EISSN 2687-2625

Academic Geriatrics Society

Eur J Geriatr Gerontol

European Journal of Geriatrics and Gerontology

2024
Volume: 6
Issue: 1
April

ORIGINAL ARTICLES

CASE REPORTS

galenos yayınevi

www.ejgg.org

EJGG
European Journal of Geriatrics and Gerontology
Academic Geriatrics Society
2024
Volume: 6 Issue: 1

Editorial Board

Publisher Contact
Address: Molla Gürani Mah. Kaçamak Sk. No: 21/1 34093 İstanbul, Turkey
Phone: +90 (530) 177 30 97
E-mail: info@galenos.com.tr / yayin@galenos.com.tr
Web: www.galenos.com.tr
Online Publication Date: April 2024
Publisher Certificate Number: 14521 **E-ISSN:** 2687-2625
International periodical journal published three times in a year.

Address for Correspondence
Academic Geriatrics Society
Güven Çarşısı Enez Sok. 2/176 Altındağ - Ankara, Turkey
info@ejgg.org

Reviewing the articles' conformity to the publishing standards of the Journal, typesetting, reviewing and editing the manuscripts and abstracts in English and publishing process are realized by Galenos.

EJGG
European Journal of Geriatrics and Gerontology
Academic Geriatrics Society
2024
Volume: 6 Issue: 1

Editorial Board

EJGG
European Journal of Geriatrics and Gerontology
Academic Geriatrics Society
2024
Volume: 6 Issue: 1

Advisory Board

EJGG
European Journal of Geriatrics and Gerontology
Academic Geriatrics Society
2024
Volume: 6 Issue: 1

Advisory Board

Please refer to the journal's webpage **(https://www.ejgg.org/)** for "Ethical Policy" and "Instructions to Authors".

The editorial and publication processes of the journal are shaped in accordance with the guidelines of the ICMJE, COPE, WAME, CSE and EASE. European Journal of Geriatrics and Gerontology is indexed in the **Emerging Sources Citation Index, TUBITAK/ULAKBIM, Scopus, EBSCO, Gale, ProQuest, Embase, J-Gate, CABI, Türk Medline, CNKI** and **Turkey Citation Index**.

The journal is published online.

Owner: The Turkish Academic Geriatrics Society

Responsible Manager: Zeynel Abidin Öztürk

EJGG
European Journal of Geriatrics and Gerontology
Academic Geriatrics Society
2024
Volume: 6 Issue: 1

CONTENTS

ORIGINAL ARTICLES

CASE REPORTS

ORIGINAL RESEARCH

DOI: 10.4274/ejgg.galenos.2023.2022-11-3

Eur J Geriatr Gerontol 2024;6(1):1-7

Malnutrition in Patients with Parkinson's Disease: Associated Clinical Factors

Murat Gültekin[1], Firuzan Fırat Özer[2], Sibel Akın[3], Ahmet Öztürk[4], Yıldız Değirmenci[5]

[1]Erciyes University Faculty of Medicine, Department of Neurology, Kayseri, Turkey
[2]Kayseri City Hospital, Clinic of Geriatrics, Kayseri, Turkey
[3]Erciyes University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, Kayseri, Turkey
[4]Erciyes University Faculty of Medicine, Department of Biostatistics, Kayseri, Turkey
[5]Düzce University Faculty of Medicine, Department of Neurology, Düzce, Turkey

Abstract

Objective: Parkinson's disease (PD) is a chronic, progressive disease commonly affecting the elderly. Among patients with PD (pwPD), those above 60 years old are considered to be at high risk of malnutrition. Weight loss is a common complaint in pwPD. Thus, we defined the risk factors for malnutrition in geriatric pwPD.

Materials and Methods: We enrolled 66 pwPD above the age of 60 years. Socio-demographic features were recorded and comprehensive geriatric assessments were evaluated. Malnutrition was assessed using a mini-nutritional assessment questionnaire. Anthropometric measurements including body mass index, mid-upper arm circumference, and calf circumference (CC) were recorded.

Results: Seven (10.6%) pwPD had malnutrition, 22 (33.3%) pwPD were at risk of malnutrition. Univariate logistic regression analysis results revealed that low CC, presence of dyskinesia, advanced Hoehn & Yahr stage, levodopa doses of ≥400 mg/day, and difficulty in swallowing (p=0.035, p=0.041, p=0.048, p=0.027 and p=0.007, respectively) were strongly related to malnutrition among the pwPD. Difficulty in swallowing was independently related to malnutrition in pwPD [odds ratio: 7.81 (confidence interval: 2.17-28.10), p=0.002].

Conclusion: PD is the second most common neurodegenerative disease in the geriatric population and is likely to cause malnutrition because of several disabling symptoms in the progressive course of the disease, such as dysphagia. To avoid or delay poorer outcomes, clinicians should be careful to identify malnutrition with appropriate screening tools during follow-up of pwPD.

Keywords: Parkinson disease, geriatric population, malnutrition, risk factors, mini-nutritional assessment

Introduction

Parkinson's disease (PD), the second most common neurodegenerative disease among the population above 65 years of age worldwide, is characterized by cardinal motor symptoms, including bradykinesia, rigidity, rest tremor, postural instability, and non-motor symptoms (1). Due to its progressive course, not only the disabling symptoms and complications, which are more likely to be seen as the disease advances, but bradykinesia itself affecting the gastrointestinal tract as well as other motor systems, autonomic involvement also acts an important role in the occurrence of malnutrition (2). In patients with PD (pwPD), there are many factors affecting malnutrition. It is stated that non-motor and motor symptoms, diagnosis in older age, higher levodopa equivalent daily dose/body weight, depression, dementia, and hallucinations are related to malnutrition among pwPD (3). Moreover, dysphagia, delayed gastric emptying, constipation, malabsorption-like disturbances in the gastrointestinal system, and weak hand-mouth coordination may affect the dietary status (4).

Address for Correspondence: Firuzan Fırat Özer, Kayseri City Hospital, Clinic of Geriatrics, Kayseri, Turkey
Phone: +90 352 315 77 00 **E-mail:** firuzozer@gmail.com **ORCID:** orcid.org/0000-0001-7470-7488
Received: 15.11.2022 **Accepted:** 24.07.2023

Cite this article as: Gültekin M, Fırat Özer F, Akın S, Öztürk A, Değirmenci Y. Malnutrition in Patients with Parkinson's Disease: Associated Clinical Factors. Eur J Geriatr Gerontol 2024;6(1):1-7

Malnutrition can be described as an imbalance between nutritional intake and requirements that eventually causes changes in body weight, body composition, and physical function (3). As a well-known entity, the prevalence of malnutrition in the geriatric population increases with aging, comorbid diseases, and the level of care (4). In accordance with aging, the reported risk of malnutrition is 3-60%, and the prevalence of malnutrition was found to be 0-24% in pwPD who are mostly geriatric (2,5). Detecting possible malnutrition early and related lifestyle characteristics is crucial. Being prone to infection, decubital ulcer, and behavioral and autonomic disorders, pwPD that do not feed well have deficits in their quality of life (6). An improved nutritional status will also improve the quality of life in pwPD.

With regard to these aspects, we investigated the possible factors affecting the risk of malnutrition in older pwPD patients who are an important part of the geriatric population.

Materials and Methods

This study was cross-sectionally designed. Sixty-six pwPD above the age of 60 were enrolled in the present study. Written approval was obtained from all patients and the relatives of patients with dementia before enrollment. Ethical approval was obtained from the Erciyes University Clinical Researches Ethics Committee (decision no: 2016/595, date 18.11.2016). The exclusion criteria were active malignancy, active infectious disease, history of cerebrovascular disease, hepatic failure, and renal failure. The socio-demographic features of the participants were recorded.

The nutritional status of the pwPD was evaluated using a mini-nutritional assessment (MNA) questionnaire, which had 18 questions with a total score of 30 (7). The normal nutrition scores were 23.5 to 30 points. Scores 17 to 23 points were considered as "risk of malnutrition", and scores below 17 points were considered "malnutrition". Study population was categorized into two groups according to MNA scores for analysis. Patients with an MNA score ≤23.5 points were defined as the group with malnutrition (including both patients with malnutrition and at risk of malnutrition), and the second group with an MNA score ≥24 points was defined as the normal nutritional status.

Anthropometric assessments of the groups were performed by height in centimeter (cm), weight measurements in kilogram (kg), body mass index [BMI (kg/m^2)], mid-upper arm circumference (MUAC) in cm, calf circumference (CC) in cm, and triceps skinfold thickness in cm. Because the participants had pwPD, the severity of PD was assessed using the Hoehn & Yahr score (8). Disease characteristic features, therapy regimens, and daily levodopa equivalent doses were recorded. Associated complaints of pwPD, including dyspepsia, constipation, and weight loss in 1 year, were also investigated by self-reported questions regarding the related symptomatology. Swallowing function was evaluated subjectively by the question "do you have difficulty swallowing solid food?".

The cognitive status of pwPD was assessed using a mini-mental status exam (MMSE). This assessment included eleven questions with a total score of 30/30 points. Since the cut-off score for cognitive impairment is 24 points, patients with an MMSE score of 24 to 30 points were considered to be normal, while mild scores between 18 and 23 points were considered "mild dementia" and those ≤17 points "severe dementia" (9).

Mood assessments for depression were performed using the geriatric depression scale which has 30 items. The scores ≥14 points were considered depression (10).

Statistics

The Shapiro-Wilks test, histogram, and q-q plots were examined to evaluate data normality. The independent samples t-test and Mann-Whitney U test were applied for continuous variables. Pearson's chi-square test or Fisher's exact test was applied for categorical variables. Univariate and multivariate binary logistic regression models were applied to examine the risk effect of variables on malnutrition. The odds ratios (ORs) were estimated using 95% confidence intervals (CIs). Significant variables with potential risk factors of malnutrition on univariate analysis with $p<0.1$ were taken into multivariate analysis including marital status, H&Y scale, levodopa dose, deep brain stimulation (DBS), difficulty in swallowing, and depression. Backward stepwise selection was applied using the likelihood ratio statistic at $p<0.10$ stringency level. Goodness of fit was assessed by the Hosmer-Lemeshow test ($p=0.840$).

Statistical Package for Social Sciences (SPSS) version 22.0 (SPSS for Windows) database was used to organize data. P values <0.05 were accepted to indicate statistical significance.

Results

Sixty-six pwPD (37 men, 29 women) above the age of 60 years participated in the study. The mean age of pwPD was 67.50 years (minimum-maximum =60-86 years). The mean BMI of pwPD was 30.13±5.04 kg/m^2 (minimum-maximum =22.9-42.0). In the study group, 37 (56.1%) pwPD had normal nutrition status, 22 (33.3%) had malnutrition risk, and 7 (10.6%) had malnutrition. Although malnutrition was more common among widowed patients, there were no statistically significant differences in terms of socio-demographic features between the patients regarding nutrition status ($p>0.05$). A comparison of the socio-demographic and clinical characteristics of pwPD according to their nutrition status is given in Table 1.

As shown in Table 1, pwPD with malnutrition had lower CC ($p=0.041$) and MUAC ($p=0.080$) than pwPD with normal nutrition. In addition, in the group of pwPD with malnutrition,

the stage of PD was more advanced (p=0.048) and levodopa daily doses were higher (p=0.027) than in the group with normal nutritional status. Dyskinesia was also more frequent in patients with malnutrition (p=0.048). Moreover, most of the pwPD in malnutrion group were under the treatment of DBS (p=0.018), had difficulty in swallowing (p=0.008) and had weight loss (p=0.020) (Table 1).

Univariate logistic regression analysis of the data revealed a strong relationship between marital status, CC, dyskinesia, stage of PD, levodopa doses, DBS procedure, difficulty in swallowing, weight loss, and malnutrition. Multiple regression analysis demonstrated an independent relationship between difficulty in swallowing and malnutrition (OR: 7.81, CI: 2.17-28.10, p=0.002). The results of the univariate and multivariate logistic regression analyzes determining the risk factors for malnutrition are shown in Table 2.

Discussion

PD is an important disabling neurodegenerative disease that interferes with patients' quality of life and is more prone to affect the geriatric population (11,12). Not only motor problems, including rigidity, tremor, postural instability, and bradykinesia, leading to dysphagia, constipation, and other problems in daily activities, but also health-related problems, such as mood changes, cognitive decline, and fatigue, may lead to malnutrition in pwPD (4). In this study, we observed that the presence of dyskinesia, advanced stages of PD, higher levodopa doses, DBS procedure, difficulty in swallowing, and depression were strongly related to malnutrition in pwPD. Among these variables, difficulty in swallowing was independently related to malnutrition in pwPD.

Malnutrition is common in pwPD but is often under-reported by both patients and clinicians. The main reasons why pwPD are at high risk of malnutrition are, first, disease characteristic features, defined as the motor findings of the disease; second, the negative effects of the disease on nutrition in older individuals, such as depression and cognitive damage, which are highly prevalent in pwPD as non-motor symptoms; and third, the drugs used for the treatment of PD (3). In addition, studies have shown that pwPD have a lower BMI than age-matched healthy controls (13). Because there is an increased risk of malnutrition reported in the literature for pwPD, it is crucial to screen nutrition in pwPD (14,15). Similar to our study, the common methods used to assess nutritional status are anthropometric measurements, including weight and BMI, and the MNA questionnaire, which is the most frequently used tool for nutritional status assessment (14).

In the literature, the prevalence of malnutrition and malnutrition risk has been stated to be up to 24% for malnutrition and 60% for malnutrition risk in PD (3-11). Similar to the literature, our results revealed a malnutrition rate of 43.9%, which approximately corresponds to half of our study population. Tomic et al. (3) examined 96 patients, and from among 96 patients, 55.2% were at risk of malnutrition, whereas 8.3% had already been malnourished. Several determinants of malnutrition have been implicated in PD patients. It has been reported that age, severity of motor symptoms, duration of the disease, and intensity of stage, especially "off" states, rigidity dominant type with "off" periods, mostly affect the nutritional status (3-16). Moreover, Fávaro-Moreira et al. (17) analyzed the risk factors of malnutrition among older adults above 65 years of age and reported that age and PD were independent risk factors for malnutrition. In the above-mentioned study, the presence of PD in older individuals was found to be independently associated with malnutrition, reflecting that PD poses a very high risk for malnutrition.

Interestingly, pwPD are shown to be overweight in the beginning stages of the disease, but as the disease progresses and the patients end up in the advanced conversely, lower BMI and weight loss are reported to be extremely common and the latter was shown to be associated with nigrostriatal depletion, cognitive impairment, deteriorated motor functions, and a poorer quality of life (18). In this study, BMI, which is one of the anthropometric determinants of malnutrition and is frequently used in clinics, was not associated with malnutrition in PD, whereas decreased MUAC and CC were closely associated with malnutrition. In this case, although it has been stated that BMI in PD patients is lower than that in normal healthy controls, especially in advanced stages, we observed that BMI alone may not be sufficient in PD patients in the evaluation of malnutrition. It may be more effective to use a valid and safe screening tool, such as MNA, in the evaluation of malnutrition in these patients. Because one of the main manifestations of malnutrition is weight loss, the possible risk factors of weight loss in pwPD may include dysphagia, which may lead to low dietary uptake, slowed gastric motility and emptying because of bradykinesia, and increased energy consumption due to levodopa-induced dyskinesia in some patients (19). Similar to the literature, our results disclosed that the risk of malnutrition was significantly higher in patients experiencing the advanced stage, in need of increased daily doses of levodopa, who had difficulty swallowing, levodopa-induced dyskinesia, and weight loss. However, the possible reasons for malnutrition in pwPD, apart from weight loss, and considered "not related" to weight loss are hyposmia, reduced appetite, changed reward mechanism due to degeneration in the mesocorticolimbic network, and decreased levels of orexin (20,21).

In this study, difficulty in swallowing was the only clinical determinant that was independently related with malnutrition in PD, and 33% of the patients had difficulty in swallowing. It has been reported that approximately 80% of pwPD develop dysphagia as the disease progresses. Swallowing disorder

Table 1. The comparison of the socio-demographic and clinical characteristics of the people with Parkinson's disease according to their nutrition status

Variables	All n=66 (100)	Nutritional status: Malnutrition (MNA score ≤23.5) n=29 (43.9)	Nutritional status: Normal (MNA score ≥24) n=37 (56.1)	p
Age	67.5 (63.0-72.0)	66.0 (63.0-73.0)	68.0 (63.0-71.0)	0.990
Gender				
Men	29 (43.9)	16 (55.2)	13 (35.1)	0.136
Women	37 (56.1)	13 (44.8)	24 (64.9)	
BMI, kg/m²	30.1±5.1	29.3±4.8	30.9±5.2	0.231
Education				
Illiterate	17 (25.8)	9 (31.0)	8 (21.9)	0.609
5 years	29 (43.9)	11 (37.9)	18 (48.6)	
Over 5 years	20 (30.3)	9 (31.0)	11 (29.7)	
Marital status				
Married	51 (77.3)	19 (65.5)	32 (86.5)	0.074
Widow	15 (22.7)	10 (34.5)	5 (13.5)	
Income				
Low	49 (74.2)	20 (69.0)	29 (78.4)	0.410
Middle/high	17 (25.8)	9 (31.0)	8 (21.6)	
MUAC, cm	29.4±3.6	28.5±4.1	30.2±3.0	0.075
CC, cm	36.1±4.4	35.6±4.4	37.9±4.1	0.035
TSF, mm	17.2±7.3	15.8±7.1	18.4±7.4	0.158
Dyskinesia				
Yes	17 (26.2)	11 (39.3)	6 (16.2)	0.048
No	48 (73.8)	17 (60.7)	31 (83.8)	
H&Y scale				
Early stages	30 (45.5)	9 (31.0)	21 (56.8)	0.048
Advanced stages	36 (54.5)	10 (69.0)	16 (43.2)	
Levodopa dose				
≥400 mg	35 (53.0)	20 (69.0)	15 (40.5)	0.027
<400 mg	31 (47.0)	9 (31.0)	22 (59.5)	
DBS				
Yes	8 (12.1)	7 (24.1)	1 (2.7)	0.018
No	58 (87.9)	22 (75.9)	36 (97.3)	
Dyspepsia				
Yes	18 (29.0)	10 (35.7)	8 (23.5)	0.400
No	44 (71.0)	18 (64.3)	26 (76.5)	
Constipation				
Yes	41 (62.1)	19 (65.5)	22 (59.5)	0.799
No	25 (37.9)	10 (34.5)	15 (40.5)	
Difficulty in swallowing				
Yes	22 (33.3)	15 (51.7)	7 (18.9)	0.008
No	44 (66.7)	14 (48.3)	30 (81.1)	
Weight loss				
Yes	25 (37.9)	16 (55.2)	9 (24.3)	0.020
No	41 (62.1)	13 (44.8)	28 (75.7)	
Depression score [(GDS) ≥14]				
Yes	28 (42.4)	16 (55.2)	12 (32.4)	0.082
No	38 (57.6)	13 (44.8)	25 (67.6)	
Cognitive impairment (MMSE score <24)				
Yes	10 (15.2)	6 (20.7)	4 (10.8)	0.315
No	56 (84.8)	23 (79.3)	33 (89.2)	

Values are stated as n (%), mean ± standard deviation or median (1st-3rd quartiles). MNA: Mini-nutritional assessment BMI: Body mass index, CC: Calf circumference, DBS: Deep brain stimulation, H&Y: Hoehn and Yahr, MUAC: Mid-upper arm circumference, TSF: Triceps skin fold thickness, GDS: Geriatric depression scale, MMSE: Mini-mental status exam

Table 2. The univariate and multivariate logistic regression analysis results, determining the risk factors of malnutrition

Variables	Univariate		Multivariate	
	OR (95% CI)	p	OR (95% CI)	p
Age	0.99 (0.91-1.08)	0.807	Not selected	
Gender Men Women	 1 2.27 (0.84-6.15)	 0.106	Not selected	
BMI (kg/m²)	0.940 (0.85-1.04)	0.230	Not selected	
Education Illiterate 5 years Over 5 years	 1 0.543 (0.16-1.83) 0.727 (0.19-2.67)	 0.324 0.630	Not selected	
Marital status Married Widow	 1 3.37 (1.001-11.345)	 0.050		
Income Low Middle/high	 1 0.61 (0.20-1.86)	 0.387	Not selected	
MUAC (cm)	0.88 (0.77-1.16)	0.080	Not selected	
CC (cm)	0.88 (0.78-0.99)	0.041	Not selected	
TSF (mm)	0.95 (0.89-1.02)	0.159	Not selected	
Dyskinesia No Yes	 1 3.34 (1.05-10.64)	 0.041	Not selected	
H&Y scale Early stages Advanced stages	 1 2.92 (1.05-8.09)	 0.040		
Levodopa dose <400 mg >400 mg	 1 3.26 (1.17-9.08)	 0.024		
DBS No Yes	 1 11.46 (1.32-99.46)	 0.027		
Dyspepsia Yes No	 1 1.81 (0.60-5.46)	 0.296	Not selected	
Constipation No Yes	 1 1.30 (0.47-3.55)	 0.615	Not selected	
Difficulty in swallowing No Yes	 1 4.59 (1.53-13.78)	 0.007	 1 7.81 (2.17-28.10)	 0.002
Weight loss No Yes	 1 3.83 (1.34-10.93)	 0.012	Not selected	
Depression No Yes	 1 2.56 (0.94-7.00)	 0.066		
Cognitive impairment No Yes	 1 2.15 (0.55-8.49)	 0.274	Not selected	

OR: Odds ratio, CI: Confidence interval, p<0.005, BMI: Body mass index, CC: Calf circumference, DBS: Deep brain stimulation, H&Y: Hoehn and Yahr, MUAC: Mid-upper arm circumference, TSF: Triceps skin fold thickness

complicates drug intake in pwPD, leads to malnutrition and aspiration pneumonia, and thus reduces quality of life and increases mortality in pwPD. Although the fundamental pathophysiology is not fully understood, dopaminergic and non-dopaminergic mechanisms play a role in the development of dysphagia in PD. Clinical assessment of dysphagia in pwPD is difficult and often yields discordant results (22). However, in this study, it was observed that pwPD who were evaluated only with a single question and described difficulty in swallowing were highly associated with the risk of malnutrition.

Study Limitations

There are some limitations to this study. The most important limitation of the study is that swallowing function was not evaluated with an objective method such as functional swallowing tests, an instrumental method such as videofluoroscopic evaluation, or a PD-specific swallowing questionnaire. However, studies in the literature have shown that a single screening question for dysphagia as difficulty in swallowing is closely related to the results of evaluations made by dysphagia diagnostic tools, both in cancer patients and older people living in the community (23,24). In addition, the relationship between a one-question dysphagia screening test and difficulty in swallowing pills was investigated in Parkinson's patients, and the sensitivity of the single question in estimating dysphagia was found to be moderate, whereas the specificity was found to be high (25). In addition, this was a cross-sectional study with a relatively small sample size. It is important to emphasize that further investigation through large-scale longitudinal studies is mandatory to detect early malnutrition risk in geriatric pwPD. Because aging and neurodegenerative diseases such as PD have a strong impact on patients' nutritional status, leading to weight loss and malnutrition via direct and indirect mechanisms, it is important to be aware of the risk of malnutrition, especially in geriatric pwPD. To prevent the damaging effects of weight loss on motor function in pwPD, especially in the geriatric population, clinicians should be aware of the risks of malnutrition, such as advanced stages of the disease, increased doses of daily levodopa, dysphagia, and dyskinesia. When swallowing dysfunction is detected, treatment approaches should be applied with pharmacological interventions and therapy by speech and language therapists. Regular screening of malnutrition in pwPD with a validated tool such as MNA alongside anthropometric measures such as body weight and BMI in follow-ups is another clue for early recognition of malnutrition and application of essential interventions for malnutrition to maintain a better quality of life in pwPD.

Conclusion

In conclusion, pwPD are at risk of malnutrition. PwPD should be regularly followed up for malnutrition by clinicians, particularly those with high risk factors associated with disease characteristics such as dysphagia. In addition, the common treatment plan for PD should include a nutritional consultation with a dietary regime.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Erciyes University Clinical Researches Ethics Committee (decision no: 2016/595, date 18.11.2016).

Informed Consent: Written approval was obtained from all patients and the relatives of patients with dementia before enrollment.

Authorship Contributions

Surgical and Medical Practices: M.G., F.F.Ö., S.A., A.Ö., Y.D., Concept: M.G., F.F.Ö., S.A., A.Ö., Y.D., Design: M.G., F.F.Ö., S.A., A.Ö., Y.D., Data Collection or Processing: M.G., F.F.Ö., S.A., Analysis or Interpretation: M.G., F.F.Ö., S.A., A.Ö., Y.D., Literature Search: M.G., F.F.Ö., Writing: M.G., F.F.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Thenganatt MA, Jankovic J. Parkinson disease subtypes. JAMA Neurol 2014;71:499-504.
2. Paul BS, Singh T, Paul G, Jain D, Singh G, Kaushal S, Chinna RS. Prevalence of Malnutrition in Parkinson's Disease and Correlation with Gastrointestinal Symptoms. Ann Indian Acad Neurol 2019;22:447-452.
3. Tomic S, Pekic V, Popijac Z, Pucic T, Petek M, Kuric TG, Misevic S, Kramaric RP. What increases the risk of malnutrition in Parkinson's disease? J Neurol Sci 2017;375:235-238.
4. Barichella M, Cereda E, Pezzoli G. Major nutritional issues in the management of Parkinson's disease. Mov Disord 2009;24:1881-1892.
5. White JV, Guenter P, Jensen G, Malone A, Schofield M. Consensus statement: Academy of Nutrition and Dietetics and American Society for Parenteral and Enteral Nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). JPEN J Parenter Enteral Nutr 2012;36:275-283.
6. Guyonnet S, Rolland Y. Screening for Malnutrition in Older People. Clin Geriatr Med 2015;31:429-437.
7. Sarikaya D, Halil M, Kuyumcu ME, Kilic MK, Yesil Y, Kara O, Ozturk S, Gungor E, Karabulut E, Balam Yavuz B, Cankurtaran M, Ariogul S. Mini nutritional assessment test long and short form are valid screening tools in Turkish older adults. Arch Gerontol Geriatr 2015;61:56-60.
8. Hoehn M, Yahr M. Parkinsonism: Onset, progression and mortality. Neurology 1967;17:427-442.
9. Güngen C, Ertan T, Eker E, Yaşar R, Engin F. [Reliability and validity of the standardized Mini Mental State Examination in the diagnosis of mild dementia in Turkish population]. Turk Psikiyatri Derg 2002;13:273-281.
10. Ertan T, Eker E. Reliability, validity, and factor structure of the Geriatric Depression Scale in Turkish elderly: are there different factor structures for different cultures? Int Psychogeriatr 200;12:163-172.

11. Kim SR, Chung SJ, Yoo SH. Factors contributing to malnutrition in patients with Parkinson's disease. Int J Nurs Pract 2016;22:129-137.
12. Bianchi VE, Herrera PF, Laura R. Effect of nutrition on neurodegenerative diseases. A systematic review. Nutr Neurosci 2021;24:810-834.
13. van der Marck MA, Dicke HC, Uc EY, Kentin ZHA, Borm GF, Bloem BR, Overeem S, Munneke M. Body mass index in Parkinson's disease: a meta-analysis. Parkinsonism Relat Disord 2012;18:263-267.
14. Sheard JM, Ash S, Silburn PA, Kerr GK. Prevalence of malnutrition in Parkinson's disease: a systematic review. Nutr Rev 2011;69:520-532.
15. Sheard JM, Ash S, Mellick GD, Silburn PA, Kerr GK. Improved nutritional status is related to improved quality of life in Parkinson's disease. BMC Neurol 2014;14:212.
16. Chen H, Zhang SM, Hernán MA, Willett WC, Ascherio A. Weight loss in Parkinson's disease. Ann Neurol 2003;53:676-679.
17. Fávaro-Moreira NC, Krausch-Hofmann S, Matthys C, Vereckeen C, Vanhauwaert E, Declercq A, Bekkering GE, Duyck J. Risk Factors for Malnutrition in Older Adults: A Systematic Review of the Literature Based on Longitudinal Data. Adv Nutr 2016;7:507-522.
18. Lee JJ, Oh JS, Ham JH, Lee DH, Lee I, Sohn YH, Kim JS, Lee PH. Association of body mass index and the depletion of nigrostriatal dopamine in Parkinson's disease. Neurobiol Aging 2016;38:197-204.
19. Pisciotta MS, Fusco D, Grande G, Brandi V, Lo Monaco MR, Laudisio A, Onder G, Bentivoglio AR, Ricciardi D, Bernabei R, Zuccalà G, Vetrano DL. Untangling the relationship between fat distribution, nutritional status and Parkinson's disease severity. Aging Clin Exp Res 2020;32:77-84.
20. Pfeiffer RF, Quigley EM. Gastrointestinal mobility problems in patients with Parkinson's disease-epidemiology, pathophysiology and guidelines for management. Cent Nerv Syst Drugs 1999;11:435-448.
21. Pålhagen S, Lorefält B, Carlsson M, Ganowiak W, Toss G, Unosson M, Granérus AK. Does L-dopa treatment contribute to reduction in body weight in elderly patients with Parkinson's disease? Acta Neurol Scand 2005;111:12-20.
22. Suttrup I, Warnecke T. Dysphagia in Parkinson's Disease. Dysphagia 2016;31:24-32.
23. Borean M, Shani K, Brown MC, Chen J, Liang M, Karkada J, Kooner S, Doherty MK, O'Kane GM, Jang R, Elimova E, Wong RK, Darling GE, Xu W, Howell D, Liu G. Development and evaluation of screening dysphagia tools for observational studies and routine care in cancer patients. Health Sci Rep 2018;1:e48.
24. Heijnen BJ, Speyer R, Bülow M, Kuijpers LM. What About Swallowing?' Diagnostic Performance of Daily Clinical Practice Compared with the Eating Assessment Tool-10. Dysphagia 2016;31:214-222.
25. Buhmann C, Bihler M, Emich K, Hidding U, Pötter-Nerger M, Gerloff C, Niessen A, Flügel T, Koseki JC, Nienstedt JC, Pflug C. Pill swallowing in Parkinson's disease: A prospective study based on flexible endoscopic evaluation of swallowing. Parkinsonism Relat Disord 2019;62:51-56.

