body composition (fat ratio and visceral adiposity ratio), especially increasing the risk factors for DM and cardiovascular diseases. Dietary interventions may reduce the risk of complications or the development of diseases associated with poor glycaemic control (prediabetic, insulin resistant, atherosclerotic, and overweight) in the elderly.

The study included elderly individuals and this is the strength of the study; while being limited to a hospital is a limitation.

The results of this study indicated that a high dietary glycaemic indexed intake and increased daily energy intake in the elderly led to poor glycaemic control, increased the risk of obesity, and were asso-

ciated with visceral adiposity and body fat ratio. Diets with a low glycaemic index as well as controlled energy consumption in prediabetic elderly people with CVD risk factors would protect them from possible negative consequences.

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