ORIGINAL RESEARCH

DOI: 10.4274/ejgg.galenos.2023.2023-5-2

Eur J Geriatr Gerontol 2024;6(1):8-11

Can Geriatric Nutrition Risk Index Predict Postoperative 90-Day Complications and Mortality in Elderly Patients with Hip Fracture?

Mustafa Yerli, Nazım Erkurt, Tahsin Olgun Bayraktar, Mehmet Selçuk Saygılı, Ali Yüce, Hakan Gürbüz

University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital, Clinic of Orthopedics and Traumatology, İstanbul, Turkey

Abstract

Objective: Malnutrition is a severe cause of increased morbidity and mortality and decreased functionality and quality of life that can be treated and prevented in the geriatric population. The geriatric nutritional risk index is used to determine the nutritional status of the geriatric population. We evaluated the ability of geriatric nutrition risk index (GNRI) values to predict 90-day complications and mortality in elderly patients with hip fractures. Our study hypothesises that low GNRI values can help predict early complications and mortality.

Materials and Methods: Patients over 65 years of age were retrospectively included in this study. Age, gender, height, weight, fracture type, hemogram, and routine biochemical values at the time of admission to the hospital, previous trauma history, and hospitalization within 90 days after surgery were evaluated from the patient's files. Surgical site infection and periprosthetic joint infections that developed in the first 90 days were recorded as early complications.

Results: The study included 1,345 patients with a mean age of 80.27±7.45. The 90-day mortality rate of the patients examined in the study was 10.6%. In addition, when we look at early complications, this rate is 4%. Statistically, although there was no significant relationship between early complications and GNRI (p=0.724), it was found to be significant with mortality (p<0.001).

Conclusion: In hip fractures with high mortality in the geriatric age group, 90-day mortality can be predicted by GNRI score calculated using albumin, height, and weight values.

Keywords: Geriatric, hip fracture, geriatric nutritional risk index

Introduction

Simple falls are common in the elderly population. Studies have shown that approximately 1 in 3 older adults fall at least once yearly, and of those who fall, approximately half fall more than once (1,2). Because of these falls, hip fracture is a common injury in elderly patients. Developing hip fractures, unfortunately, cause high mortality rates, but their frequency is gradually increasing (3). In the literature, mortality rates within 1 year range from 12% to 37% (4,5). The risk of mortality is approximately five times higher for females and approximately eight times higher for males in the first 3 months after fracture (6).

Malnutrition is a severe cause of increased morbidity and mortality and decreased functionality and quality of life that can be treated and prevented in the geriatric population (7). When it occurs with a catabolic response to surgical treatment together with malnutrition, it causes muscle loss and is associated with impaired postoperative rehabilitation, postoperative complications, worse clinical outcomes, longer length of stay, and mortality (8-10).

The geriatric nutrition risk index (GNRI) is used to determine the nutritional status of the geriatric population. It is calculated on the basis of serum albumin levels and the ratio of current body weight to ideal body weight (11). GNRI allows for the

Address for Correspondence: Mustafa Yerli, University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital, Clinic of Orthopedics and Traumatology, İstanbul, Turkey

Phone: +90 505 607 38 04 **E-mail:** mustafayerli199@gmail.com **ORCID:** orcid.org/0000-0002-2708-5812

Received: 10.05.2023 **Accepted:** 24.07.2023

Cite this article as: Yerli M, Erkurt N, Bayraktar TO, Saygılı MS, Yüce A, Gürbüz H. Can Geriatric Nutrition Risk Index Predict Postoperative 90-Day Complications and Mortality in Elderly Patients with Hip Fracture?. Eur J Geriatr Gerontol 2024;6(1):8-11

early detection and diagnosis of malnutrition, timely and appropriate administration of interventions, and identification of postoperative complications and mortality in patients on dialysis and those with cardiovascular disease (12,13).

In this study, we evaluated the ability of GNRI values to predict 90-day complications and mortality in elderly patients with hip fractures. Our study hypothesises that low GNRI values can help predict early complications and mortality.

Materials and Methods

The study was approved by the local institutional review board (University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital; decision number: E-48670771-020-212353622, date: 29.03.2023) and performed under the ethical standards laid down in the Declaration of Helsinki. All patients provided written informed consent before their inclusion in the study.

This study was planned retrospectively, and patients over the age of 65 years who applied to our hospital between 2014 and 2023 were examined for the study. Age, gender, height, weight, fracture type, hemogram, and routine biochemical values at the time of admission to the hospital, previous trauma history, and hospitalization within 90 days after surgery were evaluated from the patient's files. Patients over 65 who applied with the diagnosis of the femoral neck or intertrochanteric femur fracture were treated surgically; patients whose preoperative height, weight, and albumin values were recorded in their files, and patients with a follow-up period of at least three months were included in the study. Patients under the age of 65 years, patients whose files could not be accessed, and patients with pathological fractures were excluded.

GNRI was calculated using the formula [1.489 x albumin (g/L)]+ [41.7 x (body weight/ideal weight)] (14). While determining the ideal weight of the patients, a body mass index of 22 kg/m^2 was taken (15). An index of >98 was normal; values between 92 and 98 were determined as low risk and <92 as moderate/severe risk (16).

The neutrophil-to-lymphocyte ratio, albumin, C-reaktif protein (CRP) values, and CRP-to-albumin ratio were recorded by examining the hemogram and biochemistry tests taken routinely at the time of admission to the hospital. The Charlson comorbidity index (CCI) and American Society of Anaesthesiologists score were calculated manually based on preoperative comorbidities and patient records (17). Surgical site infection and periprosthetic joint infections that developed in the first 90 days were recorded as early complications.

Statistics

Statistical analyzes were performed using SPSS version 25.0 software. Descriptive data are presented using percentage, mean, and standard deviation. The compliance of the variables with normal distribution was examined using histogram graphs and the Kolmogorov-Smirnov test. The independent group student t-test and One-Way ANOVA test were used when evaluating the normally distributed (parametric) variables between the groups. The chi-square test was used to determine the categorical data. Cox regression analysis was performed to determine the relationship between mortality and GNRI class. Cases where the p value was under 0.05, were accepted as statistically significant.

Results

The study included 1,345 patients with a mean age of 80.27±7.45. 62.9% of the cases were female; their demographic data are shown in Table 1. The 90-day mortality rate of the patients examined in the study was 10.6%. In addition, when we look at early complications, this rate is 4%. Statistically, although there was no significant relationship between early complications and the GNRI, it was found to be significant with mortality (Table 2). A statistically significant difference was found as a result of cox regression analysis for the relationship between mortality and GNRI class (p=0.039, Figure 1).

It was observed that the albumin and hemoglobin values of the patients included in the study and CCI were significantly lower in the 90-day mortality group. Age, CRP values, neutrophil to lymphocyte and CRP to albumin ratios were significantly higher in the mortality group (Table 3).

In the study, low albumin was found to be statistically significant in patients with early complications. CRP, neutrophil to lymphocyte ratio, and CRP to albumin ratio were found to be statistically significantly higher in the group with complications. There was no statistically significant difference between the two groups in the hemoglobin values of the patients included in the study (Table 4).

Discussion

Nutritional status is essential for mortality in patients with various diseases (18-20). Studies examining the mortality rates of patients with hip fractures have shown it to be associated with malnutrition (21,22). This study found a significant relationship between malnutrition and 90-day mortality in the geriatric population after hip fracture.

The literature has reported that wound infection is more common due to surgical treatment in patients with hypoalbuminemia due to malnutrition (21,22). This study found no significant relationship between early complications and malnutrition.

Because the neutrophil-to-lymphocyte ratio, CRP, and CRP-to-albumin ratios indicate inflammatory responses, it is available in the literature where it is used to predict complications and mortality in various diseases (23-25). The results of this study were statistically significant both in the group with early complications and in the group with 90-day mortality, consistent with the literature.

Table 1. Demographic data of the patients included in the study

	Normal risk (n=523)	Low risk (n=442)	Moderate/severe risk (n=380)	Total (n=1345)	p
Age (years)	79.97±7.33	80.61±7.51	80.27±7.54	80.27±7.45	0.416*
Gender **Female [n (%)]**	332 (63.5%)	279 (63.1%)	235 (61.8%)	846 (62.9%)	0.875**
BMI (kg/m²)	25.67±2.41	25.46±2.48	25.13±2.46	25.45±2.45	0.004*
GNRI	102.96±3.54	95.11±1.62	86.79±4.37	95.82±7.36	<0.001*
Length of stay	11.91±5.73	11.99±5.23	12.62±5.51	12.13±5.51	0.124*
CCI	5.89±1.12	5.85±1.15	5.97±1.13	5.9±1.13	0.266*
ASA score [n (%)] **I** **II** **III** **IV**	 71 (13.6%) 166 (31.7%) 202 (38.6%) 84 (16.1%)	 67 (15.2%) 132 (29.9%) 172 (38.9%) 71 (16.1%)	 55 (14.5%) 135 (35.5%) 139 (36.6%) 51 (13.4%)	 193 (14.3%) 433 (32.2%) 513 (38.1%) 206 (15.3%)	0.663**
Fracture type [n (%)] **Femoral neck** **Intertrochanteric**	 206 (39.6%) 317 (60.6%)	 153 (34.6%) 289 (65.4%)	 118 (31.1%) 262 (68.9%)	 477 (35.5%) 868 (64.5%)	0.032**
Mortality [n (%)] **Releated reason** **Unreleated reason**	 7 (9.1%) 70 (90.9%)	 8 (12.9%) 54 (87.1%)	 6 (8.5%) 65 (91.5%)	 21 (10%) 189 (90%)	0.657**

*One-Way ANOVA test, **Pearson chi-square test, BMI: Body mass index, GNRI: Geriatric nutritional risk index, CCI: Charlson comorbidity index, ASA: American Society of Anaesthesiologists

Table 2. Complication and 90-day mortality rates of the patients included in the study

	Normal risk (n=523)	Low risk (n=442)	Moderate/severe risk (n=380)	Total (n=1345)	p
Complication n (%)	20 (3.8%)	21 (4.8%)	18 (4.7%)	59 (4.4%)	0.724*
90-day mortality n (%)	39 (7.5%)	40 (9%)	64 (16.8%)	143 (10.6%)	<0.001*

* Pearson chi-square test

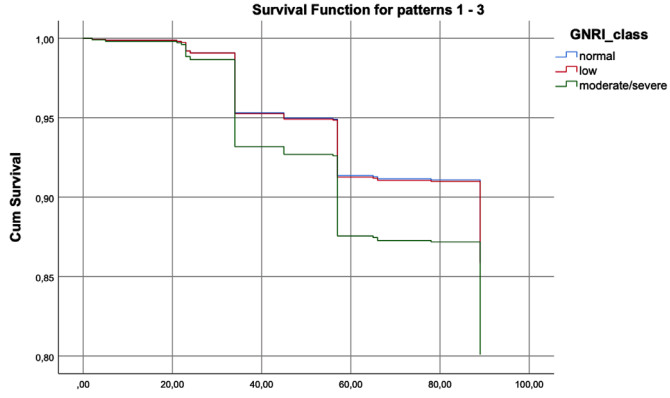

Figure 1. Cox regression analysis for the relationship between mortality and GNRI class

GNRI: Geriatric nutrition risk index, Cum: Cumulative

Table 3. Comparison of 90-day mortality and blood values of the patients included in the study

	Survived (n=1202)	Died (n=143)	p
Albumin (g/L)	37.26±4.54	32.33±4.55	<0.001*
Haemoglobin (g/dL)	11.71±1.28	10.53±0.65	<0.001*
CRP (mg/dL)	67.84±10.34	84.74±4.46	<0.001*
Neutrophil to lymphocyte ratio	4.58±0.65	5.73±0.87	<0.001*
CRP to albumin ratio	18.5±3.75	27.74±4.11	<0.001*

*Student's t-test, CRP: C-reactive protein

Table 4. Comparison of complications and blood values of the patients included in the study

	No-complicated (n=1202)	Complicated (n=143)	p
Albumin (g/L)	36.66±4.91	34.09±3.77	<0.001*
Hemoglobin (g/dL)	11.53±1.27	11.34±1.25	0.177*
CRP (mg/dL)	70.13±11.53	75.26±8.88	<0.001*
Neutrophil to lymphocyte ratio	4.74±0.75	5.1±1.33	<0.001*
CRP/albumin ratio	19.6±4.84	22.41±4.13	<0.001*

*Student's t-test, CRP: C-reactive protein

Study Limitations

This study has several limitations. First, the study is retrospective. Second, the functional status of the patients included in the study was not evaluated in the postoperative period. Finally, only the GNRI is used to assess malnutrition, and other scoring systems are not used. Despite these limitations, this study has the

highest number of patients in the literature. More precise data can be obtained using studies with more patients using other malnutrition scoring systems to be prospectively conducted in the future.

Conclusion

In hip fractures with high mortality in the geriatric age group, 90-day mortality can be predicted by GNRI score calculated using albumin, height, and weight values.

Ethics

Ethics Committee Approval: The study was approved by the local institutional review board (University of Health Sciences Turkey, Prof. Dr. Cemil Taşcıoğlu City Hospital; decision number: E-48670771-020-212353622, date: 29.03.2023) and performed under the ethical standards laid down in the Declaration of Helsinki.

Informed Consent: All patients provided written informed consent before their inclusion in the study.

Authorship Contributions

Surgical and Medical Practices: M.Y., N.E., T.O.B., M.S.S., A.Y., H.G., Concept: M.Y., N.E., T.O.B., M.S.S., A.Y., H.G., Design: M.Y., N.E., T.O.B., M.S.S., A.Y., H.G., Data Collection or Processing: M.Y., N.E., T.O.B., M.S.S., A.Y., Analysis or Interpretation: M.Y., N.E., T.O.B., M.S.S., A.Y., H.G., Literature Search: M.Y., N.E., T.O.B., M.S.S., A.Y., H.G., Writing: M.Y., N.E., T.O.B., M.S.S., A.Y., H.G.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Tosun Taşar P, Karaşahin Ö, Ural Karaman E, Serin BN, Urvasızoğlu TB, Akgöl Gür ST, Sevinç C. Factors Associated with Mortality in Geriatric Patients Presenting to the Emergency Department After Falls. Eur J Geriatric Gerontol 2021;3:171-176.
2. Çakmak G. A Comprehensive Evaluation of the Relationship Between Fall Risk and Other Geriatric Syndromes. Eur J Geriatric Gerontol 2022;4:58-63.
3. Yerli M, İmren Y, Çabuk H, Dedeoğlu SS, Yüce A, Bayraktar TO, Erkurt N, Gürbüz H. Is there a difference between traneksamic acid application routes in hip hemiarthroplasty?. Eur Res J 2022;8:560-566.
4. İğde N, Yerli M, Yüce A, Ayaz MB, Gürbüz H. The role of neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, crp and albumin to predict postoperative one-year mortality in patients with hip fractures. Medicine Science 2022;11:729-733.
5. Yerli M, Yüce A, Bayraktar TO, İğde N, Karslıoğlu B, Erkurt N, Ayaz MB, Dedeoğlu SS, İmren Y, Gürbüz H. The effects of the choice of the femoral head in hip hemiarthroplasty on radiological and clinical outcomes. Arch Curr Med Res 2022;3:31-35.
6. Haentjens P, Magaziner J, Colón-Emeric CS, Vanderschueren D, Milisen K, Velkeniers B, Boonen S. Meta-analysis: excess mortality after hip fracture among older women and men. Ann Intern Med 2010;152:380-390.
7. Catikkas NM. Malnutrition and Related Factors in Older Adults. Eur J Geriatr Gerontol 2020;2:36-40.
8. Wong AM, Xu BY, Low LL, Allen JC Jr, Low SG. Impact of malnutrition in surgically repaired hip fracture patients admitted for rehabilitation in a community hospital: A cohort prospective study. Clin Nutr ESPEN 2021;44:188-193.
9. Foss NB, Jensen PS, Kehlet H. Risk factors for insufficient perioperative oral nutrition after hip fracture surgery within a multi-modal rehabilitation programme. Age Ageing. 2007;36:538-543.
10. Malafarina V, Reginster JY, Cabrerizo S, Bruyère O, Kanis JA, Martinez JA, Zulet MA. Nutritional Status and Nutritional Treatment Are Related to Outcomes and Mortality in Older Adults with Hip Fracture. Nutrients 2018;10:555.
11. Ji Y, Geng N, Niu Y, Zhao H, Fei W, Chen S, Ren LP. Relationship between geriatric nutritional risk index and osteoporosis in type 2 diabetes in Northern China. BMC Endocr Disord 2022;22:308.
12. Sasaki M, Miyoshi N, Fujino S, Ogino T, Takahashi H, Uemura M, Matsuda C, Yamamoto H, Mizushima T, Mori M, Doki Y. The Geriatric Nutritional Risk Index predicts postoperative complications and prognosis in elderly patients with colorectal cancer after curative surgery. Sci Rep 2020;10:10744.
13. Xu J, Zhou X, Zheng C. The geriatric nutritional risk index independently predicts adverse outcomes in patients with pyogenic liver abscess. BMC Geriatr. 2019;19:14.
14. Bouillanne O, Morineau G, Dupont C, Coulombel I, Vincent JP, Nicolis I. Geriatric nutritional risk index: a new index for evaluating at-risk. Am J Clin Nutr 2005;82:777-783.
15. Kotera A. Geriatric Nutritional Risk Index and Controlling Nutritional Status Score can predict postoperative 180-day mortality in hip fracture surgeries. JA Clin Rep 2019 Sep 25;5:62.
16. Cereda E, Pusani C, Limonta D, Vanotti A. The ability of the Geriatric Nutritional Risk Index to assess the nutritional status and predict the outcome of home-care resident elderly: a comparison with the Mini Nutritional Assessment. Br J Nutr 2009;102:563-570.
17. Golsorkhtabaramiri M, Mckenzie J, Potter J. Predictability of Neutrophil to Lymphocyte Ratio in preoperative elderly hip fracture patients for post-operative short-term complications: a retrospective study. BMC Musculoskelet Disord 2023;24:227.
18. Funahashi H, Morita D, Iwase T, Asamoto T. Usefulness of nutritional assessment using Geriatric Nutritional Risk Index as an independent predictor of 30-day mortality after hip fracture surgery. Orthop Traumatol Surg Res 2022;108:103327.
19. Mireille FM, Korkic-Haliovic IK, Bakker MS, Ploeg T, Leeuwen PA, Houdijk AP. Preoperative nutrition status and postoperative outcome in elderly general surgery patients: a systematic review. J Parenter Enteral Nutr 2013;37:37-43.
20. Ballmer PE. Causes and mechanisms of hypoalbuminaemia. Clin Nutr 2001;20:271-273.
21. Chung AS, Hustedt JW, Walker R, Jones C, Lowe J, Russell GV. Increasing Severity of Malnutrition Is Associated With Poorer 30-Day Outcomes in Patients Undergoing Hip Fracture Surgery. J Orthop Trauma 2018;32:155-160.
22. Ryan S, Politzer C, Fletcher A, Bolognesi M, Seyler T. Preoperative Hypoalbuminemia Predicts Poor Short-term Outcomes for Hip Fracture Surgery. Orthopedics 2018;41:e789-e796.
23. Yüce A, Yerli M, Erkurt N, Çakar M. The Preoperative Neutrophil-Lymphocyte Ratio is an Independent Predictive Factor in Predicting 1-Year Mortality in Amputated Diabetic Foot Patients. J Foot Ankle Surg 2023;62:816-819.
24. Yüce A, Yerli M, Erkurt N, Gürbüz S, Çakar M, Adaş M. Neutrophil-lymphocyte and C reactive proteinalbumin ratios as predictors of re-surgery in adult native knee septic arthritis. J Clin Investig Surg 2022;7:191-198.
25. Chen YH, Chou CH, Su HH, Tsai YT, Chiang MH, Kuo YJ, Chen YP. Correlation between neutrophil-to-lymphocyte ratio and postoperative mortality in elderly patients with hip fracture: a meta-analysis. J Orthop Surg Res 2021;16:681.

ORIGINAL RESEARCH

DOI: 10.4274/ejgg.galenos.2023.2023-3-2
Eur J Geriatr Gerontol 2024;6(1):12-18

Restorative Effects of Virtual Nature on the Emotional Well-being of Community-dwelling Older Adults

Kenan Eren Şansal[1], Ayşe Candan Şimşek[2], Selin Aktan[3], Fulya Özbey[3], Ayça Paksoy[2]

[1]TED University, Department of Interior Architecture and Environmental Design, Ankara, Turkey
[2]Yaşar University, Department of Psychology, İzmir, Turkey
[3]Yaşar University, Department of Interior Architecture and Environmental Design, İzmir, Turkey

Abstract

Objective: Given the loss of direct nature contact due to urbanisation and demonstrated psychological benefits of nature, the question arises as to whether direct nature contact can be virtually substituted or supplemented in the elderly living in isolation from nature. Although a number of studies have demonstrated the restorative effects of virtual nature in old age, their results are inconclusive and complicated by the novelty of virtual reality (VR) experience, participants' nature connectedness and their previous nature contact. Therefore, a study was conducted for increasing our limited understanding of the subject.

Materials and Methods: Community-dwelling older adults living in highly urbanised areas of Turkey volunteered for the study. After excluding the ineligible volunteers and collecting information on sample characteristics, 60 participants, who were assigned to two study groups, watched 6-minute 360° videos of nature and urban settings on two separate occasions. On these occasions, they reported on their affective states, the restorativeness of the environments in those videos and their nature visit frequency.

Results: VR experience was new and tolerable for the majority of the participants. Unlike the urban video, the nature video significantly improved participants' affective states and was reported to be more restorative and favourable. Neither participants' nature connectedness nor their nature visit frequency, which was found to be generally low, did not have a moderating effect on the results.

Conclusion: Virtual indirect contact with nature can be effectively used, especially for those living in heavily urbanised areas, to maintain or improve psychological well-being in old age.

Keywords: Affect, aged, nature, psychological gerontology, virtual reality

Introduction

Direct contact with nature is strongly associated with marked improvements in psychological well-being (1-5). Given this effect, it is disquieting that urbanization has been increasing globally at an alarming rate (6) and has resulted in our disconnection from nature and its entities (7-9). Therefore, it is necessary to address how nature contact can be promoted in urbanized populations, including the elderly. The relevant literature indicates that some of the psychological benefits attributable to direct contact with nature can be derived from realistic nature representations using immersive virtual environment (IVE) technology. 360° videos in natural settings can be emotionally restorative and improve mood within short viewing periods among young adults (10-13). Despite these potential benefits of natural IVEs, relatively little research has been undertaken in older populations with very limited access to nature (14-16).

While it has been demonstrated that natural IVEs may not significantly improve mood and even induce fear and anxiety in the elderly (17,18), there is a growing body of empirical evidence for the restorativeness of virtual nature contact (VNC) in old age (19-22). The problem with the latter studies is that the observed restorative effects can be attributed to not only VNC but also the novelty of virtual reality (VR) experience.

Address for Correspondence: Kenan Eren Şansal, TED University, Department of Interior Architecture and Environmental Design, Ankara, Turkey
Phone: +90 534 365 92 77 **E-mail:** eren.sansal@tedu.edu.tr **ORCID:** orcid.org/0000-0002-8003-0781

Received: 15.03.2023 **Accepted:** 24.07.2023

Cite this article as: Şansal KE, Şimşek AC, Aktan S, Özbey F, Paksoy A. Restorative Effects of Virtual Nature on the Emotional Well-being of Community-dwelling Older Adults. Eur J Geriatr Gerontol 2024;6(1):12-18

Apart from the possible confounding effect of novelty, none of those studies with the aged examined whether individual differences in nature connectedness and exposure could have a moderating effect on the psychological benefits of natural IVEs. While feeling less connected to nature may weaken positive emotional reactions to simulated nature in young adults (23), there is no evidence to suggest this relationship in old age. It is also unclear whether the daily interaction of the elderly with nature alters the potency of spending additional time in virtual nature. Given that the frequency of nature visits is connected with psychological well-being (24), frequent visitors to nature who are expected to be in an elated mood state may not further benefit from VNC. Although this possibility cannot be excluded to understand the true value of natural IVEs, especially for those living isolated from nature, it has received no attention so far.

Given the absence of compelling evidence, the research question arises whether natural IVEs may substitute for or augment nature contact and support emotional restoration in older adults. Until we have a better understanding of the extent to which virtual nature contributes to the psychological well-being of the elderly, additional studies should be undertaken. Therefore, this study was conducted by recruiting elderly participants living independently in three different cities in Turkey. The current paper presents the results of this study testing three hypotheses: 1) Nature and natural environments are rarely visited by the elderly who are living in highly urbanised areas; 2) Natural IVEs can compensate for the limited or lack of direct contact with nature and restore emotional well-being in old age unlike urban IVEs; and 3) There is a moderating effect of both nature connectedness and visit frequency on the restorative effects of virtual nature in the elderly.

Materials and Methods

Participants

Due to the difficulties in finding eligible participants during the Coronavirus disease-2019 (COVID-19) pandemic, a snowball sampling method was employed. A total of 66 community-dwelling elders, living in the highly urbanized areas of Aydın, İzmir and Kocaeli, volunteered for the study. As per the ethical clearance issued by Yaşar University (decision number: 13878, date: 27.10.2021), all volunteers consented to participate after being thoroughly informed about the study protocol and the potential side effects of viewing IVEs. Two volunteers were excluded because they did not meet the inclusion criteria for medication use and cognitive functioning. Additionally, four volunteers withdrew because of scheduling constraints. The remaining 60 participants included in the analyzes were as follows: a) aged 65 or older; b) literate; c) were cognitively intact. All volunteers were screened for cognitive impairment using the standardized mini-mental state examination (SMMSE) (25). The SMMSE was translated into Turkish and validated by Güngen et al. (26). SMMSE scores <23/24 were reported to be indicative of dementia. Therefore, the volunteers who scored <24 were excluded from the study to meet the inclusion criteria; d) were able to live independently and perform the activities of daily living; e) had normal or corrected to normal vision; f) had no auditory impairment; g) did not have restricted head and neck movement as per the inclusion criteria; and h) were not taking psychotropics or more than five prescribed medications in accordance with the inclusion criteria (see Table 1 for further details on the participants).

Nature and Urban Videos

Two 360° videos were filmed in nature and urban settings. The nature video was recorded at Balçova Therapy Forest and included the main features of the environment, such as moderately dense vegetation, water, and animals. The urban video was recorded on two busy streets in Bornova, İzmir. Although there were scattered trees in the video, they constituted a negligible fraction of the content. All videos were shot from a static position to minimize visual-vestibular conflict (27). The camera height was adjusted to 120 cm to provide a natural egocentric viewpoint and a greater sense of presence in both settings (28). The edited 6-minute videos with sound were watched in a seated position using a head-mounted display (HMD) system composed of a smartphone inserted into a pair of VR goggles.

Table 1. Demographic characteristics and health status of the participants

		n		%	
Gender	Female	36		60	
	Male	24		40	
Education level	Literate	1		1.67	
	Primary school	7		11.67	
	Middle school	4		6.67	
	High school	12		20.00	
	University	36		60.00	
Chronic diseases	None	15		25.00	
	Cardiovascular	40		66.67	
	Endocrine and metabolic	19		31.67	
	Gastrointestinal	2		3.33	
	Genitourinary	3		5.00	
	Musculoskeletal and connective tissue	6		10.00	
	Neurologic	2		3.33	
	Pulmonary	4		6.67	
		Mean	**SD**	**Min**	**Max**
Age (years)		70.62	5.99	65	90
SMMSE score		28.25	1.13	25	30

Max: Maximum, Min: Minimum, SD: Standard deviation, SMMSE: Standardized mini-mental examination

Measures

The positive and negative affect schedule (PANAS) (29) was administered to track participants' affective states. The PANAS consists of 20 items rated for a given period on a 5-point scale. The responses to these items are summed to yield positive (PANAS PA) and negative affect (PANAS NA) scores. Gençöz (30) adapted the PANAS for use in Turkish and demonstrated that the psychometric properties of the scale were acceptable.

Participants' perceptions of environmental restorativeness were evaluated by using the perceived restorativeness scale (PRS) (31,32) to complement the PANAS results. PRS determines the presence of four environmental attributes (being away, coherence, compatibility, and fascination) promoting restoration of psychological and other individual resources required for effective functioning. It is composed of 26 items rated on a 7-point scale. Four PRS scores were calculated by averaging the item scores for each attribute. Özçifçi et al. (33) translated the PRS into Turkish and showed that the translated version was reliable and valid.

Since nature connectedness may impact the psychological benefits of viewing natural IVEs (23), the nature relatedness scale (NRS) (34) was also administered. The NRS measures the strength of respondents' perceived connection with nature using 21 items rated on a 5-point scale. An NRS score is calculated by averaging item scores. Çakir et al. (35) adapted the NRS for use in Turkish and demonstrated that the psychometric properties of the adapted version were satisfactory.

For assessing nature exposure, or more specifically, visit frequency in the past week, the participants were asked to choose one of three response options ("never," non-visitors; "once or twice a week," occasional visitors; and "three or more times a week," frequent visitors) and report on how often they had been outdoors in nature or natural environments. Moreover, to determine the novelty of the IVE experience, the participants were asked whether they had previously used the IVE technology.

Data Collection

Between January 24 and 30, 2022, all volunteers were evaluated on their cognitive functioning and nature connectedness using the SMMSE and NRS, respectively. In addition, they provided information about their demographic characteristics, chronic diseases, impairments, medication, and IVE experience. After screening the ineligible volunteers the remaining older adults were randomly assigned to study groups (group 1 and 2) and contacted for scheduling the video-viewing sessions. Between 31 January and 20 March 2022, each group visited their homes and watched the nature and urban videos on two separate occasions that were one week apart to eliminate any carry-over effects. While group 1 watched the nature video on the first occasion, group 2 watched it on the second occasion to minimize any bias from the novelty of using the IVE technology. On each occasion, all groups were asked to complete the PANAS before watching either the nature or urban video. Following the video-viewing session, they reported on their affective states for a second time using PANAS, completed PRS, and provided information on their nature visits during the preceding week. In addition, verbal statements of the participants and their qualitative feedback about their VR experience were recorded during the video-viewing sessions.

Statistics

To assess the normality of the data, the Kolmogorov-Smirnov and Shapiro-Wilk tests were used. Apart from these tests, skewness and kurtosis values were examined to identify the presence of non-normality. While the paired-samples t-test was used to analyze the changes in participants' PANAS PA scores, the Wilcoxon signed-rank test was used to determine the changes in PANAS NA scores and differences in PRS scores. To assess the correlates of affective responses, Spearman's correlation coefficients were computed. Additionally, Cohen's Kappa coefficients were calculated to determine the inter-rater reliability of the participants' verbal statements or feedback. All statistical analyzes were performed using the Statistical Package for the Social Sciences (version 25.0). The level of significance was set at $p<0.05$.

Results

Nature Visits

The results of our participants' nature visit frequency analysis (Figure 1) support the first hypothesis. Most of the participants, who were living independently highly urbanized areas, were non- or occasional visitors to nature. In the first video-viewing session, 42% of the participants reported that they had often visited nature or natural environments outdoors over the last week. Although the number of frequent visitors rose by 5% in the week preceding the second session, no or occasional visits were made by 53% of the participants.

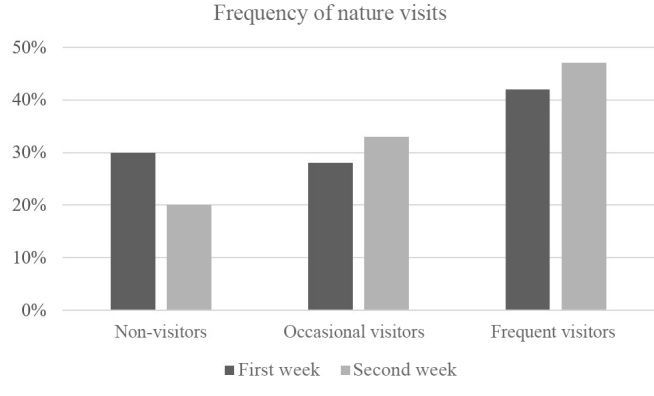

Figure 1. Frequency of participants' nature visits over two weeks

Positive and Negative Affect

To test our second hypothesis, the study groups' combined PANAS pre-test and post-test scores were compared with each other for both IVEs. The results confirmed the potential psychological benefits of interacting with nature virtually. Participants' initial pre-test PANAS PA score was found to be significantly lower [t(59)=-5.74, p<0.001] than their post-test PANAS PA score obtained after watching the nature video (Table 2). The difference between the pre-test PANAS NA and post-test PANAS NA scores was also statistically significant (Z=-3.93, p<0.001) (Table 3). Watching the urban video had a negative impact on the participants' affective states. There was a significant decrease [t(59)=5.05, p<0.001] in the PANAS PA scores following video viewing (Table 2). Moreover, being in the urban setting resulted in a significant increase (Z=-1.99, p=0.046) in the PANAS NA scores (Table 3).

Perceived Restorativeness

To validate our findings on participants' affective responses to the IVEs, the PRS scores obtained in the video-viewing sessions were compared. The results were consistent with our findings and suggested that the forest setting shown in the nature video was more restorative. There were statistically significant differences between participants' PRS scores for all four environmental attributes (being away: Z=-6.74, p<0.001; fascination: Z=-6.68, p<0.001; coherence: Z=-5.63, p<0.001; compatibility: Z=-6.30, p<0.001) (Table 4).

Table 2. Mean ± SD PANAS PA scores and paired-samples t-test results for the PANAS PA scores

		Nature		
		Mean ± SD	t	p
PANAS PA	Pre-test	35.37±6.68	-5.74	<0.001
	Post-test	39.38±6.77		
		Urban		
		Mean ± SD	**t**	**p**
PANAS PA	Pre-test	37.45±5.59	5.05	<0.001
	Post-test	33.03±8.21		

SD: Standard deviation, PANAS PA: Positive and negative affect schedule positive affect

Table 3. Median, minimum and maximum PANAS NA scores and Wilcoxon signed-rank test results for the PANAS NA scores

		Nature				
		Median	Min	Max	Z	p
PANAS NA	Pre-test	10.00	10.00	21.00	-3.931	<0.001
	Post-test	10.00	10.00	15.00		
		Urban				
		Median	**Min**	**Max**	**Z**	**p**
PANAS NA	Pre-test	11.00	10.00	23.00	-1.99	0.046
	Post-test	12.00	10.00	29.00		

PANAS NA: Positive and negative affect schedule negative affect

Correlations for the NRS Scores and Nature Visit Frequencies

To test our third hypothesis, the correlation between participants' NRS scores (mean ± standard deviation: 4.15±0.44) and the changes in their PANAS PA and NA scores (PANAS post-test scores-PANAS pre-test scores) because of the nature video viewing was calculated. The correlation was not statistically significant. Another analysis was performed to identify the correlation between participants' nature visit frequency and PANAS score differences. The results also demonstrated that there was not a significant correlation.

IVE Experience and Participant Feedback

Most (92%) participants reported that they did not use the IVE technology before. Almost none of the participants reported any adverse effects of the IVEs or complained about the HMD system. Only 5% of the participants found the HMD system heavy or reported mild nausea. However, they did not want to remove the system prematurely.

During the sessions, most participants commented on the videos. In total, 90 statements were made. These statements were categorized as positive, neutral, and negative by two assessors who were unfamiliar with the study. The level of agreement between these assessors was perfect for all categories, with Kappa coefficients in the range of 0.92 to 0.98 (p<0.001). For a perfect agreement, a third assessor, who was also not involved in the study, adjudicated the existing discrepancies. While 79% of the 48 statements made for the nature video were positive, 67% of the 42 statements about the urban video were negative. In addition, neutral statements were more (11 versus 4) for the urban video.

Discussion

Our study had both confirmatory and exploratory objectives. First, we sought to confirm the restorative effects of VNC on

Table 4. Median, minimum and maximum PRS scores and Wilcoxon signed-rank test results for the PRS scores

		Median	Min	Max	Z	p
Being away	Nature	5.40	3.00	6.00	-6.74	<0.001
	Urban	0.20	0.00	4.80		
Fascination	Nature	5.38	3.50	6.00	-6.68	<0.001
	Urban	1.19	0.00	3.75		
Coherence	Nature	6.00	2.00	6.00	-5.63	<0.001
	Urban	2.00	0.00	6.00		
Compatibility	Nature	4.44	0.89	6.00	-6.303	<0.001
	Urban	2.00	0.00	5.44		

PRS: Perceived restorativeness scale

emotional well-being in the elderly whose direct contact with nature was expected to be limited. Previous literature did not examine the role of nature connectedness and contact frequency in assessing how IVEs might affect emotional states. Therefore, to provide the first empirical evidence, we also investigated whether natural IVEs could have a beneficial effect on emotional well-being irrespective of nature connectedness and visit frequency.

Our findings confirmed that old age might account for spending no or only a very limited time outdoors in nature, and they were consistent with those of earlier studies on VNC in the elderly that did not consider the novelty of VR experience (18-22). Although our participants, who were mainly non-or occasional visitors to nature, were in a positive affective state before the video-viewing sessions, there were statistically significant improvements in their mood after watching a short nature video. Unlike the nature video, the urban video resulted in emotional degradation. Moreover, the participants found the nature video more restorative and made more positive comments. This finding supports the PANAS results and in complete accordance with the fact that individuals' evaluative judgements are congruent with their current affective state (36).

Although it seems reasonable to expect that VNC over a period of time <10 minutes is potent enough to restore psychological functioning according to our above-mentioned results and those of other research groups, it is difficult to reach any conclusions on the optimal duration and frequency of video viewing. Although 95% of our participants did not report any adverse effects of the IVEs, it is not possible to state that increasing the time spent in natural IVEs by increasing video length or viewing frequency would yield much more favorable outcomes. Given this gap in the literature, further studies on longer and more frequent video viewing sessions are required to fully understand the potential benefits of VNC in old age.

Another aim of our research was to explore whether participants' nature connectedness and frequency of nature visits had a significant effect on their self-reported affective responses because their possible effects had not been investigated in earlier studies on the elderly. Unlike McMahan et al. (23), we found that individual differences in nature connectedness did not moderate the observed effects of the natural IVE in our remarkably old sample. Since the reported levels of nature orientation may vary greatly by country (37), not only age but also cultural differences can account for the discrepancies in the obtained results. While it is not possible to generalize our results to culturally diverse elderly populations, they are of interest to other researchers for cross-cultural replication and further exploration of the mediating role of nature connectedness. Moreover, we demonstrated that there was not a significant correlation between participants' nature visit frequency and changes in their PANAS scores. This finding contradicts our expectation that frequent visitors may not benefit from the nature video because of their elevated affect in response to being in regular contact with nature. However, it is novel in terms of suggesting that natural IVEs can alter mood independently of nature contact frequency or that frequent visitors of nature can emotionally benefit from VNC. Given the novelty of these two findings, future studies on the possible moderating effects of being connected to nature and the frequency of direct nature contact should be conducted in elderly adults to verify our results.

Study Limitations

There are two limitations that should be considered when interpreting our results. First, due to the negative effect of the COVID-19 pandemic on recruiting participants, the participants aged >80 years comprised 8% of our sample. Although the oldest elderly are at a greater risk of losing their functional independence (38) and experiencing depression (39), it is erroneous to conclude that VNC may elicit highly favorable therapeutic responses in this age group. Therefore, there is a need to investigate to what extent our findings are relevant to or important for this rapidly growing segment of the population.

Second, the COVID-19 pandemic was demonstrated to restrict the time spent outdoors (TSO) in Turkish community-dwelling elderly adults (40). Therefore, the study period might have reduced participants' nature visit frequency and inflated the potency of VNC. Although the TSO may not exceed an hour in the home-dwelling (41) and institutionalized (42) elderly and that no statistically significant associations were identified between participants' reported visit frequencies and changes in affect, this inherent limitation of our study warrants consideration and should be addressed in future studies.

Conclusion

Evidently, more studies are required to fully understand the restorative effects of natural IVEs on the elderly and to recommend this technology as a substitute or supplement to natural contact. Nonetheless, two conclusions can be drawn from our results and those obtained in earlier studies. First, it is possible to conclude that brief indirect contact with nature in VR may reduce the emotional burden of urbanization and lack of direct nature contact on older adults, especially those with impaired mobility. Second, the IVE technology is generally tolerated well. Therefore, it can be considered as a non-pharmacological treatment adjunct for psychological disturbances in old age, without ignoring the fact that it may cause minor discomfort in some of the elderly.

Acknowledgements

The authors would like to thank Dr. Özge Başağaç for her help in participant recruitment and data collection.

Ethics

Ethics Committee Approval: As per the ethical clearance issued by Yaşar University (decision number: 13878, date: 27.10.2021), all volunteers consented to participate after being thoroughly informed about the study protocol and the potential side effects of viewing IVEs.

Informed Consent: All volunteers consented to participate after being thoroughly informed about the study protocol and the potential side effects of viewing IVEs.

Authorship Contributions

Concept: K.E.Ş., S.A., F.Ö., Design: K.E.Ş., Data Collection or Processing: K.E.Ş., A.C.Ş., S.A., F.Ö., A.P., Analysis or Interpretation: K.E.Ş., A.C.Ş., A.P., Literature Search: K.E.Ş., S.A., F.Ö., Writing: K.E.Ş., A.C.Ş.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Bratman GN, Anderson CB, Berman MG, Cochran B, de Vries S, Flanders J, Folke C, Frumkin H, Gross JJ, Hartig T, Kahn Jr. PH, Kuo M, Lawler JJ, Levin PS, Lindahl T, Meyer-Lindenberg A, Mitchell R, Ouyang Z, Roe J, Scarlett L, Smith JR, van den Bosch M, Wheeler BW, White MP, Zheng H, Daily GC. Nature and mental health: An ecosystem service perspective. Sci Adv 2019;5:eaax0903.
2. Frumkin H, Bratman GN, Breslow SJ, Cochran B, Kahn PH Jr, Lawler JJ, Levin PS, Tandon PS, Varanasi U, Wolf KL, Wood SA. Nature Contact and Human Health: A Research Agenda. Environ Health Perspect 2017;125:075001.
3. Jimenez MP, DeVille NV, Elliott EG, Schiff JE, Wilt GE, Hart JE, James P. Associations between Nature Exposure and Health: A Review of the Evidence. Int J Environ Res Public Health 2021;18:4790.
4. Kondo MC, Fluehr, JM, McKeon T, Branas CC. Urban green space and its impact on human health. Int J Environ Res Public Health 2018;15:445.
5. McMahan EA, Estes D. The effect of contact with natural environments on positive and negative affect: A meta-analysis. J Posit Psychol 2015;10:507-519.
6. United Nations. World urbanization prospects: The 2018 revision. New York, United Nations, 2019. https://population.un.org/wup/Publications/Files/WUP2018-Report.pdf.
7. Miller JR. Biodiversity conservation and the extinction of experience. Trends Ecol Evol 2005;20:430-434.
8. Turner WR, Nakamura T, Dinetti M. Global urbanization and the separation of humans from nature. BioScience 2004;54:585-590.
9. Zhang W, Goodale E, Chen J. How contact with nature affects children's biophilia and conservation attitude in China. Biol Conserv 2014;177:109-116.
10. Anderson AP, Mayer MD, Fellows AM, Cowan DR, Hegel MT, Buckley JC. Relaxation with immersive natural scenes presented using virtual reality. Aerosp Med Hum Perform 2017;88:520-526.
11. Browning MHEM, Mimnaugh KJ, van Riper CJ, Laurent HK, LaValle SM. Can simulated nature support mental health? Comparing short, single-doses of 360-degree nature videos in virtual reality with the outdoors. Front Psychol 2020;10:2667.
12. Mostajeran F, Krzikawski J, Steinicke F, Kühn S. Effects of exposure to immersive videos and photo slideshows of forest and urban environments. Sci Rep 2021;11:3994.
13. Yu C, Lee H, Luo, X. The effect of virtual reality forest and urban environments on physiological and psychological responses. Urban For Urban Green 2018;35:106-114.
14. Boyd F, White MP, Bell SL, Burt J. Who doesn't visit natural environments for recreation and why: A population representative analysis of spatial, individual and temporal factors among adults in England. Landsc Urban Plan 2018;175:102-113.
15. Natural England. Monitor of engagement with the natural environment: The national survey on people and the natural environment. York, Natural England, 2019. https://assets.publishing.service.gov.uk/media/5d6cd601e5274a170c435365/Monitor_Engagement_Natural_Environment_2018_2019_v2.pdf.
16. Scottish Natural Heritage. Scotland's people and nature survey participation in outdoor recreation. Inverness, Scotish Natural Heritage, 2018. https://www.nature.scot/sites/default/files/2018-12/SPANS%20-%202017-18%20Participation%20in%20outdoor%20recreation.pdf.
17. Brimelow RE, Dawe B, Dissanayaka N. Preliminary research: Virtual reality in residential aged care to reduce apathy and improve mood. Cyberpsychology Behav Soc Netw 2020;23:165-170.
18. Liu Q, Wang Y, Yao MZ, Tang Q, Yang Y. Effects of viewing an uplifting 360-degree video on emotional well-being among elderly adults and college students under immersive virtual reality and smartphone conditions. Cyberpsychology Behav Soc Netw 2020;23:157-164.
19. Appel L, Appel E, Bogler O, Wiseman M, Cohen L, Ein N, Abrams HB, Campos JL. Older Adults With Cognitive and/or Physical Impairments Can Benefit From Immersive Virtual Reality Experiences: A Feasibility Study. Front Med (Lausanne) 2020;6:329.
20. Appel L, Appel E, Kisonas E, Lewis S, Sheng LQ. Virtual reality for veteran relaxation: Can VR theraphy help veterans living with dementia who exhibit responsive behaviors? Front Virtual Real 2022;2.
21. Mosso JL, Gorini A, de la Cerda G, Obrador T, Almazan A, Mosso D, Nieto JJ, Riva G. Virtual reality on mobile phones to reduce anxiety in outpatient surgery. Stud Health Technol Inform 2009;142:195-200.
22. Scates D, Dickson JI., Sullivan K, Cline H, Balaraman R. Using nature-inspired virtual reality as a distraction to reduce stress and pain among cancer patients. Environ Behav 2020;52:895-918.
23. McMahan EA, Estes D, Murfin JS, Bryan CM. Nature connectedness moderates the effect of nature exposure on explicit and implicit measures of emotion. J Posit Psychol Wellbeing 2018;2:128-148.
24. Cox DT, Shanahan DF, Hudson HL, Fuller RA, Anderson K, Hancock S, Gaston KJ. Doses of nearby nature simultaneously associated with multiple health benefits. Int J Environ Res Public Health 2017;14:172.
25. Molloy DW, Alemayehu E, Roberts R. Reliability of a Standardized Mini-Mental Examination with the traditional Mini-Mental State Examination. Am J Psychiatry 1991;148:102-105.
26. Güngen C, Ertan T, Eker E, Yaşar R, Engin, F. Reliability and validity of the Standardised Mini-Mental State Examination in the diagnosis of mild dementia in Turkish population. Turk Psikiyatri Derg 2002;13:273-281.
27. Akiduki H, Nishiik, S, Watanabe H, Matsuoka K, Kubo T, Takeda N. Visual-vestibular conflict induced by virtual reality in humans. Neurosci Lett 2003;340:197-200.

28. Dahlquist LM, Herbert LJ, Weiss KE, Jimeno M. Visual-reality distraction and cold-pressor pain tolerance: Does avatar point of view matter? Cyberpsychology Behav Soc Netw 2010;13:587-591.

29. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: The PANAS scales. J Per Soc Psychol 1988;54:1063-1070.

30. Gençöz T. Positive and Negative Affect Schedule: A study of validity and reliability. Turkish Journal of Psychology 2000;15:19-28.

31. Hartig T, Korpela K, Evans GW, Garling T. A measure of restorative quality in environments. Hous Theory Soc 1997;14:175-194.

32. Hartig T, Kaiser FG, Bowler PA. Further development of a measure of perceived environmental restorativeness. Gavle Uppsala University 1997.

33. Özçifçi I, Kaymaz I, Tazebay I, Elmali F. Measurement of environmental restorativeness quality: Adaptation of Perceived Restorativeness Scale into Turkish. Eur J Sci Technol 2021;23:288-295.

34. Nisbet EK, Zelenski JM, Murphy SA. The Nature Relatedness Scale: Linking individuals' connection with nature to environmental concern and behaviour. Environ Behav 2009;41:715-740.

35. Çakir B, Karaarslan G, Şahin E, Ertepinar H. Adaptation of Nature Relatedness Scale to Turkish. Elementary Educ Online 2015;14:1370-1383.

36. Bless H. The consequences of mood on the processing of social information. In: Abraham Tesser, Norbert Schwarz (Eds.). Blackwell Handbook of Social Psychology: Intraindividual Processes. Malden, Blackwell Publishing, USA 2001:391-412.

37. Tam K. Concepts and measures related to connection to nature: Similarities and differences. J Environ Psychol 2013;34:64-78.

38. Arai Y, Linuma T, Takayama M, Takayama M, Abe Y, Fukuda R, Ando J, Ohta K, Hanabusa H, Asakura K, Nishiwaki Y, Gondo Y, Akiyama H, Komiyama K, Gionhaku N, Hirose N. The Tokyo Oldest Old Survey on Total Health (TOOTH): A longitudinal cohort study of multidimensional components of health and well-being. BMC Geriatr 2010;10:35.

39. Chou L, Chi I. Prevalence and correlates of depression in Chinese oldest-old. Int J Geriatr Psychiatry 2005;20:41-50.

40. Şansal KE, Balci LA, Çinar F, Çoşkunsu DK, Tanriöver SH, Uluengin MB. Relationship of daily time spent outdoors with sleep quality and emotional well-being among community-dwelling older adults during COVID-19 restrictions. Turk Geriatri Derg 2021;24:424-432.

41. Obayashi K, Saeki K, Iwamoto J, Ikada Y, Kurumatani N.Exposure to light at night and risk of depression in the elderly. J Affect Disord 2013;151:331-336.

42. Noi A, Roe J, Gow A, McNair D, Aspinall P. Seasonal differences in light exposure and associations with health and well-being in older adults: An exploratory study. HERD 2017;10:64-79.

ORIGINAL RESEARCH

DOI: 10.4274/ejgg.galenos.2023.2023-1-6

Eur J Geriatr Gerontol 2024;6(1):19-25

The Prognostic Value of Inflammation Indices in Predicting Postoperative ICU Admission and Mortality in Elderly Patients Undergoing Hip Fracture Surgery

Ökkeş Hakan Miniksar[1], Mehmet Kara[2], Muhammed Nuri Polat[2], Yeşim Andıran Şenaylı[2], Serhat Durusoy[3], Hacı Ali Olçar[3], Murat Korkmaz[3]

[1]University of Health Sciences Turkey, Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Clinic of Anesthesiology and Reanimation, Ankara, Turkey

[2]Yozgat Bozok University Faculty of Medicine, Department of Anesthesiology and Reanimation, Yozgat, Turkey

[3]Yozgat Bozok University Faculty of Medicine, Department of Orthopedics and Traumatology, Yozgat, Turkey

Abstract

Objective: This study aimed to assess the predictive impact of various inflammation indices and inflammatory biomarkers on postoperative intensive care unit (ICU) admission and mortality following hip fracture (HF) surgery in elderly patients.

Materials and Methods: We retrospectively reviewed the data of 131 geriatric patients who underwent isolated HF surgery under regional anesthesia. The patients were divided into two groups: ICU admission (ICU, n=98) and non-ICU admission (non-ICU, n=33). The patients were also grouped as survival (n=122) and non-survival (n=9) according to postoperative mortality rates. The patients' clinical characteristics and inflammation indexes were compared between the two groups, and predictors of ICU admission were determined using a multivariate regression model.

Results: Advanced age and high American Society of Anesthesiologists (ASA) scores were observed in the ICU and Non-survivor groups. Urea and creatinine levels were significantly higher in the Non-survivor group. While inflammatory indices [systemic immune-inflammation index (SII), neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio] were significantly higher in the ICU group (respectively, p=0.009, p=0.022, p=0.019), they did not differ significantly in the mortality group. Age, ASA score, and SII of the inflammation indices were determined to be independent predictors of postoperative ICU admission after HF surgery.

Conclusion: It was shown that advanced age, high ASA score, and high preoperative SII value were independent risk factors for postoperative ICU admission following HF surgery in elderly patients. SII can be used as an easily measured prognostic parameter on the ICU admission of these surgical patients in daily practice.

Keywords: Geriatrics, hip fracture, systemic immune-inflammation index, intensive care, mortality

Introduction

People on earth are getting older, and hip fractures (HF) are much more frequently seen in clinics due to aging. HF, mainly observed in elders, is a severe injury and causes a high mortality and morbidity of approximately 15-20% (1-4).

A decline in physical stamina and a rise in the prevalence of comorbidities are observed in elderly patients. Myocardial infarction, pulmonary thromboembolism, heart failure, and infectious complications account for most mortality following HFs (2-5). These high-risk HF patients are usually treated in intensive care units (ICUs) after surgery, according to their clinical history and disease progression (6). The planned postoperative ICU admission of these high-risk patients helps to minimize adverse complications. Recognizing and targeting patients with adverse outcomes is an important part of treatment planning for geriatric HF surgery. A surgical patient's decision to be admitted to the ICU is not dependent on a single

Address for Correspondence: Ökkeş Hakan Miniksar, University of Health Sciences Turkey, Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Clinic of Anesthesiology and Reanimation, Ankara, Turkey

Phone: +90 312 336 09 09 **E-mail:** hminiksar@yahoo.com **ORCID:** orcid.org/0000-0001-5645-7729

Received: 27.01.2023 **Accepted:** 11.08.2023

Cite this article as: Miniksar ÖH, Kara M, Polat MN, Andıran Şenaylı Y, Durusoy S, Olçar HA, Korkmaz M. The Prognostic Value of Inflammation Indices in Predicting Postoperative ICU Admission and Mortality in Elderly Patients Undergoing Hip Fracture Surgery. Eur J Geriatr Gerontol 2024;6(1):19-25

factor and is complex (1,2,6,7). We, clinicians, need to determine the preoperative predictors that will affect this ICU admission decision. Recognizing and targeting patients with adverse outcomes is an important part of treatment planning for geriatric HF surgery. Accurate prognostic predictors can provide valuable information on postoperative outcomes, and patients with such indicators can receive additional aggressive therapies to improve survival (4,7,8).

Several studies have shown the relationship between specific laboratory results and various factors causing ICU admission and mortality in elderly patients after HF surgery (9-11). According to previous reports, other inflammatory markers have also been associated with mortality (1-8). Therefore, in addition to these laboratory parameters, there is still a need in daily practice for an ideal readily measured marker, such as hematological parameters, to predict postoperative clinical outcomes. Nevertheless, to the best of our knowledge, no standard inflammatory biomarkers or a scoring system can be used in clinical practice to predict the postoperative outcomes of elderly HF surgery patients based on the inflammation status. Therefore, we assumed in our study that these indices could be independent predictors of ICU admission and mortality rates in elderly patients after HF surgery.

Our objective was to determine and evaluate the predictive value of several inflammatory indices and inflammatory biomarkers on prognosis in elderly patients undergoing HF surgery.

Materials and Methods

Ethical Statement

The Yozgat Bozok University Clinical Research Ethics Committee approved this retrospective observational single-center study in accordance with the Declaration of Helsinki (decision number: 2017-KAEK-189_2021.08.25_02, date: 25.08.2021). Informed consent: Retrospective study.

Study Design

This study reviewed the clinical findings of 163 patients who received isolated HFs because of minor trauma caused by falls at our department between January 2019 and May 2021. Patients included in the study had an American Society of Anesthesiologists (ASA) score of 2/3/4, were over 65 years of age, and were treated with regional anesthesia. General anesthesia, age under 65 years, hematologic abnormalities, infectious and inflammatory disease, intraoperative mortality, revision surgery, history of severe liver disease and malignancy, multiple traumas, and missing records were among the study's exclusion criteria. The study included 131 participants when the exclusion criteria were applied (Figure 1). STROBE guidelines were used during presentation preparations. (www.strobe-statement.org).

Study Participants

Demographic characteristics, comorbidities, ASA scores, intervention time, and patients' preoperative laboratory data were recorded. Both electronic and hard-copy hospital archives were evaluated to obtain data on patient files and perioperative

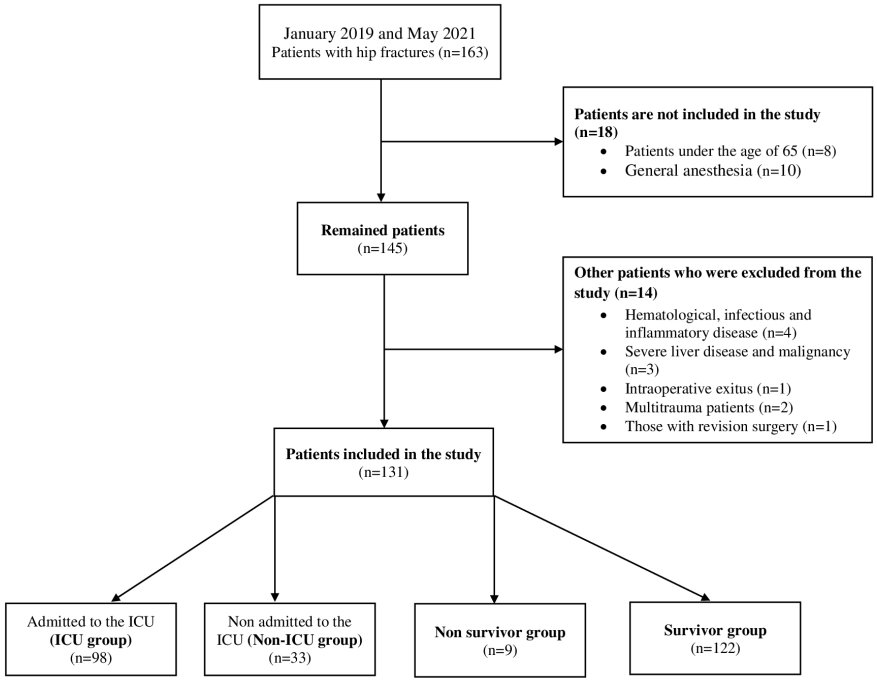

Figure 1. Flow chart of the study participants

ICU: Intensive care unit

anesthesia. The period between hospitalization and surgery was defined in days.

The patients were divided into two groups for evaluation: the ICU and Non-ICU groups. The anesthesiologist decided to admit the patient to the ICU on the basis of the patient's postoperative clinical status. This study included patients who underwent operations under regional anesthesia. For the ICU group, these patients were also evaluated as the Survivor group and Non-survivor group according to mortality. Medical departments such as cardiology, respiratory disease, or internal medicine evaluated all patients in the preoperative period. Consultation records were reviewed to evaluate the possible presence of comorbidities in the patients during the preoperative period. The patients who were admitted for the first time to the ICU were accepted. The team consisted of anesthetists, orthopedic surgeons, and internal medicine specialists who followed the patients postoperatively.

Laboratory Measurements

One day before surgery, venous blood samples [complete blood count (CBC)] were routinely taken from each patient and recorded in the hospital's medical records. Test results were obtained using a blood analyzer (Beckman Coulter®, LH 780, California, USA). The inflammatory indices were calculated from whole blood assays as follows: systemic immune-inflammation index (SII) [(neutrophils x platelets)/lymphocytes], neutrophil-to-lymphocyte ratio (NLR) (neutrophil/lymphocyte), neutrophil-to-lymphocyte, platelet ratio [neutrophil/(lymphocyte x platelet)], platelet-to-lymphocyte ratio (PLR) (platelet/lymphocyte), and mean platelet volume/platelet.

Statistics

Statistics were analyzed using IBM SPSS for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Categorical data were presented in n and frequency, while continuous data were presented in mean ± standard deviation (SD) and median (interquartile range; 25^{th}-75^{th} percentile). The Kolmogorov-Smirnov and Shapiro-Wilk tests checked the normality distribution. If more than 20% of the expected values in the cross tables were less than 5, or if at least one of the values was less than 2, Fisher's exact test was performed. All significant variables (age, ASA, SII, NLR, and PLR) were included in the multivariate logistic analysis after the univariate analysis. Factors that predict postoperative ICU admission were investigated using a backward stepwise multivariate logistic regression analysis. The Hosmer-Lemeshow test for goodness-of-fit statistics was used to determine the calibration validation and discrimination of this regression analysis. Receiver operating characteristic (ROC) curve analysis was used to determine the parameters and inflammation indices with the most significant predictive value for postoperative ICU admissions, and the areas under the curve (AUC) were calculated. A statistically significant difference was defined as a p value of 0.05.

Results

Demographic and Clinical Characteristics

A total of 131 patients in 163 met the inclusion criteria for statistical analysis with HF diagnoses who underwent surgery throughout the study period. The mean age (SD) of all patients was 82.66 (5.44), with 74 (56.5%) being female. Thirty-three patients (25.2%) and 98 patients (74.8%), respectively, comprised the Non-ICU and ICU groups. The patient's mean age in the ICU group was 83.6 years, compared with 80.4 years in the Non-ICU group (p=0.005). Nine patients (6.9%) were included in the Non-survivor group, whereas 122 patients (93.1%) were included in the Survivor group. In the Survivor group, the patients' median age ranged from 78 to 86 years; in the Non-survivor group, it was 90 to 94 (p=0.021). The difference in ASA physical status between the groups was statistically significant (p=0.002 for the ICU group and p=0.018 for the Survivor group). There was no statistically significant difference between the groups for the most common comorbidities, which were hypertension (58.0%), diabetes mellitus (29.8%), and coronary artery disease (27.5%) (Table 1).

Biochemical and Total Blood Count Parameters and Inflammation Indices

When laboratory parameters were examined, urea was significantly higher in the ICU and Non-survivor groups (p=0.002 and p=0.037, respectively). Creatinine was higher only in the Non-survivor group (p=0.047). SII (p=0.009), NLR (p=0.022), and PLR (p=0.019) inflammatory indices were significantly higher in the ICU group. Inflammatory indices did not differ significantly in the Survivor groups (Table 2).

Risk Factors for ICU Admission Using Univariate and Multivariate Analysis

The results of univariate and multivariate logistic regression analyzes for ICU admission in patients undergoing HF surgery are shown in Table 3. In univariate analysis, the following preoperative variables were found to be important predictors of postoperative ICU admission: Age [odds ratio (OR): 1.128; 95% confidence interval (CI) 1.033-1.233; p=0.008], ASA (OR: 3.332; 95% CI 1.463-7.590; p=0.004), SII (OR: 1.001; 95% CI 1.000-1.001; p=0.013), NLR (OR: 1.117; 95% CI 1.014-1.231; p=0.025), and PLR (OR: 1.005; 95% CI 1.001-1.009; p=0.027). Multivariate analysis revealed that age (OR: 1.118; 95% CI 1.015-1.231; p=0.023), ASA (OR: 2.572; 95% CI 1.101-6.007; p=0.029) and SII (OR: 1.001; 95% CI 1.000-1.001; p=0.021) were independent predictors of postoperative ICU admission. Other important variables (NLR, PLR) were not independent predictors of ICU admission. The Hosmer-Lemeshow goodness-

Table 1. Comparison of demographic and clinical characteristics between the ICU admission and mortality groups

Variables	Non-ICU group (n=33)		ICU group (n=98)		p	Non-survivor group (n=9)		Survivor group (n=122)		p
	n	%	n	%		n	%	n	%	
Age (years), mean (SD) [25-75 p.]	80	(4)	83	(6)	**0.005**[1]	90	[80-94]	81	[78-86]	**0.021**[2]
Time before surgery (days)	2	[1-2]	2	[1-2]	0.606[2]	1	[0-2]	1	[1-2]	0.376[1]
Gender, female (n=74)	16	48.5	58	59.2	0.284[#]	3	33.3	71	58.2	0.147[*]
ASA physical status, II/III/IV	7	21.2	3	3.1	**0.002**[#]	0	0.0	10	8.2	**0.018**[*]
	21	63.6	65	66.3		3	33.3	83	68.0	
	5	15.2	30	30.6		6	66.7	29	23.8	
Comorbidities, n (%)										
Hypertension, (n=76)	19	57.6	57	58.2	0.067[#]	5	55.6	71	58.2	0.877[*]
Congestive heart failure, (n=22)	4	12.1	18	18.4	0.406[*]	2	22.2	20	16.4	0.652[*]
Diabetes mellitus, (n=39)	13	39.4	26	26.5	0.162[#]	2	22.2	37	30.3	0.608[*]
Cerebrovascular disease, (n=26)	5	15.2	21	21.4	0.434[*]	4	44.4	22	18.0	0.055[*]
Arrhythmia, (n=20)	3	9.1	17	17.3	0.254[*]	3	33.3	17	13.9	0.118[*]
Coronary artery disease, (n=36)	5	15.2	31	31.6	0.067[*]	4	44.4	32	26.2	0.237[*]
Chronic renal failure, (n=9)	2	6.1	7	7.1	0.832[*]	1	11.1	8	6.6	0.602[*]
Chronic lung disease, (n=17)	2	6.1	15	15.3	0.172[*]	1	11.1	16	13.1	0.863[*]

The values are presented as the mean (SD) and median [interquartile range] for continuous variables and number and percentage for categorical variable. Compared by the [1]indipendent t-test and [2]Mann-Whitney U test for continuous variables. All statistically significant values are reported in bold. Compared by the [#]chi-square test and *Yates' correction for continuity. ICU: Intensive care unit, ASA: American Society of Anesthesiologists, MPV: Mean platelet volume, SII: Systemic immune-inflammation index, NLR: Neutrophil to lymphocyte ratio, NLPR: Neutrophil to lymphocyte, platelet ratio, PLR: Platelet to lymphocyte ratio, MPR: Mean platelet volume/platelet, SD: Standard deviation

Table 2. Comparison of laboratory parameters and inflammation indices between the ICU admission and mortality groups

Variables	Non-ICU group (n=33)		ICU group (n=98)		p[1]	Non-survivor group (n=9)		Survivor group (n=122)		p[2]
	Mean	SD	Mean	SD		Median	25-75 p.	Median	25-75 p.	
Biochemical parameters										
Glucose (mmol/L)	161	78	158	75	0.833	133	107-161	135	108-183	0.504
Sodium (mmol/L)	138	5	138	7	0.682	138	137-139	138	136-140	0.945
Urea (mg/dL)	217	61	238	92	**0.002**	239	206-254	227	186-269	**0.037**
Creatinin (mg/dL)	0.97	0.48	1.06	0.50	0.390	1.31	0.89-1.39	0.89	0.74-1.14	**0.047**
Albumin (g/dL)	3.85	0.56	4.57	5.31	0.440	3.65	3.56-3.81	3.75	3.45-4.02	0.356
Total blood count										
Hemoglobin (g/dL)	12.73	2.08	11.85	2.02	0.033	11.90	10.1-12.7	12.05	10.9-13.4	0.598
Neutrophils (x10^9 L)	0.03	0.03	0.04	0.03	0.056	0.05	0.02-0.08	0.03	0.01-0.05	0.277
Lymphocytes (x10^9 L)	1.50	0.69	1.34	0.75	0.280	0.94	0.56-2.21	1.26	0.87-1.7	0.437
Platelets (x10^9 L)	217	61	238	92	0.238	239	206-254	227	186-269	0.967
MPV (fL)	10.22	1.02	10.14	0.85	0.643	9.90	9.6-10.4	10.00	9.5-10.7	0.685
Inflammatory indices										
SII	1229.32	751.29	2132.54	1912.93	**0.009**	1210.60	1001.85-4007.51	1305.45	723.85-2466.98	0.601
NLR	6.04	3.73	8.58	5.88	**0.022**	10.02	3.44-16.76	6.71	3.80-10.52	0.385
NLPR	0.03	0.03	0.04	0.03	0.215	0.05	0.02-0.08	0.03	0.016-0.053	0.185
PLR	165.59	66.67	234.09	161.10	**0.019**	185.19	109.95-423.33	162.76	119.42-260.39	0.788
MPR	0.05	0.02	0.05	0.02	0.494	0.04	0.039-0.056	0.05	0.036-0.057	0.982

Data are presented as the mean (SD) and median [interquartile range (25.-75. percentile)] for continuous variables and number and percentage for categorical variable. Compared by the [1]Indipendent t-test and [2]Mann-Whitney U test for continuous variables. Statistical significance was set at 0.05. All statistically significant values are reported in bold.
ICU: Intensive care unit, ASA: American Society of Anesthesiologists, MPV: Mean platelet volume, SII: Systemic immune-inflammation index, NLR: Neutrophil to lymphocyte ratio, NLPR: Neutrophil to lymphocyte, platelet ratio, PLR: Platelet to lymphocyte ratio, MPR: Mean platelet volume/platelet, SD: Standard deviation

of-fit test indicated a well-calibrated model (x^2 =6.933; df =8; p=0.544).

Predictive Accuracy of SII for ICU Admission

ROC analysis determined the cut-off SII based on the differences between the ICU and Non-ICU groups. The cut-off point was established as 1001.61 (AUC of 0.646 95% CI 0.546-0.747) with 74% sensitivity and 55% specificity; p=0.012) for postoperative ICU admission SII (Figure 2).

Discussion

There is still no universal consensus, despite the large number of clinical trials that have been reported that have shown a relationship between several inflammatory markers and postoperative outcomes in elderly HF surgery patients. This study examined the relationship between postoperative ICU hospitalization, mortality, and serum inflammatory markers and indices in geriatric patients undergoing elective HF surgery. In the current study, several significant results were identified. First, patients admitted to the postoperative ICU, with observed mortality had higher ASA scores and urea levels and were older. Second, although inflammation indices (SII, NLR, and PLR) were higher in the ICU group, they did not differ significantly in the mortality group. Third, advanced age, high ASA score, and SII of the inflammation indices were determined to be independent predictors of postoperative ICU admission after geriatric HF surgery.

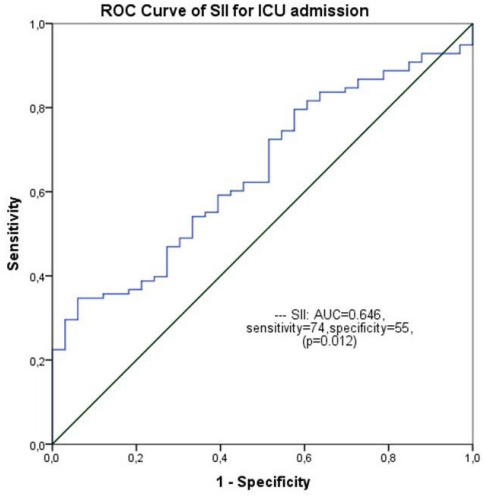

Figure 2. ROC curve of the relationship between SII and admission of ICU

ICU: Intensive care unit, SII: Systemic immune inflammation index, ROC: Receiver operating characteristic

In previous studies, advanced age was shown to be a risk factor for HF surgery (12,13). Forget et al. (12) developed a score that included age, gender, and NLR at the fifth day to estimate the risk of death at one year in elderly patients after HF surgery. Conversely, other studies have reported that advanced age is not a risk factor for mortality (14-16). In the current study, being old with a high ASA score was defined as an independent risk factor for admission to the ICU and mortality. A strong relationship between age and the ASA score is known. There is an increase in comorbidities associated with advanced age. This risky situation also contributes to postoperative mortality and ICU admission decisions. In addition, the high mean age of the included patients may have contributed to the results of our study. Although inconsistent results have been reported in the literature, our results indicate that advanced age is a significant risk factor for the prognosis of this critical surgery.

Recently, many studies have examined the relationship between inflammation and the outcomes of elderly patients. It has been reported that many inflammation markers are associated with prognosis in major orthopedic surgeries, such as HF. The most analyzed of these markers is NLR (13-18). Forget et al. (13) reported that mortality at one year was higher in patients with HF with an NLR>5 at the fifth day. The NLR value at the time of admission of elderly patients who had undergone HF surgery may be used for mortality-related risk classification, according to Temiz and Ersözlü (18) report in another investigation. On the contrary, in the study by of Altinsoy et al. (17), it was reported that there was no relationship between NLR value and postoperative short-term mortality and morbidity in patients with HF. The authors consider the small number of non-survival

Table 3. Predictors of ICU admission using univariate and multivariate analysis

Variables	Univariate analysis				Multivariate analysis			
	OR	(95% CI)		p	OR	(95% CI)		p
		Lower	Upper			Lower	Upper	
Age	1.128	1.033	1.233	**0.008**	1.118	1.015	1.231	**0.023**
ASA	3.332	1.463	7.590	**0.004**	2.572	1.101	6.007	**0.029**
SII	1.001	1.000	1.001	**0.013**	1.001	1.000	1.001	**0.021**
NLR	1.117	1.014	1.231	**0.025**	--	--	--	--
PLR	1.005	1.001	1.009	**0.027**	--	--	--	--

Hosmer–Lemeshow test (x^2=6.933; df: 8; p=0.544), Nagelkerke R Square =0.249, p<0.001. Multivariate Model's Adjusted R^2=0.183, p value <0.001.
CI: Confidence interval, OR: Odds ratio, ICU: Intensive care unit, ASA: American Society of Anesthesiologists, SII: Systemic immune inflammation index, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio

patients as the reason for this different result. Similarly, in our study, although preoperative NLR value was not associated with postoperative ICU mortality, it was associated with ICU admission. Elevated NLR was also found to be an independent predictor of admission to the ICU. There are few patients in the mortality group, and we must interpret our results cautiously.

In an experimental rat study, systemic inflammation mediators were reported as potential biomarkers in the diagnosis and prognosis of acute lung injury, a fatal complication after HF (19). In another clinical study, increased concentrations of inflammatory cytokines (tumor necrosis factor-alpha, interleukin (IL)-6, and IL-10) in elderly patients with HF represented independent risk factors for adverse postoperative outcomes (20). The underlying mechanism activates the inflammatory response of neutrophils activated after trauma. Increased stress is the cause of systemic changes that cause an increase in neutrophil counts and a decrease in lymphocyte counts. Vascular damage is induced by activated platelets and neutrophils, leading to endothelial dysfunction and coagulation disorders (21). SII, an inflammatory biomarker, depends on peripheral platelet, neutrophil, and lymphocyte counts, and it appears to be a useful prognostic indicator for some diseases (9,11). In a recent study, older patients with HF undergoing surgery had lower all-cause mortality when their SII was high (9). In our study, inflammation indices (SII, NLR, PLR) were predictors of ICU admission in univariate regression analysis, whereas SII was an independent risk factor in multivariate regression analysis. Therefore, we thought that an elevated SII level might be a possible predictor of admission to the ICU, an adverse postoperative outcome in older adults with HFs. In addition, it is crucial to determine preventive plans for postoperative ICU admission management according to this inflammation index in elderly patients with HF.

Another significant result of our study is that increased PLR, another inflammatory index, predicts admission to the ICU. Bala (22) reported that increased PLR on the second postoperative day was an effective predictor of survival in patients who underwent hemiarthroplasty. Similarly, another study showed that a high PLR (≥189) can result in increased one-year all-cause mortality in old HF patients (23). The authors reported that because PLR is an easily used simple indicator obtained during routine blood testing, it can be easily found in clinical practice. Although if the PLR level is high, the prognosis will be poor in these patients, the possible underlying mechanism is not precise. Additional research is necessary to understand the predictive ability of these inflammatory indices and to include the predictors in a new scoring system.

Furthermore, our study showed that urea and creatinine levels were significantly associated with ICU mortality and ICU admission. These risk factors have also been defined in other studies (24,25). Mosfeldt et al. (24) reported that 3-month mortality in elderly patients with HF increased threefold in those with high creatinine levels. Laulund et al. (11) concluded that high creatinine plasma levels have predictive significance for mortality in patients with HF after performing a meta-analysis of 15 studies. Preoperative correction of abnormalities in these biochemical laboratory values associated with mortality may positively affect postoperative prognosis.

Study Limitations

However, it is essential to acknowledge that this study has several limitations. First, there may be selection bias because the study was retrospective and single-centered. As a result, we are forced to rely only on the outcomes of patients at our facility. Many parameters such as the type of ICU, capacity, patient population, and anesthesiologist-surgeon relationship can affect a patient's admission to the ICU. Second, various variables contributed to the patient's admission to the ICU. Third, a thorough study with a larger sample size is required to support the existing data because there were few patients in the Non-survivor group throughout the relevant period. The conclusion of a causal association between inflammatory indices and surgical outcomes is thus limited, despite the small sample size of patients.

Conclusion

The study's primary finding is that old age, a high ASA score, and a high preoperative SII value all independently increase the probability of an elderly patient with HF being admitted to the ICU after surgery. The SII value can be employed as an easily measured prognostic parameter in the routine management of critical surgical patients. The reproducibility and generalizability of our study findings need to be examined in more extensive multicenter clinical studies.

Acknowledgement

The authors would also like to thank all of the staff in the department of anesthesiology and orthopedics and traumatology for their fundamental support during the study (Yozgat Bozok University, Medical Faculty Hospital, Yozgat, Turkey). In addition, the authors are grateful to the anesthesiologist M.D. (Ahmet Yüksek and Cevdet Yardımcı) and anesthesiology residents M.D. (Ayşegül Parlak Çıkrıkçı and Hakan Öz) for their support throughout the study.

Ethics

Ethics Committee Approval: The Yozgat Bozok University Clinical Research Ethics Committee approved this retrospective observational single-center study (decision number: 2017-KAEK-189_2021.08.25_02, date: 25.08.2021) in accordance with the Declaration of Helsinki.

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: Ö.H.M., M.K., M.N.P., Concept: Ö.H.M., M.K., M.N.P., Y.A.Ş., S.D., H.A.O., M.K., Design: Ö.H.M., M.K., M.N.P., Y.A.Ş., S.D., H.A.O., M.K., Data Collection or Processing: Ö.H.M., M.K., M.N.P., Y.A.Ş., S.D., H.A.O., M.K., Analysis or Interpretation: Ö.H.M., Literature Search: Ö.H.M., Y.A.Ş., Writing: Ö.H.M., Y.A.Ş.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Fisher AA, Davis MW, Rubenach SE, Sivakumaran S, Smith PN, Budge MM. Outcomes for older patients with hip fractures: The impact of orthopedic and geriatric medicine cocare. J Orthop Trauma 2006;20:172-178.
2. Hu F, Jiang C, Shen J, Tang P, Wang Y. Preoperative predictors for mortality following hip fracture surgery : A systematic review and meta-analysis. Injury 2012;43:676-685.
3. Durusoy S, Paksoy AE, Korkmaz M, Dağlar B, Elibol FKE. The effect of medullary fill on varus collapse in AO 31A3 intertrochanteric (reverse obliquity) fracture treated with cephalomedullary nails. Orthop Traumatol Surg Res 2021;107:102804.
4. Koval KJ, Chen AL, Aharonoff GB, Egol KA, Zuckerman JD. Clinical pathway for hip fractures in the elderly: The hospital for joint diseases experience. Clin Orthop Relat Res 2004;72-81.
5. Paksoy AE, Öner K, Polat F, Durusoy S. Is 48 h a critical cut-off point for mortality in geriatric hip fractures? Turkish J Med Sci 2020;50:1546-1551.
6. Pirat A, Candan S, Canikli S, Erkaya S, Zeyneloğlu P, Arslan G, Karaeminoğulları O. Predictors of Intensive Care Unit Admission in Geriatric Patients Undergoing Hip Replacement. Crit Care Med 2004;32:A72.
7. Onwochei DN, Fabes J, Walker D, Kumar G, Moonesinghe SR. Critical care after major surgery: a systematic review of risk factors for unplanned admission. Anaesthesia 2020;75:e62-e74.
8. Jang IY, Lee YS, Jung HW, Chang JS, Kim JJ, Kim HJ, Lee E. Clinical outcomes of perioperative geriatric intervention in the elderly undergoing hip fracture surgery. Ann Geriatr Med Res 2016;20:125-130.
9. Wang ZC, Jiang W, Chen X, Yang L, Wang H, Liu YH. Systemic immune-inflammation index independently predicts poor survival of older adults with hip fracture: a prospective cohort study. BMC Geriatr 2021;21:155.
10. Samuel D, Bhat AN, Prabhu VM. Platelet Indices as Predictive Markers of Prognosis in Critically Ill Patients: A Prospective Study. Indian J Crit Care Med 2020;24:817-822.
11. Laulund AS, Lauritzen JB, Duus BR, Mosfeldt M, Jørgensen HL. Routine blood tests as predictors of mortality in hip fracture patients. Injury 2012;43:1014-1020.
12. Forget P, Dillien P, Engel H, Cornu O, De Kock M, Yombi JC. Use of the neutrophil-to-lymphocyte ratio as a component of a score to predict postoperative mortality after surgery for hip fracture in elderly subjects. BMC Res Notes 2016;9:1-6.
13. Forget P, Moreau N, Engel H, Cornu O, Boland B, De Kock M, Yombi JC. The neutrophil-to-lymphocyte ratio (NLR) after surgery for hip fracture (HF). Arch Gerontol Geriatr 2015;60:366-371.
14. Niessen R, Bihin B, Gourdin M, Yombi JC, Cornu O, Forget P. Prediction of postoperative mortality in elderly patient with hip fractures: A single-centre, retrospective cohort study. BMC Anesthesiol 2018;18:5-7.
15. Özbek EA, Ayanoğlu T, Olçar HA, Yalvaç ES. Is the preoperative neutrophil-to-lymphocyte ratio a predictive value for postoperative mortality in orthogeriatric patients who underwent proximal femoral nail surgery for pertrochanteric fractures? Ulus Travma ve Acil Cerrahi Derg 2020;26:607-612.
16. Miniksar OH, Kaçmaz O. The effect of neutrophil-lymphocyte ratio on admission to postoperative intensive care and mortality in elderly patients undergoing hip fracture surgery with spinal anesthesia. Eur Res J 2021;7:628-634.
17. Altinsoy S, Çatalca S, Sayin M, Ergil J. The effect of neutrophil to lymphocyte ratio on postoperative early mortality and morbidity in hip fracture intensive care patients. Anestezi Derg 2018;26:234-237.
18. Temiz A, Ersözlü S. Admission neutrophil-to-lymphocyte ratio and postoperative mortality in elderly patients with hip fracture. Ulus Travma ve Acil Cerrahi Derg 2019;25:71-74.
19. Gan L, Sun T, Li B, Tian J, Zhang J, Chen X, Zhong J, Yang X, Li Q. Serum miR-146a and miR-150 as Potential New Biomarkers for Hip Fracture-Induced Acute Lung Injury. Mediators Inflamm 2018;2018:8101359.
20. Sun T, Wang X, Liu Z, Chen X, Zhang J. Plasma concentrations of pro- and anti-inflammatory cytokines and outcome prediction in elderly hip fracture patients. Injury 2011;42:707-713.
21. Fisher A, Srikusalanukul W, Fisher L, Smith P. The neutrophil to lymphocyte ratio on admission and short-term outcomes in orthogeriatric patients. Int J Med Sci 2016;13:588-602.
22. Bala MM. The benefit of dynamic neutrophil-lymphocyte ratio and systemic immune-inflammation index in predicting survival in patients undergoing hemiarthroplasty. Eur Rev Med Pharmacol Sci 2022;26:3878-3885.
23. Wang Z, Wang H, Yang L, Jiang W, Chen X, Liu Y. High platelet-to-lymphocyte ratio predicts poor survival of elderly patients with hip fracture. International Orthopaedics 2021;45:13-21.
24. Mosfeldt M, Pedersen OB, Riis T, Worm HO, Mark SVD, Jorgensen HL, Duus BL, Lauritsen JB. Value of routine blood tests for prediction of mortality risk in hip fracture patients. Acta Orthop 2012;83:31-35.
25. Seyedi HR, Mahdian M, Khosravi G, Bidgoli MS, Mousavi SG, Razavizadeh MR, Mahdian S, Mohammedzadeh M. Prediction of mortality in hip fracture patients: Role of routine blood tests. Arch Bone Jt Surg 2015;3:51-55.

ORIGINAL RESEARCH

DOI: 10.4274/ejgg.galenos.2023.2023-3-6
Eur J Geriatr Gerontol 2024;6(1):26-30

Clinical Frailty Scale and Body Mass Index as an Independent Predictor of 2-year Mortality at Hospitalized Patients

Yelda Öztürk, Arzu Okyar Baş, Merve Güner, Serdar Ceylan, Meltem Koca, Mert Esme, Cafer Balcı, Burcu Balam Doğu, Mustafa Cankurtaran, Meltem Halil

Hacettepe University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, Ankara, Turkey

Abstract

Objective: This study aimed to investigate the effect of the clinical frailty scale (CFS) and body mass index (BMI) on the 2-year mortality prediction in hospitalized internal medicine patients.

Materials and Methods: A prospective observational study was conducted between January 2019 and February 2020. Subjects (18 years and older) admitted to the internal medicine wards and expected to stay for at least 72 h were included. Participants were evaluated within 48 h of admission. The Charlson comorbidity index (CCI) was calculated. Anthropometric measurements and handgrip strength were obtained within 48 h. CFS was used for frailty assessment. Cox regression analysis was performed for mortality analysis.

Results: One hundred eighteen patients were included. Fifty-eight of the (49.2%) patients were 65 years and over. In multivariate analysis, BMI and CFS were independently associated with 2-year mortality, regardless of age, sex, and CCI. Hazard ratios for BMI and CFS were 0.898 [95% confidence interval (CI), 0.840-0.961; p=0.002] and 1.313 (95% CI, 1.002-1.719; p=0.048), respectively.

Conclusion: Higher CFS scores and lower BMI scores are independently associated with 2-year mortality in hospitalized internal medicine patients.

Keywords: Body mass index, clinical frailty scale, frailty, hospitalization, mortality

Introduction

Frailty is a state of increased vulnerability to stressors and is also associated with multiple physiological systems that are interrelated with each other (1). It is a global public healthcare issue as the world is aging. Subjects living with frailty are at a growing risk of adverse outcomes, including hospitalization and mortality, causing higher healthcare costs (2). It is a known fact that subjects with frailty can dynamically transition between states (3). Therefore, it is crucial to detect and manage subjects who are living with frailty.

The prevalence of frailty in geriatric inpatients ranges from 48.8% to 80%, depending on the evaluation tool used (4). There are several frailty instruments such as the FRAIL scale, Edmonton frailty scale, and clinical frailty scale (CFS) (3,5-7). CFS is an easy and quick scale. It was developed to determine frailty in older adults and includes items such as comorbidity, cognitive impairment, and function (8). It assesses frailty using visual and written charts with nine graded pictures, ranging between 1 (very fit) and 9 (terminally ill). A score of ≥5 represents patients who are frail. CFS has been shown to be widely used in multiple settings. Several studies have been conducted, especially in hospital settings, and assessed its associations with adverse outcomes (9).

Body mass index (BMI) is also known to be a factor related to mortality. It is an index of malnutrition (10). Malnutrition (both undernutrition and obesity) plays a key role in the pathogenesis of frailty and sarcopenia (11). A recently published meta-analysis revealed a high overlapping prevalence of malnutrition

Address for Correspondence: Yelda Öztürk, Eskişehir City Hospital, Clinic of Geriatrics, Eskişehir, Turkey
Phone: +90 533 615 12 86 **E-mail:** yeldaozturk67@gmail.com **ORCID:** orcid.org/0000-0003-3847-0967
Received: 27.03.2023 **Accepted:** 16.08.2023
Cite this article as: Öztürk Y, Okyar Baş A, Güner M, Ceylan S, Koca M, Esme M, Balcı C, Doğu BB, Cankurtaran M, Halil M. Clinical Frailty Scale and Body Mass Index as an Independent Predictor of 2-year Mortality at Hospitalized Patients. Eur J Geriatr Gerontol 2024;6(1):26-30

and frailty in hospitalized older patients (12). On the other hand, obesity has a close relationship with type 2 diabetes mellitus and coronary artery disease (13). However, there are conflicting results regarding its effect on mortality, changing from condition to condition (14,15).

Obesity paradox, a term used to describe that overweight and obese patients with a particular disease may have better outcomes than normal weight patients, is another concern (16,17). For example, it has been claimed that the strength of the association between obesity and mortality weakens with increasing age (18). There is wide heterogeneity between studies regarding the relationship between obesity and mortality, especially in older patients (19).

In light of these data, we determined the effect of CFS and BMI on 2-year mortality in hospitalized internal medicine patients.

Materials and Methods

This prospective observational study was conducted between January 2019 and February 2020. Subjects (18 years and older), admitted to the internal medicine wards of a university hospital and expected to stay for at least 72 h, were included. Written informed consents were obtained from all participants.. Participants were evaluated within 48 h of admission, and they were followed up for at least 2 years or until death. The baseline characteristics of patients, including comorbidities, were recorded. The Charlson comorbidity index (CCI) was calculated (20).

Anthropometric measurements including height, weight, calf circumference (CC), and mid-upper arm circumference (MAC) were taken. Height and weight were measured while standing and recorded in meters and kilograms, respectively (TEM-BEKO 035x040, İstanbul, Turkey). BMI was calculated by dividing body weight in kilograms by height in meters squared (kg/m^2). CC was measured in the sitting position with 90^o of knee flexion at the largest level of the leg. MAC was measured when the elbow was at 90^o flexion. CC and MAC were recorded in centimeters. Handgrip strength (HGS) was measured by Takei digital grip strength dynamometer (Takei Scientific Instruments Co, Niigata, Japan) at a 90^o flexion of the elbow with a neutrally rotated forearm and reported in kilograms. The thresholds of 16 kg for females and 27 kg for males were used, as recommended by EWGSOP-2 (21). The highest value of the three measurements was considered (22). Mini nutrition assessment-short form (MNA-SF), and nutritional risk score-2002 (NRS-2002) were performed to screen for malnutrition. Patients were grouped as malnourished (score ≤7), at-risk (score 8-11), and normal (score 12-14) according to the MNA-SF score (23). When the NRS-2002 score was ≥3, it meant nutritionally at risk (24). Frailty was assessed using the 9-point CFS. The score ranged from 1 to 9 (25). The study was approved by the Hacettepe University Non-Interventional Clinical Research Ethics Committee (decision number: 2019/07-28, date: 07.03.2019).

Statistics

The IBM SPSS Statistics program version 23.0 was used for statistical analysis. The normality of variables was examined using visual (histograms and probability plots) and analytical methods. Categorical variables are presented as numbers and frequencies. Normally distributed variables are presented as mean ± standard deviation, non-normally distributed variables are presented as median (IQR, 25p-75p). Patients were divided into two groups as younger (<65 years) and older (≥65 years) to present baseline characteristics of patients. The χ^2 or Fisher's exact test was used to compare differences between the categorical variables as appropriate. Mann-Whitney U and Student's t-tests were used to compare non-normally and normally distributed variables, respectively. Cox regression analysis was performed to define the factors associated with 2-year mortality. Four models were constructed. Model 1 included age and sex; model 2 included age, sex, and CCI; model 3 included age, sex, CCI, and BMI; model 4 included age, sex, CCI, BMI, and CFS. The findings are shown as hazard ratios (HRs) and the corresponding 95% confidence interval (CI). The proportional hazard assumption and model fit were assessed using residual (Schoenfeld and Martingale) analysis. All analyzes were considered statistically significant when the p value was <0.05.

Results

A total of 118 patients were included in the analysis. Subjects were divided into two groups as younger (n=60) and older (n=58). The baseline characteristics of the patients are presented in Table 1. Causes of hospitalization, length of stay, CCI, MAC, CC, and MNA-SF categories were not different between the groups. Median BMI values of the younger and older groups were 25.8 (22.7-29.9), and 29.1 (25.5-32.1), respectively (p=0.008). The rate of patients with risk of malnutrition according to NRS-2002 was higher in the older group (p=0.001). The median CFS score was higher in the older group than the youngers (p>0.001). The rates of patients with low muscle strength were 38.6% (n=22) in the younger group and 74.5% (n=41) in the older group (p<0.001).

During the 2-year follow-up, 28.8% of patients died (21.7% of younger group, 36.2% of older group). Age (p=0.015), CCI (p=0.021), BMI (p=0.032) and CFS (p=0.001) were significantly associated with 2-year mortality in the univariate model (Table 2). Four different models were created and are presented in Table 3. In model 4, which included age, sex, CCI, BMI, and CFS, BMI and CFS were independently associated with 2-year mortality. The HRs for BMI and CFS were 0.898 (95% CI, 0.840-0.961; p=0.002) and 1.313 (95% CI, 1.002-1.719; p=0.048), respectively.

Table 1. Baseline characteristics of younger and older patients			
	<65 years (n=60)	≥65 years (n=58)	p
Sex, female	39 (65.0)	27 (46.6)	0.044
Illiterate	6 (10.0)	16 (27.6)	<0.001
Causes of hospitalization			
Malignancy	5 (8.3)	7 (12.1)	0.502
Infectious disease	5 (8.3)	7 (12.1)	0.502
Rheumatic disease	3 (5.0)	5 (8.6)	0.434
Gastrointestinal disease	7 (11.7)	10 (17.2)	0.389
Hematologic disease	16 (26.7)	5 (8.6)	0.010
Endocrine disease	8 (13.3)	2 (3.4)	0.054
Pulmonary disease	6 (10.0)	3 (5.2)	0.323
Nephrology disorders	5 (8.3)	11 (19.0)	0.092
Cardiovascular disease	5 (8.3)	8 (13.8)	0.344
Length of hospital stay, days	12.8 (8.8-19.7)	10.8 (7.8-17.0)	0.391
Charlson comorbidity index	2 (1-3)	2 (1-3)	0.191
Body mass index, kg/m²	25.8 (22.7-29.9)	29.1 (25.5-32.1)	0.008
Mid-upper arm circumference, cm	28 (24-30)	27 (25-30)	0.606
Calf circumference, cm	34 (31-37)	35 (31-37)	0.793
NRS-2002, at risk (≥3)	13 (21.7)	30 (51.7)	0.001
MNA-SF score ≤11	28 (43.8)	36 (56.3)	0.093
Clinical frailty scale	3 (2-4)	4 (4-5)	<0.001
Low handgrip strength, kg	22 (38.6)	41 (74.5)	<0.001

Numbers are means ± SD, medians (25^{th}-75^{th} percentiles), or frequencies (%), as appropriate
MNA-SF: Mini nutrition assessment-short form, NRS-2002: Nutritional risk score-2002, SD: Standard deviation

Table 2. Univariable analysis associated to 2-year mortality		
	95% CI	p
Age	1.032 (1.006-1.058)	0.015
Sex	1.335 (0.682-2.1615)	0.400
Charlson comorbidity index	1.266 (1.036-1.547)	0.021
Body mass index	0.934 (0.877-0.994)	0.032
Clinical frailty scale	1.406 (1.140-1.735)	0.001
Low handgrip strength	1.445 (0.697-2.995)	0.322

CI: Confidence interval

Discussion

This prospective cohort study demonstrated the independent effect of CFS and BMI on 2-year mortality prediction in hospitalized internal medicine patients. Whereas a higher CFS score was associated with a higher mortality risk, a lower BMI was associated with a higher mortality risk, regardless of age, sex, and CCI. In our study population, older patients had a higher CFS score. The rate of patients with low HGS and at risk of malnutrition was higher in the older group. This is not surprising as they are leading and challenging geriatric syndromes, especially for hospitalized older patients (12,26).

Recently, CFS has been widely used to predict adverse outcomes such as mortality in various settings (9). Although it was validated in geriatric patients (≥65 years), there are emerging studies suggesting its use at all ages (25). Welford et al. (27) revealed that a higher CFS score was associated with a poor prognosis in hemato-oncology clinics. They supported the use of CFS in inpatients of any age. In another study, CFS was used in 18 years and older patients with cancer at an intensive care unit and was found to be associated with worse clinical outcomes among oncologic critically ill patients (28).

A multicenter retrospective cohort study with a median (IQR) age of 63.7 years (49.1-74.0 years) concluded that CFS predicted 1-year mortality well in critically ill patients (HR 1.26, 95% CI 1.21-1.31) after adjusting for confounders (29). A prospective multicenter cohort study was conducted in younger critically ill patients and supported the use of CFS in younger adults, not just in older adults (30). The results of our study are consistent with the literature. One-point increment in CFS was associated with 1.3-fold mortality risk in hospitalized internal medicine patients, regardless of age, sex, and comorbidities.

Another highlighted point of our study is the independent effect of BMI on mortality. We concluded that higher BMI scores were associated with lower mortality risk. A recently published, large sample size study conducted in geriatric medical departments presented the protective effect of BMI on mortality. They used standard BMI categories according to the World Health Organization in their study and emphasized the requirement of an ideal BMI for vulnerable groups (31). This result was similar to ours. In our study, the median (IQR) BMI scores were 25.8

Table 3. Multivariable Cox regression analysis associated to 2-year mortality

	Model-1		Model-2		Model-3		Model-4	
	CI 95%	p	CI 95%	p	CI 95%	p	CI 95%	p
Age	1.032 (1.006-1.058)	0.017	1.031 (1.003-1.060)	0.029	1.037 (1.011-1.063)	0.005	1.018 (0.987-1.050)	0.254
Sex	1.245 (0.635-2.441)	0.524	1.261 (0.643-2.474)	0.500	1.173 (0.597-2.305)	0.643	1.406 (0.672-2.945)	0.366
CCI			1.227 (1.002-1.504)	0.048	1.326 (1.076-1.634)	0.008	1.238 (0.991-1.547)	0.060
BMI					0.890 (0.830-0.954)	0.001	0.898 (0.840-0.961)	0.002
CFS							1.313 (1.002-1.719)	0.048

Model 1 age, sex; model 2 age, sex, CCI; model 3 age, sex, CCI, BMI; model 4 age, sex, CCI, BMI, CFS
BMI: Body mass index, CCI: Charlson comorbidity index, CFS: Clinical frailty scale, CI: Confidence interval

(22.7-29.9) and 29.1 (25.5-32.1) for younger and older patients, respectively. On the other hand, we did not categorize patients according to BMI because the thresholds should be different for geriatric patients and patients living with frailty. In the light of these data, we evaluated BMI as a continuous variable and showed its effect on mortality irrespective of age, sex, CCI, and CFS. This striking point will provide a basis for future study designs. Kanenawa et al. (32) presented a study similar to ours. They determined the impact of CFS on 2-year mortality after hospitalization for heart failure, regardless of stratification based on age, sex, BMI, and left ventricular ejection fraction. Therefore, they suggested the use of CFS as a prognostic tool in clinical settings.

Study Limitations

There are some limitations to our study. First, CFS was not validated in younger patients. However, as there are so many studies supporting its use in younger patients, we used it for younger patients. Second, we evaluated BMI as a continuous variable and did not categorize it. We planned to investigate the effect of a 1-point change in BMI. Therefore, there are conflicting results regarding its use, especially for older adults. In this field, large sample size studies are needed, and the cut-off values for BMI should be assessed anew. In contrast, we highlighted the importance of using CFS and assessing BMI in hospitalized patients, regardless of age, sex, and CCI.

Conclusion

Higher CFS and lower BMI scores are independently associated with 2-year mortality in hospitalized internal medicine patients. Future comprehensive studies on the use of CFS in hospitalized patients and updating BMI cut-off values according to frailty and age categories are needed.

Ethics

Ethics Committee Approval: The study was approved by the Hacettepe University Non-Interventional Clinical Research Ethics Committee (decision number: 2019/07-28, date: 07.03.2019).

Informed Consent: Written informed consents were obtained from all participants.

Authorship Contributions

Surgical and Medical Practices: Y.Ö., M.G., M.K., M.H., Concept: Y.Ö., M.G., M.K., C.B., B.B.D., M.C., M.H., Design: Y.Ö., M.K., M.H., Data Collection or Processing: Y.Ö., M.G., S.C., M.K., B.B.D., M.C., M.H., Analysis or Interpretation: Y.Ö., A.O.B., M.G., S.C., M.E., C.B., B.B.D., M.C., M.H., Literature Search: Y.Ö., A.O.B., M.G., S.C., M.E., M.H., Writing: Y.Ö., A.O.B., M.G., S.C., M.K., M.E., C.B., M.H.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet 2013;381:752-762.
2. Hoogendijk EO, Afilalo J, Ensrud KE, Kowal P, Onder G, Fried LP. Frailty: implications for clinical practice and public health. Lancet 2019;394:1365-1375.
3. Dent E, Martin FC, Bergman H, Woo J, Romero-Ortuno R, Walston JD. Management of frailty: opportunities, challenges, and future directions. Lancet 2019;394:1376-1386.
4. Rezaei-Shahsavarloo Z, Atashzadeh-Shoorideh F, Gobbens RJJ, Ebadi A, Ghaedamini Harouni G. The impact of interventions on management of frailty in hospitalized frail older adults: a systematic review and meta-analysis. BMC Geriatr 2020;20:526.
5. Morley JE, Vellas B, van Kan GA, Anker SD, Bauer JM, Bernabei R, Cesari M, Chumlea WC, Doehner W, Evans J, Fried LP, Guralnik JM, Katz PR, Malmstrom TK, McCarter RJ, Gutierrez Robledo LM, Rockwood K, von Haehling S, Vandewoude MF, Walston J. Frailty consensus: a call to action. J Am Med Dir Assoc 2013;14:392-397.
6. Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. Age Ageing 2006;35:526-529.
7. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, Mitnitski A. A global clinical measure of fitness and frailty in elderly people. Cmaj 2005;173:489-495.
8. Rockwood K, Theou O. Using the Clinical Frailty Scale in Allocating Scarce Health Care Resources. Can Geriatr J 2020;23:210-215.

9. Church S, Rogers E, Rockwood K, Theou O. A scoping review of the Clinical Frailty Scale. BMC Geriatr 2020;20:393.
10. Cederholm T, Jensen GL, Correia MITD, Gonzalez MC, Fukushima R, Higashiguchi T, Baptista G, Barazzoni R, Blaauw R, Coats A, Crivelli A, Evans DC, Gramlich L, Fuchs-Tarlovsky V, Keller H, Llido L, Malone A, Mogensen KM, Morley JE, Muscaritoli M, Nyulasi I, Pirlich M, Pisprasert V, de van der Schueren MAE, Siltharm S, Singer P, Tappenden K, Velasco N, Waitzberg D, Yamwong P, Yu J, Van Gossum A, Compher C; GLIM Core Leadership Committee; GLIM Working Group. GLIM criteria for the diagnosis of malnutrition - A consensus report from the global clinical nutrition community. Clin Nutr 2019;38:1-9.
11. Cruz-Jentoft AJ, Kiesswetter E, Drey M, Sieber CC. Nutrition, frailty, and sarcopenia. Aging Clin Exp Res 2017;29:43-48.
12. Ligthart-Melis GC, Luiking YC, Kakourou A, Cederholm T, Maier AB, de van der Schueren MAE. Frailty, Sarcopenia, and Malnutrition Frequently (Co-) occur in Hospitalized Older Adults: A Systematic Review and Meta-analysis. J Am Med Dir Assoc 2020;21:1216-1228.
13. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, Khan SS, Mookadam F, Krasuski RA, Ahmed H. Association Between Obesity and Cardiovascular Outcomes: A Systematic Review and Meta-analysis of Mendelian Randomization Studies. JAMA Netw Open 2018;1:e183788.
14. Li J, Li D, Wang X, Zhang L. The impact of body mass index on mortality rates of hip fracture patients: a systematic review and meta-analysis. Osteoporos Int 2022;33:1859-1869.
15. Kittiskulnam P, Johansen KL. The obesity paradox: A further consideration in dialysis patients. Semin Dial 2019;32:485-489.
16. Bosello O, Vanzo A. Obesity paradox and aging. Eat Weight Disord 2021;26:27-35.
17. Donini LM, Busetto L, Bischoff SC, Cederholm T, Ballesteros-Pomar MD, Batsis JA, Bauer JM, Boirie Y, Cruz-Jentoft AJ, Dicker D, Frara S, Frühbeck G, Genton L, Gepner Y, Giustina A, Gonzalez MC, Han HS, Heymsfield SB, Higashiguchi T, Laviano A, Lenzi A, Nyulasi I, Parrinello E, Poggiogalle E, Prado CM, Salvador J, Rolland Y, Santini F, Serlie MJ, Shi H, Sieber CC, Siervo M, Vettor R, Villareal DT, Volkert D, Yu J, Zamboni M, Barazzoni R. Definition and Diagnostic Criteria for Sarcopenic Obesity: ESPEN and EASO Consensus Statement. Obes Facts 2022;15:321-335.
18. Wang Z. Age-dependent decline of association between obesity and mortality: a systematic review and meta-analysis. Obes Res Clin Pract 2015;9:1-11.
19. Dramé M, Godaert L. The Obesity Paradox and Mortality in Older Adults: A Systematic Review. Nutrients 2023;15:1780.
20. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373-383.
21. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, Schneider SM, Sieber CC, Topinkova E, Vandewoude M, Visser M, Zamboni M; Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48:16-31.
22. Ozturk Y, Deniz O, Coteli S, Unsal P, Dikmeer A, Burkuk S, Koca M, Cavusoglu C, Dogu BB, Cankurtaran M, Halil M. Global Leadership Initiative on Malnutrition criteria with different muscle assessments including muscle ultrasound with hospitalized internal medicine patients. JPEN J Parenter Enteral Nutr 2022;46:936-945.
23. Sarikaya D, Halil M, Kuyumcu ME, Kilic MK, Yesil Y, Kara O, Ozturk S, Gungor E, Karabulut E, Balam Yavuz B, Cankurtaran M, Ariogul S. Mini nutritional assessment test long and short form are valid screening tools in Turkish older adults. Arch Gerontol Geriatr 2015;61:56-60.
24. Bolayir B, Arik G, Yeşil Y, Kuyumcu ME, Varan HD, Kara Ö, Güngör AE, Yavuz BB, Cankurtaran M, Halil MG. Validation of Nutritional Risk Screening-2002 in a Hospitalized Adult Population. Nutr Clin Pract 2019;34:297-303.
25. Özsürekci C, Balcı C, Kızılarslanoğlu MC, Çalışkan H, Tuna Doğrul R, Ayçiçek GŞ, Sümer F, Karabulut E, Yavuz BB, Cankurtaran M, Halil MG. An important problem in an aging country: identifying the frailty via 9 Point Clinical Frailty Scale. Acta Clin Belg 2020;75:200-204.
26. Daly RM, Iuliano S, Fyfe JJ, Scott D, Kirk B, Thompson MQ, Dent E, Fetterplace K, Wright ORL, Lynch GS, Zanker J, Yu S, Kurrle S, Visvanathan R, Maier AB. Screening, Diagnosis and Management of Sarcopenia and Frailty in Hospitalized Older Adults: Recommendations from the Australian and New Zealand Society for Sarcopenia and Frailty Research (ANZSSFR) Expert Working Group. J Nutr Health Aging 2022;26:637-651.
27. Welford J, Rafferty R, Hunt K, Short D, Duncan L, Ward A, et al. The Clinical Frailty Scale can indicate prognosis and care requirements on discharge in oncology and haemato-oncology inpatients: A cohort study. Eur J Cancer Care (Engl) 2022;31:e13752.
28. Osatnik J, Matarrese A, Leone B, Cesar G, Kleinert M, Sosa F, Roberti J, Ivulich D. Frailty and clinical outcomes in critically ill patients with cancer: A cohort study. J Geriatr Oncol 2022;13:1156-1161.
29. Subramaniam A, Ueno R, Tiruvoipati R, Srikanth V, Bailey M, Pilcher D. Comparison of the predictive ability of clinical frailty scale and hospital frailty risk score to determine long-term survival in critically ill patients: a multicentre retrospective cohort study. Crit Care 2022;26:121.
30. Bagshaw M, Majumdar SR, Rolfson DB, Ibrahim Q, McDermid RC, Stelfox HT. A prospective multicenter cohort study of frailty in younger critically ill patients. Crit Care 2016;20:175.
31. Ryg J, Anru PL, Engberg H, Jorgensen MG, Masud T, Christensen K, Andersen-Ranberg K. Association of Body Mass Index With All-Cause Mortality in Acutely Hospitalized Older Patients. J Am Med Dir Assoc 2022;23:507-513.
32. Kanenawa K, Isotani A, Yamaji K, Nakamura M, Tanaka Y, Hirose-Inui K, Fujioka S, Mori S, Yano M, Ito S, Morinaga T, Fukunaga M, Hyodo M, Ando K. The impact of frailty according to Clinical Frailty Scale on clinical outcome in patients with heart failure. ESC Heart Fail 2021;8:1552-1561.

ORIGINAL RESEARCH

DOI: 10.4274/ejgg.galenos.2023.2023-7-3
Eur J Geriatr Gerontol 2024;6(1):31-38

Problems Experienced by Physicians Treating Elderly Patients in the Palliative Care Process and Solution Proposals

Ayşe Gülay Şahan[1], Asli Kilavuz[2]

[1]Balıkesir University Faculty of Health Sciences, Department of Gerontology, Balıkesir, Turkey
[2]Ege University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, İzmir, Turkey

Abstract

Objective: This study aimed to determine the opinions of physicians treating elderly patients in palliative care units in government and private health institutions about the problems experienced and the solution proposals for these problems.

Materials and Methods: From qualitative research designs, a single case design was adopted. The study group consisted of 16 physicians determined using the maximum variation, convenience, and criterion sampling methods from purposive sampling methods. The data obtained using the "personal information form" and the "interview form", were analyzed using descriptive and content analysis methods.

Results: In the palliative care process, problems related to chronic diseases were most common in elderly patients, followed by problems related to neuropsychiatry and pain, respectively. While routine treatment proposals came to the fore in solving problems arising from chronic diseases, medication and related specialist support were emphasized to solve problems caused by pain, oncology, and the gastrointestinal system.

Conclusion: Because elderly patients in the palliative care process experience multiple problems, it is recommended that physicians adopt an individualized approach, including a comprehensive evaluation with an interdisciplinary team, to solve these problems.

Keywords: Palliative care, problems in palliative care, solutions in palliative care, physician, elderly patient

Introduction

Today, with the increase in the average age worldwide, the care of the elderly has become more important. Because individuals have the right to spend their last days in quality and peace, palliative care is considered among the most important human rights today (1).

The Latin word "palliate (palliare)" means protective or inclusive. "Palliative" means "mitigating, soothing, or temporary remedy" in English (2). Palliative care is a medical concept that does not have a single generally accepted definition (3). It has been defined differently in different sources and its definition has changed over time (4). According to the widely accepted definition, palliative care is an approach in which appropriate medical treatment methods are offered simultaneously to meet the physical, psychosocial, and spiritual needs of patients and their family (caregiver) in the terminal period of any life-threatening illness, focusing on reducing the problems and increasing the quality of life (5).

Consistent with the criteria determined by the World Health Organization, each country has created a plan and strategy regarding the palliative care process according to the country's health system, culture, beliefs, and needs. In Turkey, the first palliative care practices began in the 1990s (6). In 2010, the Ministry of Health developed a palliative care organization model, and as of the beginning of 2010, 10 palliative care centers, most of which are located within university hospitals, have been established. According to the latest data, palliative care services are provided with 5,302 beds in 396 health institutions under the Ministry of Health in Turkey (7). In addition, this service is provided in care centers affiliated with the Ministry of Family and Social Services.

Address for Correspondence: Asli Kilavuz, Ege University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, İzmir, Turkey
Phone: +90 532 353 65 70 **E-mail:** asli.kilavuz@ege.edu.tr **ORCID:** orcid.org/0000-0002-0474-9911
Received: 16.07.2023 **Accepted:** 03.09.2023

Cite this article as: Şahan AG, Kilavuz A. Problems Experienced by Physicians Treating Elderly Patients in the Palliative Care Process and Solution Proposals. Eur J Geriatr Gerontol 2024;6(1):31-38

At the institutional level, the palliative care process begins with diagnosis and covers holistic and humanistic care, and functional and emotional care and support. Palliative care, a multidisciplinary healthcare service, requires team effort. The palliative care team, whose aim is to increase the quality of life rather than life expectancy (8), includes physicians (family physicians, anesthesiologists, algologists, oncologists, surgeons), nurses, pharmacologists, dietitians, psychologists, social service specialists, and grief counselors (9). The most important group in the team-providing palliative care services are physicians with the responsibility for diagnosis, treatment, and organization (6).

This study aimed to determine the opinions of physicians treating elderly patients in palliative care units in government and private health institutions regarding the problems experienced in the palliative care process and the solution proposals for these problems, and whether there are differences and similarities between the opinions of physicians in the two groups.

Materials and Methods

This study has a qualitative approach in which a single case study design from qualitative research designs was adopted. The study was conducted between January 2023 and March 2023.

Participants

One government institution and two private institutions with palliative care centers were included in the study. The study group consisted of 16 physicians who were determined using maximum diversity, easy accessibility, and criterion sampling methods from purposive sampling methods. Eight physicians were working in government institutions and eight were in private institutions. The number of beds in the palliative care service in the government institution was 18, whereas the total number of beds in the two private palliative care centers was 74. The number of patients hospitalized in palliative care services per month is 30 in government institutions and 10 in private institutions. The inclusion criteria were working in palliative care centers/services of government and private health institutions in the city where the study was conducted and volunteering to participate in the study. The exclusion criteria were being employed in the relevant centers but not volunteering to participate in the study.

Data Collection and Analysis

The data were obtained using the "personal information form" and "interview form" developed by the researchers. Personal information forms were used to determine the characteristics of the participants, whereas the interview form was used to investigate the opinions of the participants about the problems experienced in the palliative care process and the solution proposals for these problems. The preparation of data collection tools followed the stages of preparing possible questions according to the conceptual framework, presenting the forms to expert opinions, making the necessary corrections according to expert opinions, conducting the pilot testing, and giving the final shape to the forms.

The study was approved by the Medical Research Ethics Committee of Ege University (approval number: E-99166796-050.06.04-994509, date: 17.11.2022) and was conducted in accordance with the principles of the Declaration of Helsinki. Necessary permissions were obtained from the health directorate and private care centers of the city where the research was conducted. Before the interview, the interviewee was informed about the purpose of the study, the informed consent form was read, and written consent was obtained. In addition, the interviews were tape-recorded by taking verbal consent.

Statistics

Descriptive analysis and content analysis methods were used. Analysis of data included coding the data into the conceptual framework, presenting the data, and interpreting the data. The findings were grouped under six themes: pain, gastrointestinal system, nutrition, oncological diseases, chronic diseases, and neuropsychiatry. Tables with codes and frequency (frequency of physicians' opinions in government institutions/frequency of physicians' opinions in private institutions) values for the problems and solutions within the scope of each theme were created. For example, the value (4/5) in the table indicates that 4 of the relevant theme or code reflects the opinion of physicians working in government institutions, whereas 5 reflects the opinion of physicians working in private institutions. To support the findings with direct quotations, participant statements were included. During the analysis process, direct quotations were numbered to represent the institutions and rankings of the physicians GP1,..., GP8 for physicians working in government institutions [GP1,..., GP8 for physicians working in government institutions (G: Government institutions, P: Physician) and PP1,..., PP8 for physicians working in private institutions (P: Private institutions, P: Physician)].

Validity and Reliability

To ensure validity, personal information and interview questions were prepared in accordance with the main and subcategories of palliative care. To ensure reliability, the consistency obtained from analyzing the data at two different times was calculated as. Eighty nine using the percentage of agreement formulas. A value of 70% and above indicates the reliability of a study (10,11).

Results

Eight physicians were working in government institutions, 8 were in private institutions, 7 were female, 9 were male, and 12

were married. Five participants aged between 24 and 58 years were specialist physicians and 11 were general practitioners. The seniority of the participants varied between 6 months and 36 years, and the working period in the palliative care service ranged from 2 months to 14 years. Only one participant was permanently working in the palliative care service and only one stated to receive palliative care training.

Our study findings are tabulated and interpreted below within the framework of the sub-problems of the research (Table 1-6).

When the problems related to pain and suggestion proposals were examined, they mostly concentrated on general pain, joint pain, and bone pain. General pain-related problems were experienced more in government institutions, and narcotic analgesics were suggested as a solution. Joint pain problems were mostly experienced in private institutions, and painkillers were proposed as a solution (Table 1). Sample expressions are given below:

"Our patients mostly express general pain. Bone and joint pain are also common conditions. In this case, we preferred painkillers and narcotic agents. Sometimes we can provide physical therapy, algology or psychologist support" (GP3).

"We encounter complaints in different parts of the body and joint and bone pains, which are quite intense. In addition to

Table 1. Problems related to pain in the palliative care process in government and private health institutions and solution proposals

Theme		Code
Pain	**Problem (*f*)**	**Proposal (*f*)**
	General pain (7/5)	Narcotic analgesics (7/1), painkillers (6/2), physiotherapy (1/5), algologist support (4/1), alternative medicine (3/2), algorithm based treatment (3/1), exercise (-/2), psychologist support (1/-), neurologist support (1/-), related expert support (-/1)
	Joint pain (6/6)	Painkillers (6/3), physiotherapy (1/5), algologist support (4/-), narcotic analgesic (3/-), exercise (-/3), massage (-/2), neurologist support (1/-), related expert support (-/1), alternative medicine (-/1), algorithm based treatment (-/1), hot/cold application (-/1)
	Bone pain (6/3)	Painkillers (6/-), physiotherapy (1/3), algologist support (3/-), narcotic analgesic (3/-), hot/cold application (-/2), massage (-/2), exercise (-/2) neurologist support (1/-), alternative medicine (-/1), positioning (-/1), algorithm based treatment (-/1)
	Wound pain (2/4)	Painkillers (2/3), narcotic analgesic (-/2), algorithm based treatment (-/1)
	Post-surgical pain (-/4)	Algorithm based treatment (-/2), painkillers (-/1), narcotic analgesic (-/1), physical therapy (-/1)
	Neuropathic pain (-/2)	Physical therapy (-/2), painkillers (-/1), related expert support (-/1), algorithm based treatment (-/1)
	Gastrointestinal pains (-/2)	Painkillers (-/1), narcotic analgesic (-/1), massage (-/1), exercise (-/1)
	Vascular pain (-/2)	Painkillers (-/1), narcotic analgesics (-/1)
	Positional pain (-/1)	Painkillers (-/1), positioning (-/1), hot/cold application (-/1), massage (-/1)
	Regional pain (-/1)	Painkillers (-/1), narcotic analgesics (-/1)

f: Frekans, (..../....): Number of physicians working in government institutions supporting the relevant theme or code/number of physicians working in private institutions supporting the relevant theme or code

Table 2. Problems related to the gastrointestinal system in the palliative care process in overnment and private health institutions and solution proposals

Theme		Code
Gastrointestinal system	**Problem (*f*)**	**Solution (*f*)**
	Constipation (8/7)	Medication (5/4), exercise (2/6), surgical intervention (2/2), laxative agents (2/2), dietitian support (4/-), massage (1/-), nutritional support product (2/-), follow-up fluid balance (-/1), increasing oral fluid intake (1/2), consultation (-/1)
	Diarrhea (2/6)	Dietitian support (1/4), medication (1/3), follow-up fluid balance (-/2), increasing oral fluid intake (-/2), consultation (-/1), hygiene (-/1)
	Gas and bloating (3/4)	Medication (2/3), dietitian support (1/3), exercise (-/1), consultation (-/1)
	Indigestion (4/-)	Dietitian support (3/-), exercise (1/-)
	Oral/dental problems (-/3)	Daily oral care (-/3), dentist support (-/2)
	Dyspepsia (2/-)	Medication (2/-)
	Low oral intake (1/-)	Dietitian support (1/-)
	Acid reflux (1/-)	Medication (1/-)

f: Frekans, (..../....): Number of physicians working in government institutions supporting the relevant theme or code/number of physicians working in private institutions supporting the relevant theme or code

painkillers, physical therapy, and hot-cold applications, we perform alternative medicine applications such as mesotherapy and ozone" (PP2).

The problems related to the gastrointestinal system were constipation, diarrhea, gas, and bloating. Additionally, the problems and solutions in government and private health institutions were similar in terms of constipation, bloating, and gas, whereas they differed in terms of diarrhea and oral/dental problems (Table 2). Sample expressions are listed below:

"The most common gastrointestinal problem in bedridden elderly patients is constipation. Additionally, we encountered diarrhea, gas, and bloating complaints. In this case, we applied treatments such as medication, dietitian support, laxative agents, and increasing oral fluid intake" (GP4).

"The most common condition we encounter is constipation. Therefore, we recommend dietitian support, drug combinations, laxative agents, increasing oral fluid intake, and in-bed exercises (PP4).

The problems related to nutrition and solutions were concentrated on swallowing difficulties, loss of appetite, chewing problems, nutritional disorders, and weight loss. Within the context of nutrition, the problems and intensities

Table 3. Nutritional problems in the palliative care process in government and private health institutions and solution proposals

Theme		Code
Nutrition	**Problem (*f*)**	**Solution (*f*)**
	Swallowing difficulty (6/5)	PEG (5/3), dietitian support (4/3), nutritional support product (4/1), nasogastric nutrition (1/3), enteral nutrition (3/-) oral aqueous food (1/1), parenteral nutrition (1/1), nutrition monitoring (1/-), specialist nurse support (-/1)
	Loss of appetite (5/4)	Dietitian support (1/3), nutritional support product (1/2), vitamin-mineral supplement (1/-), weight monitoring (-/1), specialist nurse support (-/1), psychologist support (-/1))
	Chewing difficulty (4/5)	PEG (1/2) nutritional support product (1/2), enteral nutrition (1/-), weight monitoring (-/1), specialist nurse support (-/1)
	Nutritional disorder (4/4)	Dietitian support (2/2), nutritional support product (1/2), peg (1/1), specialist nurse support (-/1), snack (-/1), nutrition follow-up (-/1)
	Weight loss (3/4)	Nutritional support product (2/1), dietitian support (1/2), vitamin-mineral supplement (1/-), psychologist support (-/1), snack (-/1), weight monitoring (-/1), specialist nurse support (-/1)
	Temporary swallowing function (-/2)	Dietitian support (-/2) nutritional support product (-/1), internal medicine specialist support (-/1)
	Food refusal (-/1)	Psychologist support (-/1), snack (-/1)

PEG: Percutaneous endoscopic gastrostomy, *f*: Frekans, (..../....): Number of physicians working in government institutions supporting the relevant theme or code/number of physicians working in private institutions supporting the relevant theme or code

Table 4. Problems related to oncology patients in the palliative care process in government and private health institutions and solution proposals

Theme		Code
Oncology patients	**Problem (*f*)**	**Solution (*f*)**
	General pain (4/9)	Algorithmic pain treatment (1/3), medication (1/1), narcotic analgesic (1/1), consultation (1/-), psychologist support (-/1), psychiatrist support (-/1), neurologist support (-/1), physiotherapy (-/1)
	Chemotherapy-related side effects (4/3)	Medication (1/2), consultation (1/-), specific treatment (1/-), dietitian support (1/-), psychologist support (-/1), psychiatrist support (-/1)
	Nausea (3/3)	Medication (1/2), specific treatment (1/-), dietitian support (1/1), consultation (1/-)
	Nutritional disorder (2/2)	Parenteral nutrition (1/1), PEG (1/-), ng probe (1/-), nutrition monitoring (-/1)
	Loss of appetite (1/3)	Consultation (1/-), medication (-/1), nutrition monitoring (-/1)
	Vomiting (2/1)	Specific treatment (1/-), dietitian support (1/1), consultation (1/-), medication (-/1)
	Psychiatric disorders (1/2)	Socialization support (-/2), referral to a specialist (1/-)
	Movement restriction (1/2)	Physical therapy support (1/1), psychologist support (-/1)
	Radiotherapy-induced pain (1/1)	Painkillers (1/1), narcotic analgesic (1/-)
	Decubitus ulcers (-/1)	Wound care (-/1), oncologist support (-/1), psychiatrist support (-/1), psychologist support (-/1)
	Neuropathy (1/-)	Neurologist support (1/-), algologist support (1/-)

f Frekans, PEG: Percutaneous endoscopic gastrostomy, ng probe: Nasogastric Probe (..../....): Number of physicians working in government institutions supporting the relevant theme or code/number of physicians working in private institutions supporting the relevant theme or code

experienced in government and private health institutions were similar, but the solution proposals differed (Table 3). Sample expressions are presented below:

"With regard to nutrition, we usually observe difficulty in swallowing, loss of appetite, nutritional disorder, and weight loss. As a solution, we recommend percutaneous endoscopic gastrostomy (PEG) or enteral nutrition. We receive dietitian support or recommend nutritional support products" (GP3).

"The nutritional problems we experience in elderly patients include loss of appetite, difficulty in swallowing, chewing problems, and weight loss. When necessary, we can recommend nutritional support products, nasogastric nutrition, and nutrition with PEG. We can obtain relevant specialist and dietitian support" (PP6).

The problems experienced in the palliative care process of oncology patients and solution proposals were concentrated on general pain, side effects due to chemotherapy, nausea, nutritional disorder, and loss of appetite. There was a difference between government and private health institutions in terms of the intensity of the general pain problem, whereas there were similarities in terms of the intensity of other problems (Table 4). Sample expressions are listed below:

Table 5. Problems related to chronic diseases in the palliative care process in government and private health institutions and solution proposals

Theme		Code
Chronic diseases	**Problem (*f*)**	**Solution (*f*)**
	Diabetes (7/8)	Routine treatment (3/5), laboratory (5/1), dietitian support (2/3), consultation (3/-), endocrine support (-/2), neurologist support (-/2), psychologist support (-/2), positioning (1/-)
	Hypertension (5/7)	Routine treatment (4/4), blood pressure monitoring (4/2), dietitian support (2/2), consultation (3/-), endocrine support (-/3), neurologist support (-/3), psychologist support (-/2) positioning (1/-), vitamin D support (-/1)
	Cardiovascular diseases (5/6)	Routine treatment (3/3), cardiologist support (-/4) laboratory (3/-), dietitian support (2/1), endocrine support (-/3), neurologist support (-/3), psychologist support (-/3), consultation (2/-), radiology (1/-), positioning (1/-), ambulance support (-/1)
	Osteoporosis (2/5)	Routine treatment (-/4), gynecologist support (-/2), consultation (1/-), dietitian support (1/1), vitamin D support (-/1),
	Osteoarthritis (2/5)	Routine treatment (-/3), dietitian support (1/1), consultation (1/-), vitamin D support (-/1)
	Movement restriction (1/-)	Consultation (1/-), dietitian support (1/-)
	Multiple drug use (1/-)	Consultation (1/-)

f: Frekans, (..../....): Number of physicians working in government institutions supporting the relevant theme or code/number of physicians working in private institutions supporting the relevant theme or code

Table 6. Problems related to neuropsychiatry in the palliative care process in government and private health institutions and solution proposals

Theme		Code
Neuropsychiatry	**Problem (*f*)**	**Solution (*f*)**
	Depression (5/8)	Psychologist support (4/6), psychiatrist support (1/6), medication (1/4), family education (1/-), medication use information (1/-), social activity (-/1), family psychologist support (-/1)
	Fear of death (5/8)	Psychologist support (4/6), family psychologist support (2/3), medication (1/4), psychiatrist support (1/4), consultation (1/-), medication use information (1/-)
	Intense anxiety (4/6)	Psychologist support (4/4), medication (2/3), psychiatrist support (-/4), family psychologist support (1/2), family psychiatrist support (-/2), consultation (1/-)
	Loneliness (2/4)	Psychologist support (3/3), psychiatrist support (1/2), medication use information (1/-), medication (-/1), social activity (-/1)
	Delirium (2/2)	Medication (2/2), psychologist support (1/1), family psychologist support (1/1), consultation (1/-), family education (1/-), social activity (-/1)
	Sleeping disorder (1/3)	Medication (1/1), psychiatrist support (-/2), family education (1/-), psychologist support (-/1)
	Intense hallucination (1/-)	Neurologist support (1/-), psychologist support (1/-)
	Memory problems (1/-)	Medication (1/-), family education (1/-)

f: Frekans, (..../....): Number of physicians working in government institutions supporting the relevant theme or code / Number of physicians working in private institutions supporting the relevant theme or code

"General pain and chemotherapy-related side effects are common problems in oncology patients. Nausea, vomiting, and loss of appetite are common complaints. As in pain treatment, we use painkillers and receive support from algologists and neurologists" (GP1).

"The pain management of such patients is essential. These patients may also have social and psychological needs during treatment. In addition to drug treatment, socialization and psychologist support may be required" (PP7).

When the findings related to the theme of chronic diseases were examined, the problems and solution suggestions in the palliative care process focused on diabetes, hypertension, and cardiovascular diseases. The problems experienced within the scope of this theme are more common in private health institutions in general (Table 5). Sample expressions are given below:

"Chronic diseases such as heart failure, hypertension, and diabetes are generally in all our patients. We apply routine treatments, follow-up, and consultation when necessary" (GP3).

"Chronic diseases are the underlying diseases of our palliative care patients. These include hypertension, diabetes, and heart disease. For the solution, we plan treatment in line with the recommendations of our endocrine, neurology, gynecology, and cardiology specialists" (PP4).

Within the scope of the neuropsychiatry theme, the problems experienced in the palliative care process and solutions were concentrated on depression, fear of death, intense anxiety, and loneliness, which were more common in private health institutions (Table 6). Sample expressions are presented below:

"Neuropsychiatric complaints are quite common. Depression, fear of death, sleep disorders, and delirium are the most common complaints. We often administer medication, and when necessary, we receive support from a psychologist or psychiatrist for the patient and his family" (GP8).

"I have observed sleep disorders, depression, anxiety, delirium attacks, and fear of death. In this case, in addition to drug treatment, we provide both psychologist and psychiatrist support to the patient and his family" (PP7).

Discussion

When the results were evaluated in general, the most common problems were seen to be due to chronic diseases in the palliative care process, followed by neuropsychiatric and pain-related problems.

In a study conducted by Göksel et al. (12), the most common diagnosis of hospitalization in palliative care centers was oncological diseases (35%), neurological diseases (22%), and chronic diseases (11%), while pain was the most common symptom (25%). Although these results are similar to our results, they differ in terms of the frequency of the problems, which can be explained by the difference in the study groups of the two studies.

The results of our study are consistent with the conclusion that neuropsychiatric disorders such as depression and anxiety are important problems encountered in the palliative care process in a study conducted by Jacobsen et al. (13). These results suggest that patients treated with palliative care need psychiatric support throughout the process.

Similar to our study, in the studies conducted by Gültekin et al. (14) and Henson et al. (15), one of the reasons why patients needed palliative care was pain. These results indicate that pain is one of the most important problems in the palliative care process.

In our study, in addition to the problems experienced intensively in the palliative care process, nutrition, oncology, and gastrointestinal system-related problems were also experienced. Similarly, in a study conducted by Güler Bayındır et al. (16) one of the reasons for the hospitalization of palliative care patients was found to be nutritional problems.

When the relevant literature is examined, the majority of patients in palliative care centers were elderly people with cancer which is consistent with our results (17-20). In a study conducted by Komaç et al. (21) the result that 33% of patients in the palliative care service had oncology-related problems supports our study results. This may be because palliative care practices were initiated with the aim of reducing the pain and care of cancer patients (22), as well as revealing the similarity of the problems experienced in the palliative care process in different societies.

In our study, disease-specific treatment came to the forefront in the solution of problems arising from chronic diseases, whereas medication and related specialist support came to the forefront in the solution of problems arising from pain, oncology, and the gastrointestinal system. Consistent with these results, in the study conducted by Yılmaz and Bahat (23), the use of analgesics was the most commonly used strategy in the management of pain in older adults. In another study, Ankay Yılbaş and Çelebi (24) stated that analgesics were frequently used with antidepressant drugs to improve the quality of life by reducing the level of pain felt by a terminal patient, and that psychiatric support should be provided to patients without sufficient social and familial support.

In our study, it was observed that dietitian support was adopted for the solution of nutrition-related problems, and psychologist or psychiatrist support was mostly adopted as a solution for neuropsychiatry-related problems. In line with this result, the study conducted by Kaya (25), suggested that patients in the

palliative service should receive consultation support from other clinicians, and support services should be provided to patients and their relatives with psychiatrists, psychologists, moral support units, physiotherapists, and social workers. Suggesting similar solution proposals in our research and other studies on the problems experienced in the palliative care process shows the consistency of the research results.

Study Limitations

Our study has some strengths and limitations. The strength of our research is that physicians, who are one of the stakeholders of the palliative care team, which is a multidisciplinary health service that includes functional and emotional care and support, reveal their opinions in a holistic and in-depth manner regarding the problems experienced in the palliative care process and solution proposals. On the other hand, the limitation of the research is the scarcity of physicians included in the study and the research findings consisting only of physicians' opinions.

Conclusion

According to the results of our study, patients in the palliative care process experience multiple problems, and an individualized approach should be adopted as a result of a comprehensive evaluation with a multidisciplinary team to solve these problems. Multiple problems experienced in the palliative care process result in multiple solution proposals, which reveals the importance of cooperation between specialists and increasing the number of physicians working in palliative care centers/services. In addition, the acceptance of palliative care as a specialty will make palliative care services more professional and enable patients receive more qualified health care.

Acknowledgements

We thank the physicians who voluntarily participated in this study.

Ethics

Ethics Committee Approval: The study was approved by the Medical Research Ethics Committee of Ege University (approval number: E-99166796-050.06.04-994509) and was conducted in accordance with the principles of the Declaration of Helsinki.

Informed Consent: Informed consent was obtained from all participants.

Authorship Contributions

Concept: A.G.Ş., A.K., Design: A.G.Ş., A.K., Data Collection or Processing: A.G.Ş., A.K., Analysis or Interpretation: A.G.Ş., Literature Search: A.G.Ş., A.K., Writing: A.G.Ş., A.K.

Conflict of Interest: No conflicts of interest were declared by the authors.

Financial Disclosure: This research received no external funding. This study is related to the topic of a doctoral thesis.

References

1. Hebert K, Moore H, Rooney J. The Nurse Advocate in End-of-Life Care. Ochsner J 2011;11:325-329.
2. Kabalak AA, Öztürk H, Çağıl H. End of life care organization; palliative care. Yoğun Bakım Dergisi 2013;11:56-70.
3. Pastrana T, Jünger S, Ostgathe C, Elsner F, Radbruch L. A matter of definition--key elements identified in a discourse analysis of definitions of palliative care. Palliat Med 2008;22:222-232.
4. Meier D, McCormick E. Benefits, Services, and Modes of Subspecialty Palliative Care; Available at: 2015.
5. World Helath Organization. Available at: https://www.who.int/cancer/palliative/definition/en/ (Accessed on April 16, 2023)
6. Sertdemir Batbaş C, Yakar B, Pirinçci E. Palliative care and hospice. STED 2021;30:136-143.
7. Sağlık Bakanlığı. Palyatif Bakım Hizmetleri. Available at: https://khgmozellikli.saglik.gov.tr/svg/palyatif.php (Accessed on May 21, 2023)
8. WPCA (Worldwide Palliative Care Alliance). Global Atlas of Palliative Care at the End of Life. London: WHO; 2014.
9. Shoemaker LK, Estfan B, Induru R, Walsh TD. Symptom management: an important part of cancer care. Cleve Clin J Med 2011;78:25-34.
10. Miles MB, Huberman AM. Qualitative Data Analysis: An Expanded Sourcebook. Thousand Oaks, CA: Sage Publications 1994.
11. Tavşancıl E, Aslan AE. İçerik analizi ve uygulama örnekleri. İstanbul: Epsilon Yayınlar 2001.
12. Göksel F, Şenel G, Oğuz G, Özdemir T, Aksakal H, Türkkanı MH, Küçük A, Eğin ME, Gultekin M, Silbermann M. Development of palliative care services in Turkey. Eur J Cancer Care (Engl) 2020;29:e13285.
13. Jacobsen R, Liubarskiene Z, Møldrup C, Christrup L, Sjøgren P, Samsanaviciene J. Barriers to cancer pain management: a review of empirical research. Medicina (Kaunas) 2009;45:427-433
14. Gültekin M, Özgül N, Olcayto E, Tuncer M. Türkiye'de palyatif bakım hizmetlerinin mevcut durumu. Türk Jinekolojik Onkoloji Dergisi 2010;13:1-6. [Turkish]
15. Henson LA, Maddocks M, Evans C, Davidson M, Hicks S, Higginson IJ. Palliative Care and the Management of Common Distressing Symptoms in Advanced Cancer: Pain, Breathlessness, Nausea and Vomiting, and Fatigue. J Clin Oncol 2020;38:905-914.
16. Güler Bayındır A, Tuncer Ö, Demiralın MÖ, Erdoğan i, Gündemir M, Işıl AM. Evaluation of palliative care patients: single center experience. Medical Journal of İzmir Hospital 2020;24:207-212.
17. Morrison RS, Meier DE. Clinical practice. Palliative care. N Engl J Med 2004;350:2582-2590.
18. Adsersen M, Thygesen LC, Neergaard MA, Bonde Jensen A, Sjøgren P, Damkier A, Groenvold M. Admittance to specialized palliative care (SPC) of patients with an assessed need: a study from the Danish palliative care database (DPD). Acta Oncol 2017;56:1210-1217.
19. Gomes B, Pinheiro MJ, Lopes S, de Brito M, Sarmento VP, Lopes Ferreira P, Barros H. Risk factors for hospital death in conditions needing palliative care: Nationwide population-based death certificate study. Palliat Med 2018;32:891-901.
20. Robinson J, Gott M, Frey R, Ingleton C. Circumstances of hospital admissions in palliative care: A cross-sectional survey of patients admitted to hospital with palliative care needs. Palliat Med 2018;32:1030-1036.
21. Komaç A, Elyiğit F, Türemiş C, Gram E, Akar H. Retrospective analysis of hospitalized patients in Tepecik Training and Research Hospital Internal Medicine Palliative Care Unit. FNG & Bilim Tıp Dergisi 2016;2:1-3.

22. Koç A. Palliative care in Turkish medical history. Journal of Anesthesia–JARSS 2021;29:159-164.

23. Yılmaz O, Bahat G. Yaşlıda hastane temelli palyatif bakım ve hospis. (Editör: Naharcı, M. İ.) Yaşlının Hastanedeki Serüveni. 1. Baskı. Ankara: Turkiye Klinikleri 2019;32-44.

24. Ankay Yılbaş A, Çelebi N. Pain management and difficulties in palliative care. Journal of Anesthesia–JARSS 2014;22:124-134.

25. Kaya A. Türkiye'de ve Dünya'da palyatif bakım. Acıbadem Hemşirelik Dergisi 2015;82.

ORIGINAL RESEARCH

DOI: 10.4274/ejgg.galenos.2023.2023-8-4
Eur J Geriatr Gerontol 2024;6(1):39-45

Determination of Dysphagia with Different Tools in Turkish Nursing Home Residents

Emine Sumru Savaş[1], Numan Demir[2], Asli Kilavuz[1], Zeliha Fulden Saraç[1]

[1]Ege University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics,, İzmir, Turkey
[2]Hacettepe University Faculty of Physical Therapy and Rehabilitation, Ankara, Turkey

Abstract

Objective: The eating assessment tool-10 (EAT-10) is a self-administered questionnaire for dysphagia screening. Whether EAT-10 is a convenient tool for screening swallowing problems in nursing home residents is debatable. The Yale swallow protocol (YSP) is an easily administered, reliable, and validated swallow screening protocol. The aim of this study was to assess dysphagia using EAT-10 and YSP in nursing home residents.

Materials and Methods: Residents without eating or cognitive problems were enrolled in the study. The EAT-10, YSP, mini-nutritional assessment-short form, body mass index, hospitalizations for any reason/pneumonia-associated hospitalizations in the last year, comorbidities, and diet type were evaluated.

Results: Ninety-nine residents were enrolled in this study. Dysphagia risk was 31.3% with EAT-10 and 18.2% with YSP. There was a fair agreement between EAT-10 and YSP. Dysphagia defined by YSP was associated with malnutrition risk.

Conclusion: The risk of dysphagia in nursing home residents without documented prior swallowing disorder or complaints was high and variable with different tools, where self-reported dysphagia was higher. Nutritional status was associated with YSP-defined dysphagia risk but not with EAT-10.

Keywords: Aged, nursing home, dysphagia, eating assessment Tool-10, Yale swallow protocol

Introduction

Dysphagia is a frequent health problem in the aging population, and it is becoming more critical as the population ages worldwide (1). Dysphagia's potential consequences include aspiration pneumonia, ranking as the second most prevalent infection among residents of nursing homes (2,3). It may also lead to malnutrition, dehydration, and social-emotional problems (4,5). Swallowing difficulty increases with aging, and the significance of dysphagia in frail older adults is more substantial because it may be life-threatening (6). Dysphagia is a spectrum of disorders experienced during the passage of food from the mouth to the stomach (7). In a review with a comprehensive literature search, in long-term care residents, the occurrence of dysphagia has been documented with varying rates, ranging from 7% to 40% (8). It is not detected routinely and systematically despite severe complications and high prevalence (9). If detected, the prevalence may be diverse in different settings and populations with different screening and/or assessment methods, depending on the executor. Videofluoroscopic swallowing study (VFSS) and fiberoptic endoscopic evaluation of swallowing (FEES) provide dynamic imaging of swallow function. However, they are invasive and require specialized equipment and qualified personnel (6). Screening methods are necessary to identify people at risk of aspiration or malnutrition and to rapidly identify and refer to patients with dysphagia for further evaluation (9). However, performing further studies in older patients with low functionality might not always be practical. The eating assessment tool-10 (EAT-10) is a self-administered questionnaire designed to screen for dysphagia across diverse clinical settings, accommodating the broad spectrum of underlying causes (9,10). A systematic review suggested the

Address for Correspondence: Asli Kilavuz, Ege University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics,, İzmir, Turkey
Phone: +90 532 353 65 70 **E-mail:** asli.kilavuz@ege.edu.tr **ORCID:** orcid.org/0000-0002-0474-9911
Received: 20.08.2023 **Accepted:** 18.09.2023

Cite this article as: Savaş ES, Demir N, Kilavuz A, Saraç ZF. Determination of Dysphagia with Different Tools in Turkish Nursing Home Residents. Eur J Geriatr Gerontol 2024;6(1):39-45

use of bedside clinical assessments involving liquids, such as water, alongside oximetry as a recommended approach for identifying individuals with dysphagia (11). The Yale swallow protocol (YSP) is a validated bedside screening protocol known for its user-friendly administration, reliability, non-invasive nature, and incorporation of a concise cognitive assessment (12-16). Research evaluating dysphagia in Turkish nursing home residents with any tool is scarce to date. In addition, the suitability of the EAT-10 as a convenient tool for screening swallowing issues among nursing home residents remains a subject of debate. The difference between the two screening tools is that the EAT-10 is a self-administered, symptom-specific screening tool that assesses dysphagia only in a questionnaire style, whereas the YSP is a three-step test used to determine the risk of aspiration by having individuals drink water in addition to the questionnaire. Because YSP is a validated tool and there is no study investigating dysphagia with EAT-10 in comparison with YSP at nursing homes in the literature, we aimed to explore dysphagia with EAT-10 and YSP in Turkish nursing home residents.

Materials and Methods

This was a cross-sectional study. Residents of a nursing home in İzmir, Turkey, were screened in two weeks in September 2018. Residents aged 60 years and older, participants conscious enough to answer the questions, and those who can consume water or receive food orally, such as aqueous food or normal food, were included in the study. Older individuals with pre-existing swallowing difficulty, enteral tube feeding, head position restrictions in bed, and tracheostomy tube were excluded. Besides, the residents who did not want to join the study and residents with a negative "brief cognitive screen" were also excluded from the study. All of the assessments were performed by two medical doctors who were trained for the protocols (12,13).

Measures

Diet (regular diet, use of a thickener, oral nutritional supplement, soft diet), number of hospitalizations in the last 12 months, hospitalizations with pneumonia diagnosis in the last 12 months, and comorbidities were noted. The EAT-10 screening test was applied to all participants (9,10). Afterwards, YSP was performed for the residents.

The EAT-10 questionnaire comprises 10 items, with each item scored on a scale of 0 to 4. A score of 0 denotes "no problem", while a score of 4 signifies a "severe problem". An EAT-10 score of ≥3 indicates the existence of swallowing challenges (9,10). The EAT-10 is validated in adult Turkish patients (4).

The YSP is a dependable and validated bedside screening tool for assessing the risk of aspiration. It encompasses a concise cognitive assessment, an examination of the oral mechanism, and a 3-ounce water swallow challenge. This challenge involves drinking water from a cup or straw, with observed reactions such as coughing, choking, and voice alterations serving as endpoints (14-18). Successful completion of the YSP necessitates sufficient cognitive capacity and proper oral function to engage in uninterrupted water consumption without experiencing coughing either during the act or immediately after finishing the 3-ounce intake (17). Failure criteria for YSP include interrupted drinking, an inability to consume the entire quantity, or the occurrence of coughing during or shortly after drinking (17). The concise cognitive evaluation consists of inquiries like "what is your name?," "where are you currently?," and "what year is it?" (15,17). Participants with one or more omitted or incorrect responses were not included in the study.

Body mass index was equal to weight divided by the square of height (kg/m^2).

Nutritional status was evaluated using the mini nutritional assessment-short form (MNA-SF) (19). The MNA-SF comprises 6 questions, with the cumulative score ranging from 12 to 14 indicating a normal nutritional status, 8 to 11 points suggesting a risk of malnutrition, and 0 to 7 points indicating malnourishment. The Turkish validity of the scale was proved by Sarıkaya (20).

The study received approval from the Ethics Committee of Ege University (approval number: 70198063-050.06.04, date: 19.04.2018) and was conducted in alignment with the ethical guidelines outlined in the Declaration of Helsinki. Informed consent was obtained from all participants.

Statistics

Statistical analyzes were conducted using IBM SPSS Statistics 25.0 software. Numeric data are reported as mean ± standard deviations, and as medians and minimum-maximum values where available. Data normality was assessed using the Shapiro-Wilk test. Categorical variables are presented as frequencies and percentages. To assess the distinctions between the two groups divided by EAT-10 scores (0-2 and 3-4) and YSP scores (successful and unsuccessful), the chi-square test and Mann-Whitney U test were employed. The agreement between EAT-10 and YSP was evaluated by the Kappa coefficient. Binary logistic regression analysis was used to identify potential risk factors associated with dysphagia. Statistical significance was established at a p value of <0.05.

Results

Out of 181 residents, those who did not want to join the study (n=15), those with preexisting swallowing difficulty (n=5), and those with a negative "brief cognitive screen" (n=62) were excluded. Finally, 99 residents were enrolled in the study

(Figure 1). More than half of the residents were female (63.6%) and over 75 years of age (60.6%). As there were no residents with thickener use or oral nutritional supplement intake in our study group, the diet of the participants was classified into two groups: a regular and soft diet. Only 40% of the residents were evaluated as having normal nutritional status. The risk of dysphagia was observed in 31.3% of the residents with EAT-10 and 18.2% of the residents with YSP. The characteristics of the participants are shown in Table 1.

The median MNA-SF score was lower, and the number of residents at risk of malnutrition was higher among residents at risk for dysphagia with YSP (p=0.009, and p=0.023, respectively) than among residents not at risk for dysphagia with YSP. A higher number of residents at dysphagia risk with EAT-10 were on a soft diet than residents without dysphagia risk (p=0.032). No other significant relationship was observed among YSP, EAT-10, and other variables (Table 2).

A moderate level of concurrence was observed between EAT-10 and YSP (κ=0.231, p=0.014). In the binary logistic regression analysis, dysphagia defined by YSP was associated with nutritional status, and residents at risk of malnutrition had four times more swallowing problems diagnosed with YSP (odds ratio, 4.205, 95% confidence interval 1.129-15.652, p=0.032). The risk of dysphagia with EAT-10 was not associated with any of these factors. The number of "hospitalizations for any reason" and "pneumonia-associated hospitalizations" in the last year were similar among older patients with and without dysphagia risk by both instruments (Table 2).

Discussion

We report that dysphagia risk in Turkish nursing home residents was variable with EAT-10 and YSP, and the agreement among the tools was fair. Poor nutritional status was associated with dysphagia risk with YSP alone.

In our study, dysphagia risk was found in 31.3% of residents with EAT-10. Similar to our study, in a systematic review, the combined prevalence of three studies screening for dysphagia with EAT-10 in nursing homes was reported as 36.11% (21). Although there has been no validation study of the EAT-10 in the identification of dysphagia in older adults, this questionnaire has been the most frequently used questionnaire in the included studies.

The risk of dysphagia did not differ according to the older age group (≥75 years) in our study with both instruments, although the effect of aging on swallowing function has been described in previous studies, with a higher impact in the oldest age group (22,23). Dysphagia is defined higher in patients with functional declines and comorbidities, although there are studies that are not able to show the association of dysphagia and comorbidities in accordance with our results (24,25). The insignificance of age and other variables may have occurred because of the sample size of this study. Dysphagia is a highly prevalent clinical finding in older patients with pneumonia, and nearly half of nursing home residents with dysphagia have been reported to develop aspiration pneumonia in the last year (26-28). EAT-10 may also provide useful information on aspiration risk (29). However, the number of hospitalizations for any reason and pneumonia-associated hospitalizations in the last year were similar among older patients with and without dysphagia risk by both instruments in our study. This may be due to the retrospective design of the study. An evident connection emerged between dysphagia and malnutrition, both among nursing home residents and individuals residing in assisted-living facilities (30). In a systematic review (31), impaired functioning and swallowing challenges were the factors consistently linked to inadequate nutrition among nursing home residents. In a review by Zhang et al. (32), it was reported that dehydration, malnutrition, and aspiration pneumonia were among the common complications of dysphagia. Furthermore, in a recent study, EAT-10 was found to correlate with the nutritional status of older individuals in need of long-term care (33). Tagliaferri et al. (34) noted that 37.8% of individuals at risk of dysphagia experienced malnutrition, and their study demonstrated a significant and negative correlation between EAT-10 and MNA-SF scores. In our study, most residents exhibited vulnerability to malnutrition. Nonetheless, although an association between dysphagia risk and poor nutritional status was observed solely with YSP, not EAT-10, our knowledge base lacks any prior studies delving into the connection between YSP and the risk of malnutrition.

Distinguishing patients with dysphagia involves a range of methods, including assessments, interviews, observation of indicative cues, and trials involving swallowing (6,11). The prevalence of dysphagia in older persons may particularly vary according to the instrument used, depending on whether it is a screening questionnaire or a clinical examination such as volume viscosity swallowing test (VVST), and depending on

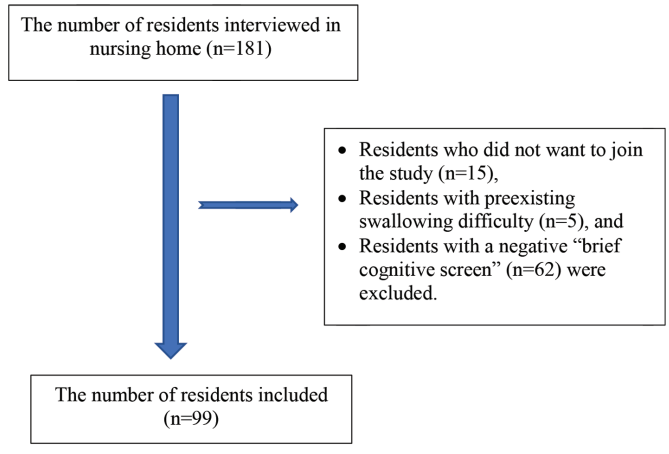

Figure 1. Flow chart for the participants included in the study

the settings, comorbidities present, and the sample chosen. The prevalence ranges from 27% to 91% in different settings with varying characteristics in older people (24). It has been shown that most older persons who live in elderly care centers do not benefit from the correct diagnosis and/or treatment of dysphagia (35). To be practical for use by nurses within nursing homes, the tool should exhibit simplicity by comprising fewer items, minimizing the need for extensive training. EAT-10 determines self-perceived dysphagia symptoms of patients (4,11,36). Research investigating dysphagia in nursing homes and long-term care facilities with YSP is scarce (37), although there are various studies with the same or different amounts of water (12,14,38). In a recent study, Greek-EAT-10 and FEES scores were significantly correlated (39). On the other hand, a recent study has highlighted potential shortcomings in the construct validity of EAT-10, prompting a consideration for enhancing the instrument to enhance its suitability for regular application in both clinical settings and research endeavors (40). In a study from a nursing home in Turkey, dysphagia was investigated with EAT-10 and 100 cc water drinking test (41). There was no patient identified to be at risk for dysphagia in the aforementioned study, and there are many methodological issues such as defining dysphagia with scores ≥2 for EAT-10 (41). In the present study, dysphagia risk was higher with EAT-10 (31.3%) than with YSP (18.2%) among Turkish nursing home residents, and a moderate level of concurrence was observed between EAT-10 and YSP. Likewise, the prevalence of dysphagia varies by screening questionnaires (11.4% to 33.7%) and by clinical explorations such as VVST (23%) in community-living older adults (42). However, we could not locate other studies comparing EAT-10 and YSP in the literature in relation to dysphagia in nursing home residents. Nevertheless, in a recent study using VFSS as a reference standard, both EAT-10 and VVST as clinical bedside assessments were shown to discriminate dysphagia (9). In addition, in a very recent study from Turkey, the gugging swallowing screen was shown to correlate negatively with EAT-10 in healthy older people (43). In a cohort study, YSP was

Table 1. Characteristics of nursing home residents

Variables		Total population (n=99)
Age, years (range)[a]		76.2±7.7 (62-98)
Age groups, n (%)	<75 years	39 (39.4)
	≥75 years	60 (60.6)
Female, n (%)		63 (63.6)
BMI, kg/m^{2}[a]		27.1±4.9
Number of comorbidities		1.2±0.9
Diabetes mellitus, n (%)		13 (13.1)
Hypertension, n (%)		44 (44.4)
Coronary artery disease, n (%)		15 (15.2)
Cerebrovascular disease, n (%)		13 (13.1)
Other diseases, n (%)[b]		28 (28.3)
EAT-10 score[a]		2.5±3.8
MNA-SF score[a]		10.9±2.0
Hospitalization for any reason in the last year, n (%)		27 (27.3)
Pneumonia-associated hospitalization in the last year, n (%)		5 (5.1)
EAT-10 categories, n (%)	Score ≥3	31 (31.3)
	Score <3	68 (68.7)
Yale swallow protocol, n (%)	Unsuccessful	18 (18.2)
	Successful	81 (81.8)
Nutritional status, n (%)[c]	Normal nutritional status	40 (40.4)
	At-risk	53 (53.5)
	Malnourished	6 (6.1)
Diet, n (%)	Soft diet	5 (5.1)
	Regular diet	94 (94.9)

BMI: Body mass index, EAT-10: Eating assessment tool-10, MNA-SF: Mini nutritional assessment-short form
[a]Values are given as means (± standard deviations), [b]Other diseases: Fracture, thyroid disease, depression, renal failure, gastroesophageal reflux disease, chronic obstructive pulmonary disease, [c]MNA-SF scores from 0 to 7 points indicate malnutrition, scores >7 to 11 indicate the risk of malnutrition

established as a valid and dependable tool within post-acute care settings, encompassing long-term care facilities (37). Furthermore, in a recent assessment of dysphagia screening methods in residential care contexts, YSP emerged as one of the instruments characterized by exceptional diagnostic accuracy values (44).

Study Limitations

Among the limitations of this study are the relatively modest participant count and the absence of validation for dysphagia diagnosis via assessment techniques such as VFSS and FEES. The strength of this study is that it is the first study to investigate dysphagia with EAT-10 and YSP comparatively at nursing homes in the literature.

Conclusion

The risk of dysphagia exhibited variations depending on the assessment tools employed, with EAT-10 and YSP demonstrating a moderate level of agreement. Although there is no consensus on how to identify dysphagia in nursing homes, poor nutritional status was associated with only dysphagia screened by YSP in our study. There were no swallowing disorder complaints in the older residents enrolled in our study, and the presence of dysphagia risk reveals the importance of evaluating swallowing disorders with simple screening tools such as EAT-10 and YSP. The predictive values of the YSP and self-reported EAT-10 questionnaire need to be studied with prospective studies.

Table 2. Characteristics of nursing home residents in relation to dysphagia risk by EAT-10 and YSP

Variables	EAT-10 score <3 (n=68)	EAT-10 score ≥3 (n=31)	p	YSP (successful) (n=81)	YSP (unsuccessful) (n=18)	p
Age, years[a]	76.25 (62-98)	75.97 (62-95)	0.907	75.95 (62-95)	77.11 (65-98)	0.696
Age groups, n (%)						
<75 years of age	29 (42.6)	10 (32.3)	0.380	33 (40.7)	6 (33.3)	0.606
≥75 years of age	39 (57.4)	21 (67.7)		48 (59.3)	12 (66.7)	
Gender, n (%)						
Female	42 (61.8)	21 (67.7)	0.655	51 (63.0)	12 (66.7)	1.000
Male	26 (38.2)	10 (32.3)		30 (37.0)	6 (33.3)	
BMI, kg/m²[a]	26.7 (17.8-42.0)	27.9 (17.8-38.3)	0.182	27.0 (17.8-42.0)	24.9 (19.6-31.7)	0.081
MNA-SF score[a]	11 (2-14)	11 (5-14)	0.546	11 (2-14)	10.5 (5-12)	0.009
Diabetes mellitus, n (%)	10 (14.7)	3 (9.7)	0.749	13 (16.0)	0 (0)	0.118
Hypertension, n (%)	17 (54.8)	27	0.193	37 (45.7)	7 (38.9)	0.794
CAD, n (%)	12 (17.6)	(39.7)	0.378	13 (16)	2 (11.1)	0.732
CVD, n (%)	10 (14.7)	3 (9.7)	0.749	11 (13.6)	2 (11.1)	1.000
Other diseases, n (%)[b]	17 (25)	11 (35.5)	0.338	25 (30.9)	3 (16.7)	0.264
Number of comorbidities[a]	1 (0-3)	1 (0-3)	0.900	1 (0-3)	1 (0-3)	0.098
Nutritional status, n (%)[c]						
Normal nutritional status	28 (41.2)	12 (38.7)	0.588	37 (45.7)	3 (16.7)	0.023
At risk of malnutrition	40 (58.8)	19 (61.3)		44 (54.3)	15 (83.3)	
Diet, n (%)						
Soft diet	1 (1.5)	4 (12.9)	0.032	3 (3.7)	2 (11.1)	0.223
Regular diet	67 (98.5)	27 (87.1)		78 (96.3)	16 (88.9)	
Hospitalization for any reason in the last year, n (%)						
No hospitalization	48 (70.6)	24 (77.4)	0.628	61 (75.3)	11 (61.1)	0.249
≥1 hospitalization	20 (29.4)	7 (22.6)		20 (24.7)	7 (38.9)	
Pneumonia-associated hospitalization in the last year, n (%)	4 (5.9)	1 (3.2)	1.000	5 (6.1)	0 (0)	0.581

BMI: Body mass index, CAD: Coronary artery disease, CVD: Cerebrovascular disease, EAT-10: Eating assessment tool-10, MNA-SF: Mini nutritional assessment-short form, YSP: Yale swallow protocol

[a]Values are given as medians (minimum-maximum), [b]Other diseases: Fracture, thyroid disease, depression, renal failure, gastroesophageal reflux disease, chronic obstructive pulmonary disease, [c]MNA-SF scores from 0 to 7 points indicate "malnutrition", scores >7 to 11 indicate "the risk of malnutrition"

Acknowledgements

We thank the nursing home residents who voluntarily participated in this study.

Ethics

Ethics Committee Approval: The study received approval from the Ethics Committee of Ege University (approval number: 70198063-050.06.04, date: 19.04.2018) and was conducted in alignment with the ethical guidelines outlined in the Declaration of Helsinki.

Informed Consent: Informed consent was obtained from all participants.

Authorship Contributions

Concept: E.S.S., N.D., A.K., Z.F.S., Design: E.S.S., N.D., A.K., Z.F.S., Data Collection or Processing: E.S.S., A.K., Analysis or Interpretation: E.S.S., N.D., A.K., Z.F.S., Literature Search: E.S.S., N.D., A.K., Z.F.S., Writing: E.S.S., N.D., A.K., Z.F.S.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: This study received no external funding.

References

1. Achem SR, Devault KR. Dysphagia in aging. J Clin Gastroenterol 2005;39:357-371.
2. Marik PE, Kaplan D. Aspiration pneumonia and dysphagia in the elderly. Chest 2003;124:328-336.
3. Tanner DC. Lessons from nursing home dysphagia malpractice litigation. J Gerontol Nurs 2010;36:41-46.
4. Demir N, Serel Arslan S, İnal Ö, Karaduman AA. Reliability and Validity of the Turkish Eating Assessment Tool (T-EAT-10). Dysphagia 2016;31:644-649.
5. Farri A, Accornero A, Burdese C. Social importance of dysphagia: its impact on diagnosis and therapy. Acta Otorhinolaryngol Ital 2007;27:83-86.
6. Park YH, Bang HL, Han HR, Chang HK. Dysphagia screening measures for use in nursing homes: a systematic review. J Korean Acad Nurs 2015;45:1-13.
7. Shaker R. Oropharyngeal Dysphagia. Gastroenterol Hepatol (N Y) 2006;2:633-634.
8. Namasivayam AM, Steele CM. Malnutrition and Dysphagia in long-term care: a systematic review. J Nutr Gerontol Geriatr 2015;34:1-21.
9. Rofes L, Arreola V, Mukherjee R, Clavé P. Sensitivity and specificity of the Eating Assessment Tool and the Volume-Viscosity Swallow Test for clinical evaluation of oropharyngeal dysphagia. Neurogastroenterol Motil 2014;26:1256-1265.
10. Belafsky PC, Mouadeb DA, Rees CJ, Pryor JC, Postma GN, Allen J, Leonard RJ. Validity and reliability of the Eating Assessment Tool (EAT-10). Ann Otol Rhinol Laryngol 2008;117:919-924.
11. Bours GJ, Speyer R, Lemmens J, Limburg M, de Wit R. Bedside screening tests vs. videofluoroscopy or fibreoptic endoscopic evaluation of swallowing to detect dysphagia in patients with neurological disorders: systematic review. J Adv Nurs 2009;65:477-493.
12. Suiter DM, Sloggy J, Leder SB. Validation of the Yale Swallow Protocol: a prospective double-blinded videofluoroscopic study. Dysphagia 2014;29:199-203.
13. Warner HL, Suiter DM, Nystrom KV, Poskus K, Leder SB. Comparing accuracy of the Yale swallow protocol when administered by registered nurses and speech-language pathologists. J Clin Nurs 2014;23:1908-1915.
14. Suiter DM, Leder SB. Clinical utility of the 3-ounce water swallow test. Dysphagia 2008;23:244-250.
15. Leder SB, Suiter DM, Lisitano Warner H. Answering orientation questions and following single-step verbal commands: effect on aspiration status. Dysphagia 2009;24:290-295.
16. Leder SB, Suiter DM, Murray J, Rademaker AW. Can an oral mechanism examination contribute to the assessment of odds of aspiration? Dysphagia 2013;28:370-374.
17. Leder SB, Suiter DM, Agogo GO, Cooney LM Jr. An Epidemiologic Study on Ageing and Dysphagia in the Acute Care Geriatric-Hospitalized Population: A Replication and Continuation Study. Dysphagia 2016;31:619-625.
18. Yale Swallow Protocol. Accessed on 13 February 2022 at: https://www.sasspllc.com/wp-content/uploads/2014/12/Yale-Swallow-Protocol.pdf.
19. Rubenstein LZ, Harker JO, Salvà A, Guigoz Y, Vellas B. Screening for undernutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). J Gerontol A Biol Sci Med Sci 2001;56:366-372.
20. Sarıkaya D. A validity study of long and short (MNASF) forms of mini nutritional assessment (MNA) test in geriatric patients. Hacettepe University Faculty of Medicine Internal Diseases Specialty Thesis Ankara, 2013, Accessed on 04 September 2023, at: http://www.openaccess.hacettepe. edu.tr:8080/xmlui/handle/11655/913.
21. Doan TN, Ho WC, Wang LH, Chang FC, Nhu NT, Chou LW. Prevalence and Methods for Assessment of Oropharyngeal Dysphagia in Older Adults: A Systematic Review and Meta-Analysis. J Clin Med 2022;11:2605.
22. Ahn DH, Yang HE, Kang HJ, Do KH, Han SC, Jang SW, Lee JH. Changes in etiology and severity of dysphagia with aging. Eur Geriatr Med 2020;11:139-145.
23. Zayed AM, Afsah O, Elhadidy T, Abou-Elsaad T. Screening for oropharyngeal dysphagia in hospitalized COVID-19 patients: a prospective study. Eur Arch Otorhinolaryngol 2023;280:2623-2631.
24. Ortega O, Martín A, Clavé P. Diagnosis and Management of Oropharyngeal Dysphagia Among Older Persons, State of the Art. J Am Med Dir Assoc 2017;18:576-582.
25. Serra-Prat M, Palomera M, Gomez C, Sar-Shalom D, Saiz A, Montoya JG, Navajas M, Palomera E, Clavé P. Oropharyngeal dysphagia as a risk factor for malnutrition and lower respiratory tract infection in independently living older persons: a population-based prospective study. Age Ageing 2012;41:376-381.
26. Cabre M, Serra-Prat M, Palomera E, Almirall J, Pallares R, Clavé P. Prevalence and prognostic implications of dysphagia in elderly patients with pneumonia. Age Ageing 2010;39:39-45.
27. Cook IJ, Kahrilas PJ. AGA technical review on management of oropharyngeal dysphagia. Gastroenterology 1999;116:455-478.
28. Loeb M, Neupane B, Walter SD, Hanning R, Carusone SC, Lewis D, Krueger P, Simor AE, Nicolle L, Marrie TJ. Environmental risk factors for community-acquired pneumonia hospitalization in older adults. J Am Geriatr Soc 2009;57:1036-1040.
29. Bartlett RS, Kenz MK, Wayment HA, Thibeault SL. Correlation Between EAT-10 and Aspiration Risk Differs by Dysphagia Etiology. Dysphagia 2022;37:11-20.
30. Lindroos E, Saarela RK, Soini H, Muurinen S, Suominen MH, Pitkälä KH. Caregiver-reported swallowing difficulties, malnutrition, and mortality among older people in assisted living facilities. J Nutr Health Aging 2014;18:718-722.
31. Tamura BK, Bell CL, Masaki KH, Amella EJ. Factors associated with weight loss, low BMI, and malnutrition among nursing home patients: a systematic review of the literature. J Am Med Dir Assoc 2013;14:649-655.

32. Zhang PP, Yuan Y, Lu DZ, Li TT, Zhang H, Wang HY, Wang XW. Diagnostic Accuracy of the Eating Assessment Tool-10 (EAT-10) in Screening Dysphagia: A Systematic Review and Meta-Analysis. Dysphagia 2023;38:145-158.

33. Wakabayashi H, Matsushima M. Dysphagia Assessed by the 10-Item Eating Assessment Tool Is Associated with Nutritional Status and Activities of Daily Living in Elderly Individuals Requiring Long-Term Care. J Nutr Health Aging 2016;20:22-27.

34. Tagliaferri S, Lauretani F, Pelá G, Meschi T, Maggio M. The risk of dysphagia is associated with malnutrition and poor functional outcomes in a large population of outpatient older individuals. Clin Nutr 2019;38:2684-2689.

35. Daniels SK, Anderson JA, Willson PC. Valid items for screening dysphagia risk in patients with stroke: a systematic review. Stroke 2012;43:892-897.

36. Burgos R, Sarto B, Segurola H, Romagosa A, Puiggrós C, Vázquez C, Cárdenas G, Barcons N, Araujo K, Pérez-Portabella C. [Translation and validation of the Spanish version of the EAT-10 (Eating Assessment Tool-10) for the screening of dysphagia]. Nutr Hosp 2012;27:2048-2054.

37. Ward M, Skelley-Ashford M, Brown K, Ashford J, Suiter D. Validation of the Yale Swallow Protocol in Post-Acute Care: A Prospective, Double-Blind, Multirater Study. Am J Speech Lang Pathol 2020;29:1937-1943.

38. DePippo KL, Holas MA, Reding MJ. Validation of the 3-oz water swallow test for aspiration following stroke. Arch Neurol 1992;49:1259-1261.

39. Printza A, Kyrgidis A, Pavlidou E, Triaridis S, Constantinidis J. Reliability and validity of the Eating Assessment Tool-10 (Greek adaptation) in neurogenic and head and neck cancer-related oropharyngeal dysphagia. Eur Arch Otorhinolaryngol 2018;275:1861-1868.

40. Wilmskoetter J, Bonilha H, Hong I, Hazelwood RJ, Martin-Harris B, Velozo C. Construct validity of the Eating Assessment Tool (EAT-10). Disabil Rehabil 2019;41:549-559.

41. Alp HB, Erdeo F, Tat AM, Tat MN, Altuntaş Yılmaz N, Koçaker A. Investigation of the effects of depression on the functional capacity, swallowing function and quality of life in geriatric individuals in the nursing home. Journal of Human Sciences 2019;16:968-977.

42. Halter JB, Ouslander JG, Studenski S, High KP, Asthana S, Supiano MA, Ritchie C. eds. Hazzard's Geriatric Medicine and Gerontology. 7th ed. McGraw-Hill; 2017. Accessed on 15 February-2022. https://accessmedicine.mhmedical.com/content.aspx?bookid=1923&sectionid=143987225

43. Umay E, Eyigor S, Karahan AY, Gezer IA, Kurkcu A, Keskin D, Karaca G, Unlu Z, Tıkız C, Vural M, Aydeniz B, Alemdaroglu E, Bilir EE, Yalıman A, Sen EI, Akaltun MS, Altındag O, Keles BY, Bilgilisoy M, Ozcete ZA, Demirhan A, Gundogdu I, Inanir M, Calik Y. The GUSS test as a good indicator to evaluate dysphagia in healthy older people: a multicenter reliability and validity study. Eur Geriatr Med 2019;10:879-887.

44. Estupiñán Artiles C, Regan J, Donnellan C. Dysphagia screening in residential care settings: A scoping review. Int J Nurs Stud 2021;114:103813.

ORIGINAL RESEARCH

DOI: 10.4274/ejgg.galenos.2023.2023-8-7
Eur J Geriatr Gerontol 2024;6(1):46-52

Positive Aspects of Caregiving Questionnaire for Family Caregivers of People with Dementia: Psychometric Properties of the Turkish Version

Merve Aliye Akyol[1], Burcu Akpınar Söylemez[1], Özlem Küçükgüçlü[1], Pınar Soysal[2], Bilgehan Özkaya Sağlam[3], Baran Gül[3], İzlem Sözeri Eser[1,3], Didem Öz[4,5]

[1]Dokuz Eylül University Faculty of Nursing, Department of Internal Medicine Nursing, İzmir, Turkey
[2]Bezmialem Vakıf University Faculty of Medicine, Department of Geriatric Medicine, İstanbul, Turkey
[3]Dokuz Eylül University Faculty of Nursing, Department of Internal Medicine Nursing, İzmir, Turkey
[4]University of California, Global Brain Health Institute, San Francisco, United States of America
[5]Dokuz Eylül University Faculty of Medicine, Department of Neurology; Dokuz Eylül University, Institute of Health Sciences, Department of Neurosciences, İzmir, Turkey

Abstract

Objective: Negative and positive aspects of caregiving (PAC) coexist. Ignoring the PAC limits the overall understanding of caregiving adaptation and thus undermines the development of initiatives. This study aimed to translate the PAC Questionnaire (PACQ) into Turkish and assess its psychometric properties of the Turkish version of the positive aspects of caregiving questionnaire (T-PACQ).

Materials and Methods: This study used a descriptive and methodological approach. After linguistic validity, we conducted a convenience sample of 222 family caregivers of people living with dementia, all home dwellings, using a socio-demographic form, Beck depression inventory, and T-PACQ. Factor analysis [exploratory factor analyses and confirmatory factor analyses (CFA)], analyses of discriminant validity, internal consistency (using Cronbach's alpha), item-total and item-sub-dimensions correlations, ceiling and floor effects, and Hotelling's t-squared test were conducted.

Results: The linguistic validity of the instrument was satisfactory. The total explained variance of the instrument consisting of two domains and 10 items was determined to be 48.40%. According to CFA, model fit indices were ≥0.90. The value of Cronbach's alpha was found to be 0.80. No response bias or ceiling-floor effects were observed.

Conclusion: This instrument is a short and robust measurement tool for assessing family caregivers' perceptions of the PAC. It could be used to engage in appropriate initiatives for family caregivers and assess their effectiveness.

Keywords: Caregivers, caregiving, dementia, psychometrics

Introduction

Dementia is a concern for public health around the world, according to the World Health Organization. More than 55 million people have dementia, with the majority (over 60%) residing in low- and middle-income countries such as Turkey, and over 10 million new cases are diagnosed annually (1). There were approximately 800,000 people living with dementia (PwD) in Turkey in 2019, and the number is projected to rise to 3 million by the year 2050 (2). With a 277% increase expected between 2019 and 2050, the demand for PwD caregivers will rise in the Turkish society.

Dementia is one of the leading causes of disability and dependence in people aged 65 years and older worldwide. PwDs,

Address for Correspondence: Merve Aliye Akyol, Dokuz Eylül University Faculty of Nursing, Department of Internal Medicine Nursing, İzmir, Turkey
Phone: +90 533 405 75 19 **E-mail:** merve.akyol@deu.edu.tr **ORCID:** orcid.org/0000-0001-5107-266X

Received: 29.08.2023 **Accepted:** 23.11.2023

Cite this article as: Akyol MA, Akpınar Söylemez B, Küçükgüçlü Ö, Soysal P, Özkaya Sağlam B, Gül B, Sözeri Eser İ, Öz D. Positive Aspects of Caregiving Questionnaire for Family Caregivers of People with Dementia: Psychometric Properties of the Turkish Version. Eur J Geriatr Gerontol 2024;6(1):46-52

their caregivers, families, and society as a whole have to deal with the financial, social, psychological, and physical effects of this condition. The main source of informal care and a key factor in supporting dementia care in the community is family caregiving. In 2019, informal caregivers (most commonly family members and friends) provided an average of 5 h of daily care to PwD (1). Maintaining this valuable source of informal care for PwD requires a significant focus on encouraging caregivers to successfully adapt to this process. Research in the caregiving of PwD places great emphasis on negative aspects and decreases the burden and associated health consequences, but little attention has been given to the positive aspects (3). However, the process of caring for someone includes both negative and positive aspects. Therefore, disregarding the positive aspects of caregiving (PAC) would hinder understanding of the entirety of the process that family caregivers go through while coping with PwD (4). Strengthening caregiver adaptation includes going beyond reducing the caregiver burden to enhancing PAC (3). PAC is thought to be a protective factor for caregivers' quality of life (4) and can reduce the negative effects on health outcomes (5).

In sum, PAC is a positive appraisal response that results from effective coping with a difficult caregiving situation. Recognizing and promoting PAC can help lessen the effect of negative experiences and feelings that arise while caring for someone (6). To assess family caregivers' perceptions of PAC, valid and reliable measurement tools are required. There is only one valid and reliable scale in Turkish (7), but using the 42-item scale takes time. The PAC questionnaire (PACQ) is a short (10 item) and robust tool based on the stress-coping model (8). Some aspects of the spiritual or moral dimensions of caregiving have been neglected in previously developed instruments. The PACQ also addresses this aspect. The PACQ consists of 10 items structured into two 5-point Likert subdimensions: patient-caregiver relationship and caregiver's psychological well-being. Exploratory factor analysis (EFA) revealed that the factor loadings were suitable (min: 0.531 to max: 0.875). Internal consistency was high for the overall questionnaire (0.785). Because of its usefulness, ease of use and understanding, quick implementation time, and good psychometric values, it will likely be implemented in clinical practice.

Materials and Methods

Aim

The research adapted the PACQ into the Turkish language and to test the psychometric properties of the Turkish version of the positive aspects of caregiving questionnaire (T-PACQ) among family caregivers of PwD.

Design

Using a descriptive, methodological, and cross-sectional research design, the psychometric properties of the T-PACQ were examined. The study followed standard reporting guidelines for the development and validation of scales in the fields of health, social science, and behavioral research (9). The PACQ was translated into Turkish and back-translated from Turkish into English, and linguistic validation tests were performed. Subsequently, construct validation and reliability assessment were examined for T-PACQ.

Linguistic Validation

First, Dr. İbrahim Abdollahpour, the original developer of the questionnaire, granted permission to translate the PACQ and evaluate T-PACQ psychometric properties. The questionnaire was originally written in English, and the research team independently translated it into Turkish. The meaningfulness, linguistic accuracy, and conceptual equivalence of each item were then evaluated by the researchers. A bilingual professional translator with no prior familiarity with the questionnaire translated the items from Turkish to English (10). During the last step of adaptation, the team met online to discuss questionnaire translations. The researchers compared the English translation to the original. Dr. İbrahim Abdollahpour confirmed the back-translation via e-mail, and no changes were made to the questionnaire items.

The items of T-PACQ relevance and meaningfulness to the target population were evaluated using face validity. At this stage, 14 family caregivers of PwD participated. The researchers designed an anonymous form that included the following questions: what general comments do you have about the questionnaire? Is the number of questions appropriate? Do you think the question order makes sense? Did you have any difficulty understanding or responding to any question? What opinions do you have regarding each statement? Was the questionnaire overall simple and easy to understand? Have you had any challenges with the statement rating? Do you have any recommendations?

The content validity was examined by seven experts, including two nursing academicians (one an expert in psychometric research and the other in geriatric nursing), two clinic nurses (one with eight years of clinical experience in geriatrics and over five years of clinical experience in neurology), and three physicians (one neurologist and two geriatricians). Experts rated each item on a four-point scale, ranging from inappropriate (1) to appropriate (4).

Construct Validation and Reliability Assessment

Setting and Sample

Sample sizes of 10 participants per survey question and/or 200-300 observations are recommended for use in scale development and validation studies (9). To conduct EFA and confirmatory factor analyses (CFA), it was necessary to collect data from at least 200 individuals, which would mean 20 responses per scale item (10 items in total). The study was

conducted between May and September 2022 in a neurology and geriatrics outpatient clinic in Turkey. A total of 222 family caregivers of PwD who were all home-dwelling were recruited. Samples were chosen using convenience sampling with non-probability. To be included in the study, caregivers needed to meet the following criteria: they had to be the primary family caregiver for a PwD, be responsible for his/her daily activities, have cared for a PwD for at least six months, have lived in the same house, have voluntarily agreed to participate in the study, be literate in Turkish, and be at least 18 years old. The following were the requirements for caregiver exclusion: people having difficulty hearing or speaking, and people with any psychological illness (self-reported).

Data Collection

A socio-demographic form of PwD and their caregivers, the Beck depression inventory (BDI), and the T-PACQ were used to collect the study data.

Socio-demographic Data: The form was designed to collect socio-demographic data about PwD and their caregivers, including age, sex, years of formal education, duration of disease (years), and marital status.

BDI: Twenty one items were responded to in four options, measuring depression-related attitudes and symptoms. The total score is determined by summing together the points awarded to the right of each question that was answered. The range of the score that can be obtained from the inventory is 0-63 (0-16 points for normal or mild mood disorder, 17 points and above for depressed). Higher scores indicate greater depressive symptoms in individuals (11). Both the total scale and sub-dimension Cronbach's alpha for the Turkish population were quite high (12). The Beck depression scale was used in this study for discriminant validity assessment.

PACQ: On a Likert-type questionnaire, 10 questions were answered with a response ranging from strongly disagree (0) to strongly agree (4). The questionnaire includes two sub-dimensions: patient and caregiver relationship (item 1 + item 2 + item 3 + item 4) and caregiver's psychological well-being (item 5 + item 6 + item 7 + item 8 + item 9 + item 10). The two subdimensions are added together to obtain the total score (min: 0, max: 40). Higher scores indicate positive satisfaction with the caregiving process. Cronbach's alpha scores for both the questionnaire and its sub-dimensions were found to be in the higher ranges (8).

Each caregiver contacted a researcher face to face before the survey began to obtain information about the study and provide written consent.

Ethics

The first author of the original questionnaire provided written permission for the psychometric testing of the T-PACQ. The Dokuz Eylül University Non-Invasive Research Ethics Committee approved the study (decision number: 2022/15-13, date: 20.04.2022). Each caregiver provided their informed consent to participate in the study after being provided with information regarding the purpose and methodology of the research being conducted.

Statistics

Analysis of Moment Structures (AMOS) 25.0 and (SPSS) 24.0 were used in the analysis. We used a confidence interval of 95% ($p<0.05$).

For face validity, the responses were analyzed descriptively. The item content validity index (I-CVI) and scale levels (S-CVI) were evaluated for expert opinions (13-16). The level of expert agreement was tested using Kendall's W analysis.

Construct validity was evaluated using EFA, CFA, and discriminant validity. Using participant entry codes, the study sample was divided at random. EFA was used on one of these halves to examine the measurement model, and CFA was used on the other half to confirm the model. Both the Kaiser-Meyer-Olkin (KMO) coefficient and the Barlett sphericity test were used to determine whether or not the data were suitable for factor analysis. For testing the necessary EFA assumptions, the KMO was used to be greater than 0.60, and the Bartlett test for sphericity was used to have a significance level of less than 0.05. To investigate domain identification, the principal components EFA with a Varimax rotation was employed. The data's assumed normality was tested using the skewness and kurtosis indices. If the eigenvalue was at least 1 and the factor loadings were at least 0.30, it was thought that the factors and items were being kept well. The following variables were analyzed for CFA: Pearson chi-square (χ^2), degree of freedom (df), root mean square error of approximation (RMSEA), goodness-of-fit index (GFI), and comparative fit index (CFI) (13,17,18).

The reliability of the questionnaire was calculated using Cronbach's alpha (18-20), item-total correlation, ceiling and floor effects, and Hotelling's t-squared test for response bias (16,20). Cronbach's coefficient was used to conduct the reliability analysis, and a value of 0.60 or higher was regarded as satisfactory (13,15).

Results

Linguistic Validation

Items were remarkably similar to the originals after translation and back translation and did not require alteration (Supplementary Material 1).

Face validity testing was performed on 14 family caregivers of PwD aged (mean) 59.21±8.30 years (range: 41-71), 78.6% of

whom were female, 85.7% of whom were retired or unemployed, 42.9% of whom were bachelor graduates, 71.4% of whom were children of PwD, and more than 57.1% of caregivers stated that their income was the same as their expenses. The quantity and order of items were considered appropriate by all caregivers, and they had no difficulties with the statement ratings. The T-PACQ was deemed relevant and understandable by most respondents. No changes were made to the questionnaire items. I-CVI for ten items ranged from 0.90 to 1, and the S-CVI was 0.98. The ratings for each item were similar, with no statistically significant differences (Kendall W: 0.18, p=0.23). As a result, all items were retained in the questionnaire.

Construct Validation and Reliability Tests

The mean age of caregivers (n=222) was 54.72±12.07 years (range: 19-84), 76.6% (n=170) were female, 72.5% (n=161) were married, 58.6% (n=130) stated that their income was the same as their expenses, and 38.3% (n=84) had a bachelor's degree. Most caregivers (67.6%, n=150) were children of PwD, and their patients had Alzheimer's type dementia (57.7%, n=128) (Table 1).

The KMO coefficient was found to be 0.74 and a Bartlett sphericity test χ^2 of 300.64 (p<0.001), indicating that the data were appropriate for factor analysis. Within the EFA, two factors were identified: the first explained 34.13% of the total variance and the second explained 14.27%. These factors explained 48.40% of the total variance. Factor loadings for factor 1 (patient and caregiver relationship) ranged from 0.36 to 0.93, and factor 2 (caregiver's psychological well-being) ranged from 0.40 to 0.74 (Table 2).

The CFA applied to the two-factor solution showed that this model was suitable. CFI: 0.94, GFI: 0.91, χ^2/df: 1.47, p<0.001, and RMSEA: 0.06 were the model fit indices that were determined (Figure 1). There was a moderately positive correlation between patient and caregiver relationships and the caregiver's psychological well-being subscales using Pearson product-moment correlation (r=0.469, p<0.001). The discriminant validity test found a statistically significant difference between the two groups (t=2.369, p=0.01). Non-depressed participants had higher T-PACQ scores (25.51±8.54) than depressed participants (22.26±8.92).

The overall Cronbach's alpha was 0.80 (patient and caregiver relationship: 0.72, caregiver's psychological well-being: 0.71). Hotelling's t-squared test was 284.06, p<0.001, suggesting no response bias. No floor or ceiling effects were determined (=0.01%). All of the item-total correlations were satisfactory, with values ranging from 0.39 to 0.68 from 0.64 to 0.81 for the patient and caregiver relationship, and from 0.43 to 0.75 for the caregiver's psychological well-being (Table 3).

Table 1. Descriptive characteristics of the sample (n=222)

Caregivers	n	%
Sex		
Female	170	76.6
Male	52	23.4
Income status		
Income less than expenditure	44	19.8
Income equal to expenditure	130	58.6
Income more than expenditure	48	21.6
Working status		
Working	63	28.4
Not working	159	71.6
Marital status		
Married	161	72.5
Single	61	27.5
Educational status		
Literate/elementary school	59	26.5
High school	57	25.7
University	85	38.3
Postgraduate	21	9.5
Relationship with the patient		
Spouse	53	23.9
Children	150	67.6
Other family member	19	8.5
	X	**SD**
Age (years)	54.72	12.07
Caregiving period (months)	39.57	30.52
Patients		
Age (years)	77.92	9.42
Diagnosis (years)	42.13	31.31
	n	**%**
Sex		
Female	137	61.7
Male	85	38.3
Marital status		
Married	144	64.9
Single	78	35.1
Educational status		
Illiterate	34	15.3
Literate/elementary school	112	50.5
High school	41	18.5
University	28	12.6
Postgraduate	7	3.1
Types of dementia		
Alzheimer's disease	128	57.7
Frontotemporal dementia	13	5.9
Vascular dementia	19	8.6
Lewy body dementia	25	11.3
Parkinson's disease dementia	10	4.6
Unknown	27	12.1

X: Mean, SD: Standard deviation

Discussion

The PACQ was initially developed in English and then translated into Turkish. Its psychometric qualities were then examined in Turkish family caregivers of PwD. To demonstrate that the T-PACQ provides valid and reliable PAC process scores among Turkish family carers of PwD, we used face and content validity assessments, EFA, CFA, discriminant validity, and reliability testing. The best psychometric performance was produced by retaining the original version's 10 item, two-factor structure.

This study is the first to examine PACQ's reliability and validity in a different language and context (8); therefore, we lack any variables to compare. Findings showed that the questionnaire was easily completed by the intended sample because all questions were easily understood and considered relevant. The T-PACQ seems to measure the concept it is supposed to measure, as the content validity scores were all above the minimally needed levels (19). This suggests that the experts could reach a satisfactory compromise.

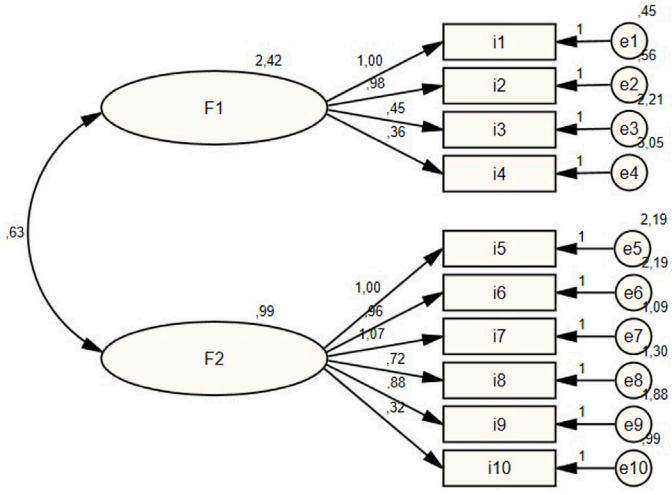

Figure 1. Confirmatory factor analysis of T-PACQ

T-PACQ: Turkish version of the positive aspects of caregiving questionnaire

Similar to the initial study, the T-PACQ was found to have a two-factor structure (8), with the items strongly correlating with each factor. This indicated that both factors in a strong factor structure measured the intended concept. Because all of the factor loadings and fit indices obtained from the CFA were within the ranges stated in the literature, it was concluded that the factor structure of the instrument gave the best feasible fit (21,22). The initial study (8) did not include CFA, so we did not have any variables to compare. Discriminant validity is used to examine whether the concept being measured is different from other concepts (9). Scores on the T-PACQ were expected to be statistically different between the depressed and nondepressed groups. Similarly, caregivers' self-rated health was significantly associated with PACQ scores in the initial study (8). These construct validity results suggest that the questionnaire can provide valid data on PAC for family caregivers of PwD.

The T-PACQ was found to provide highly reliable results. Cronbach's α was approximately the same as that found in the initial study (total α: 0.78, patient and caregiver relationship: 0.71, and caregiver's psychological well-being: 0.70) (8). Additionally, there was no potential for significant response bias according to the Hotelling t-square test results, which showed that people answered questions based on their opinions, not outside factors (16,23). The floor and ceiling effect was 0.01%,

Table 2. Factor loadings, exploratory factor analysis (n=111)

Items*	Factor 1: patient and caregiver relationship	Factor 2: caregiver's psychological well-being
1. Do you feel that, caring your patient has resulted in more dependency feeling to him/her?	0.92	
2. Do you feel that, comparing to the past, you have become closer to your patient?	0.93	
3. Do you feel that, due to caring your patient, your life has become more meaningful?	0.46	
4. Do you believe that caring your patient, due to providing a compensation opportunity for appreciate him/her, donates a satisfaction feeling to you?	0.36	
5. Did you believe that, as a result of caring your patient, you have become a better human comparing to your past?		0.58
6. Do you believe that collaboration in caring your patient has brought your family members closer together?		0.68
7. Do you think that your faith, in the time of caring your patient, has provided a source of power and peace for you?		0.74
8. Did you believe that, during caring your patient, you have learned many useful things?		0.61
9. Do you believe that caring your patient has spiritual/moral remuneration?		0.59
10. Do you believe that caring your patient has been beneficial for your patient?		0.40
Explained variance (%)	34.13	14.27

*Turkish version of instrument was administered to the caregivers

Table 3. Item-total and item-sub-dimensions' correlation scores (n=222)

Sub-dimensions	Item	Item-total correlation (r)*	Item-subdimension correlation (r)*
Patient and caregiver relationship	Item 1	0.65	0.81
	Item 2	0.63	0.81
	Item 3	0.68	0.68
	Item 4	0.56	0.64
Caregiver's psychological well-being	Item 5	0.64	0.67
	Item 6	0.55	0.64
	Item 7	0.65	0.75
	Item 8	0.55	0.61
	Item 9	0.62	0.69
	Item 10	0.39	0.43

*p<0.001

which is much less than the 20% limit and shows that this bias did not exist (16,23).

Study Limitations

Participants in the survey were family members of PwD who received routine care at a neurology and geriatrics outpatient clinic in Turkey. Common generalizations are limited by the use of a non-random sample approach because bias may exist. Reliability, and especially validity, is an increasing and never-ending process. Therefore, a larger population can be used to evaluate the questionnaire's validity and reliability. Assessment of the time variation of the questionnaire was not performed. These should be considered in future studies.

Conclusion

The results show that the T-PACQ is a strong two-factor structure that provides valid and reliable results about PAC for family caregivers of PwD. Using T-PACQ will demonstrate value for assessing caregivers' perceptions of the PAC and engage in appropriate interventions for caregivers as the number of people with dementia rises in Turkey and worldwide. Because of its practicality, simplicity, and short application time, it is expected to be a measurement tool preferred by health professionals.

Ethics

Ethics Committee Approval: The first author of the original questionnaire provided written permission for the psychometric testing of the T-PACQ. The Dokuz Eylül University Non-Invasive Research Ethics Committee approved the study (decision number: 2022/15-13, date: 20.04.2022).

Informed Consent: Informed consent was obtained.

Authorship Contributions

Concept: M.A.A., B.A.S., Ö.K., P.S., B.Ö.S., B.G., İ.S.E., D.Ö., Design: M.A.A., B.A.S., Ö.K., P.S., B.Ö.S., B.G., İ.S.E., D.Ö., Data Collection or Processing: M.A.A., P.S., B.Ö.S., B.G., İ.S.E., Analysis or Interpretation: M.A.A., B.A.S., Literature Search: M.A.A., B.A.S., Ö.K., P.S., B.Ö.S., B.G., İ.S.E., D.Ö., Writing: M.A.A., B.A.S., Ö.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. World Health Organization. (2022). Dementia. Retrieved from https://www.who.int/news-room/fact-sheets/detail/dementia. Accessed 16 July 2023.
2. GBD 2019 Dementia Forecasting Collaborators. Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019. Lancet Public Health 2022;7:105-125.
3. Wang J, Li X, Liu W, Yang B, Zhao Q, Lü Y, Xiao M. The positive aspects of caregiving in dementia: A scoping review and bibliometric analysis. Front Public Health 2022;10:985391.
4. Johansson MF, McKee KJ, Dahlberg L, Summer Meranius M, Williams CL, Marmstål Hammar L. Negative Impact and Positive Value of Caregiving in Spouse Carers of Persons with Dementia in Sweden. Int J Environ Res Public Health 2022;19:1788.
5. Morimoto H, Takebayashi Y. Antecedents and Outcomes of Enrichment Among Working Family Caregivers of People With Dementia: A Longitudinal Analysis. J Gerontol B Psychol Sci Soc Sci 2021;76:1060-1070.
6. Dias R, Santos RL, Sousa MF, Nogueira MM, Torres B, Belfort T, Dourado MC. Resilience of caregivers of people with dementia: a systematic review of biological and psychosocial determinants. Trends Psychiatry Psychother 2015;37:12-19.
7. Gönen Şentürk S, Akpınar Söylemez B, Akyol MA, Isik AT, Küçükgüçlü Ö. Psychometric properties of the Turkish version of the scale for positive aspects of caregiving experience. Perspect Psychiatr Care 2022;58:1651-1656.
8. Abdollahpour I, Nedjat S, Noroozian M, Salimi Y, Majdzadeh R. Positive Aspects of Caregiving Questionnaire. J Geriatr Psychiatry Neurol 2017;30:77-83.
9. Boateng GO, Neilands TB, Frongillo EA, Melgar-Quiñonez HR, Young SL. Best Practices for Developing and Validating Scales for Health, Social, and Behavioral Research: A Primer. Front Public Health 2018;6:149.
10. Maneesriwongul W, Dixon JK. Instrument translation process: a methods review. J Adv Nurs 2004;48:175-186.

11. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561-571.
12. Hisli N. A reliability and validity study of Beck Depression Inventory in a university student sample. J Psychol 1989;7:3-13.
13. Çam MO, Baysan-Arabaci L. Qualitative and quantitative steps on attitude scale construction. Journal of Research and Development in Nursing 2010;12:59-71.
14. Crestani AH, Moraes AB, Souza APR. Content validation: clarity/relevance, reliability and internal consistency of enunciative signs of language acquisition. Codas 2017;29:e20160180.
15. Leech NL, Barrett KC, Morgan GA. SPSS for intermediate statistics: Use and interpretation. New York, L. Erlbaum Associates, 2008.
16. Nunnally JC, Bernstein IH. Psychometric Theory. 3rd edition, New York, McGraw-Hill, 2010.
17. Polit DF, Beck CT, Owen SV. Is the CVI an acceptable indicator of content validity? Appraisal and recommendations. Res Nurs Health 2007;30:459-467.
18. Souza AC, Alexandre NMC, Guirardello EB. Psychometric properties in instruments evaluation of reliability and validity. Epidemiol Serv Saude 2017;26:649-659.
19. Sousa VD, Rojjanasrirat W. Translation, adaptation and validation of instruments or scales for use in cross-cultural health care research: a clear and user-friendly guideline. J Eval Clin Pract 2011;17:268-274.
20. Streiner DL, Kottner J. Recommendations for reporting the results of studies of instrument and scale development and testing. J Adv Nurs 2014;70:1970-1979.
21. DeVellis RF. Scale Development, Theory and Applications. 4th edition, New Delhi, India, SAGE Publication Inc, 2016.
22. Johnson B, Christensen L. Educational Research: Quantitative, Qualitative, and Mixed Approaches. 3rd edition, California, SAGE Publication, 2014, pp 199-222.
23. Rattray J, Jones MC. Essential elements of questionnaire design and development. J Clin Nurs 2007;16:234-243.

Supplementary Material 1. Turkish version of the positive aspects of caregiving questionnaire (T-PACQ)

Bakım Vermenin Olumlu Yönleri Ölçeği	Kesinlikle katılmıyorum	Katılmıyorum	Kararsızım	Kararsızım	Kesinlikle katılıyorum
1. Hastanıza bakım verdiğiniz için onunla aranızda daha fazla bağlılık oluştuğunu hissediyor musunuz?					
2. Geçmişe kıyasla hastanızla daha yakın olduğunuzu düşünüyor musunuz?					
3. Hastanıza bakım verdiğiniz için hayatınızın daha anlamlı hale geldiğini düşünüyor musunuz?					
4. Bakım vermenin hastanıza borcunuzu ödeme fırsatı verdiği için memnuniyet duymanızı sağladığını düşünüyor musunuz?					
5. Hastanıza bakım vermenin bir sonucu olarak, geçmişinize kıyasla daha iyi bir insan olduğunuza inanıyor musunuz?					
6. Hastanızın bakımında yaptığınız işbirliğinin aile üyelerini birbirlerine daha yakınlaştırdığına inanıyor musunuz?					
7. Hastanıza bakım verirken inancınızın size güç ve huzur kaynağı olduğunu düşünüyor musunuz?					
8. Hastanıza bakım verirken birçok yararlı şey öğrendiğinize inanıyor musunuz?					
9. Hastanıza bakım vermenin manevi mükâfatı olduğuna inanıyor musunuz?					
10. Verdiğiniz bakımın hastanız için yararlı olduğuna inanıyor musunuz?					

ORIGINAL RESEARCH

DOI: 10.4274/ejgg.galenos.2023.2023-9-1
Eur J Geriatr Gerontol 2024;6(1):53-57

Gastric Mucosal Changes and Frequency of *Helicobacter pylori* in Patients with Gastroenterostomy

Semih Sezer[1], Bülent Ödemiş[2]

[1]University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Gastroenterology, Ankara, Turkey
[2]University of Health Sciences Turkey, Ankara Bilkent City Hospital, Clinic of Gastroenterology, Ankara, Turkey

Abstract

Objective: We investigated endoscopic and pathological changes in the gastric mucosa and the frequency of *Helicobacter pylori* (Hp) infection in patients undergoing gastroenterostomy surgery.

Materials and Methods: Patients who were admitted to our hospital between November 2009 and April 2010 and who had previously undergone gastroenterostomy surgery for any reason were included in the study. The control group consisted of patients without gastroenterostomy who underwent routine endoscopy.

Results: Hp was positive in 10 of 70 patients with gastroenterostomy (14.3%) and in 30 of 50 patients (60%) in the control group. The difference between the two groups was statistically significant (p<0.001). Intestinal metaplasia was detected in 22 of 70 patients (31.4%) and in 8 of 50 patients (16%) in the gastroenterostmy and control groups, respectively (p=0.054). Atrophic gastritis was detected in 42 of 70 patients (60%) and in 15 of 50 patients (30%). The difference was statistically significant (p<0.01). Dysplasia and adenocarcinoma were detected in 4 (5.5%) patients (dysplasia in 1 patient, adenocarcinoma in 3 patients) in the gastroenterostomy group, but not in the control group (p<0.02).

Conclusion: This study showed that the frequency of enterogastric reflux increased in patients who underwent gastroenterostomy and correspondingly decreased Hp's frequency. The incidence of atrophic gastritis and dysplasia from precancerous gastric lesions is significantly higher in patients who undergo gastroenterostomy. In light of these results, because enterogastric reflux and Hp have a synergistic damage effect on the gastric mucosa, we recommend that patients with gastroenterostomy should be tested for Hp, and if positive, they should be eradicated, and biopsies should be taken from the distal remnant gastric mucosa close to the stoma line.

Keywords: Aging, cell biology, geriatric care management, geriatric palliative care, geriatrics

Introduction

Reflux of bile, pancreatic, and small intestinal secretions from the duodenum into the stomach is called enterogastric reflux. In general, these secretions are not normally found in the stomach. Insufficient pyloric function plays an important role in the reflux of duodenal contents into the stomach (1). Enterogastric reflux in the stomach increases by 30-100% after subtotal gastrectomy, pyloroplasty, and cholecystectomy (2,3). Billroth-I (B-I) is a gastroduodenostomy procedure that can be performed end-to-end or side-to-side. In a Billroth-II (B-II) operation, a side-to-side gastrojejunostomy is performed. The decisive difference between B-I and B-II is that in B-I, the duodenal passage remains intact. Because of the nature of the anastomosis, antrectomy is typically performed in B-I as a rule. In cases requiring more extensive resection, B-II and Roux-en-Y (R-Y) surgery are preferred because of postoperative complications. In R-Y surgery, the afferent loop coming from the duodenum is connected more distally to the efferent jejunum segment anastomosed to the stomach. Therefore, bile reflux into the stomach is less common in R-Y surgery than in B-II surgery (4). If gastric emptying is not sufficient and delayed, gastric contents, including excess bile, remain for a prolonged time and have harmful effects on the gastric mucosa. Biliated duodenal

Address for Correspondence: Semih Sezer, University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Gastroenterology, Ankara, Turkey
Phone: +90 505 260 51 70 **E-mail:** ssezer1970@hotmail.com **ORCID:** orcid.org/0000-0002-0458-1450
Received: 01.09.2023 **Accepted:** 23.11.2023

Cite this article as: Sezer S, Ödemiş B. Gastric Mucosal Changes and Frequency of *Helicobacter pylori* in Patients with Gastroenterostomy. Eur J Geriatr Gerontol 2024;6(1):53-57

content can cause damage to the gastric mucosa with local effects. Duodenal contents combine with gastric secretions in the stomach and cause mucosal damage (1). Histopathological evaluations of the gastric mucosa are graded as mild, moderate, and severe according to the modified Sydney classification based on chronic inflammation, neutrophil activity, glandular atrophy, intestinal metaplasia, and *Helicobacter pylori* (Hp) density (5).

The coexistence of enterogastric reflux and Hp infection is thought to increase damage to the gastric mucosa (6). In the long term, after gastric surgery, the reflux of bile back into the stomach is a factor in the development of stomach ulcers and stomach cancer. Chronic epithelial damage, particularly due to enterogastric reflux, may facilitate cancer development by increasing mucosal cell proliferation (7).

Although Hp infection is highly prevalent in our country and has been investigated in various conditions, it has not been adequately studied in patients who have undergone gastrectomy. In addition, it remains controversial whether eradication should be applied when Hp infection is detected after gastrectomies (8). We investigated the endoscopic and pathological findings in the gastric mucosa and the frequency of Hp infection in patients undergoing gastroenterostomy.

Materials and Methods

Patients who were admitted to the Gastroenterology Clinic of Türkiye Yüksek İhtisas Hospital between November 2009 and April 2010 and who had previously undergone gastroenterostomy surgery for any reason were included in the study. The control group consisted of patients without gastroenterostomy who underwent routine endoscopy. The study was designed as a single-center cross-sectional study. Written consent from each patient was obtained before entering the study. Patients with B-II, R-Y, and simple gastroenterostomy (SG) were included in the study. Patients who had previously undergone Hp eradication therapy and those who had been taking antibiotics and proton pump inhibitors (PPI) within the last 3 months were excluded from the study. The control group consisted of patients who had requested endoscopy for any reason, had not previously undergone Hp eradication therapy, and had not used antibiotics or PPIs in the last 3 months. All endoscopic procedures were performed using video endoscopes with local throat anesthesia (xylocain 10%) following at least 12 h of fasting. The endoscopic appearance of dense bile and bile sludge on an edematous, hyperemic, and easily vulnerable mucosa was evaluated as endoscopic enterogastric reflux. In patients with gastroenterostomy, biopsy samples were obtained from four quadrants of the remnant mucosa close to the stoma and the proximal gastric remnant mucosa. In the control group, biopsies were obtained from all four quadrants of the antrum and corpus. All biopsies were evaluated using giemsa stain by a single pathologist. The Sydney classification was used to evaluate pathological findings. In addition, pathologically reactive gastropathy findings suggestive of enterogastric reflux (gland structures with cystic changes, hypercellularity in gastric pits, smooth muscle fibers between glands, foveolar hyperplasia, capillary congestion and vasodilation in superficial lamina propria) were examined. As a standard practice, the pathological evaluation of enterogastric reflux in patients undergoing gastric surgery was performed in the remnant gastric mucosa close to the stoma. Therefore, enterogastric reflux evaluation was not conducted in the proximal remnant mucosa. Endoscopic and pathologic findings of patients with or without previous gastric surgery were compared according to enterogastric reflux and Sydney classification Table 1 (5). The correlation between the endoscopic and pathological findings was evaluated. Ethical approval for the study was obtained from the Clinical Ethics Committee of Türkiye Yüksek İhtisas Hospital (decision number: 242, date: 04.08.2010).

Statistics

Statistical evaluation was performed using SPSS vs. 18.0 (SPSS Inc., IL, USA). Two-sample t-test when comparing different data, chi-square test when multiple variables need to be compared, Mann-Whitney U test when it is necessary to compare data whose distributions are shown not to be homogeneous; was used. In cases where p-values were less than 0.05, the result was considered statistically significant.

Results

Seventy patients who underwent gastroenterostomy surgery and 50 control patients who underwent upper gastrointestinal

Table 1. Modified Sydney classification

	Histopatological grade		
	Mild	Moderate	Severe
Chronic inflammation	+	++	+++
Neutrophilic infiltrate	<1/3	1/3-2/3	>2/3
Atrophy	<1/3	1/3-2/3	>2/3
Intestinal metaplasia	+	++	+++
Hp density	+	++	+++

Hp: *Helicobacter pylori*

endoscopy for various reasons were included in the study. The distribution of the 70 patients with gastroenterostomy was as follows: 7 patients with R-Y anastomosis (10%), 18 patients with SG (25%), and 45 patients (64%) with B-II. The mean age was 62.7±4.4 years in patients with R-Y anastomosis, 58.9±2.2 years in SG patients, 63±1.5 years in B-II patients, and 55.4±1.9 years in the control group. There was no statistically significant difference in the mean age between the groups of gastroenterostomy patients. The mean time elapsed after the operation was 10.4±2.5 years in patients with R-Y anastomosis, 18.1±2.3 years in patients with SG, and 14.7±2.1 years in patients with B-II. The reason for gastroenterostomy was peptic ulcer in 50 of the 70 patients, adenocarcinoma in 19, and neuroendocrine tumor in one patient. When the groups were examined, 5 (71.4%) patients in the R-Y group were operated on for peptic ulcer and 2 (28.6%) patients for adenocarcinoma. In the SG group, all 18 (100%) patients underwent surgery for peptic ulcer, whereas in the B-II group, 27 (60%) patients underwent surgery for peptic ulcer, 17 (37.8%) for adenocarcinoma, and one patient for neuroendocrine tumor. Demographic characteristics and statistics are provided in Table 2.

Distal Gastric Biopsy Examinations in Patients with Gastroenterostomy

Hp was positive in 10 of 70 patients with gastroenterostomy (14.3%) and in 30 of 50 patients (60%) in the control group. The difference between the two groups was statistically significant (p<0.001). Intestinal metaplasia was detected in 22 of 70 patients (31.4%) and in 8 of 50 patients (16%) in the gastroenterostmy and control groups, respectively (p=0.054). Pathologic activity according to Sydney classification was positive in 32 of 70 patients (48.6%) and in 25 of 50 (25%) patients. No significant difference was found (p=0.6). Chronic inflammation was positive in 58 of 70 patients (82.9%) and in 46 of 50 patients (92%) in the gastroenterostomy and control groups, respectively. No significant difference was found (p=0.1). Atrophic gastritis was found in 42 of 70 patients (60%) and 15 of 50 patients (30%). The difference was significant (p<0.01). Dysplasia and adenocarcinoma were detected in 4 (5.5%) patients (dysplasia in 1 patient, adenocarcinoma in 3 patients) in the gastroenterostomy group but not in the control group. A comparison of distal gastric biopsy samples from gastroenterostomy patients and control group patients is provided in Table 3.

Proximal Gastric Biopsy Examinations in Patients with Gastroenterostomy

In the gastroenterostomy and control groups, 14 of 70 patients (20%) and 31 of 50 patients (62%) were positive for Hp. The difference between the two groups was significant (p<0.001). The rate of intestinal metaplasia was detected in 13 of 70 patients (18.6%) and in 7 of 50 patients (14%) (p=0.5). Atrophic gastritis was detected in 31 of 70 patients (44.3%) and in 12 of 50 (24%) patients. The difference was statistically significant (p<0.02). Activity was positive in 34 of 70 patients (48.6%) and in 25 of 50 (50%) patients. There was no statistically significant difference (p=0.8). Chronic inflammation was detected in 61 of 70 patients (88.4%) and in 44 of 50 patients (88%). There was no statistically significant difference (p=0.9). Proximal gastric biopsies of patients with gastroenterostomy revealed

Table 2. Demographic characteristics of patients

Patients undergoing gastroenterostomy	70 (n)		R-Y	7 (10%)
			B-II	45 (65%)
			SG	18 (25%)
Control group	50 (n)			
Age	Gastroenterostomy		R-Y	62.7±4.4
			B-II	63±1.5
			SG	58.9±2.2
	Control			55.4±1.9
Duration of time after gastroenterostomy	R-Y			10.4±2.5 (year)
	SG			18.1±2.3 (year)
	B-II			14.7±2.1 (year)
Reason for the gastroenterostomy procedure	R-Y	Peptic ulcer		5 (71.4%)
		Adenocarcinoma		2 (28.6%)
	SG	Peptic ulcer		18 (100%)
	B-II	Peptic ulcer		27 (60%)
		Adenocarcinoma		17 (37.8%)
		Neuroendocrine tumor		1 (2.2%)

R-Y: Roux-en-Y, B-II: Billroth-II, SG: Simple gastroenterostomy

neuroendocrine tumors in one patient (1.4%) and dysplasia in one patient (2%) in the control group. The difference was not statistically significant (p=0.6). As a rule, pathologic evaluation of enterogastric reflux in patients with gastroenterostomy was performed on the remnant gastric mucosa close to the stoma; therefore, enterogastric reflux evaluation was not performed on the proximal remnant mucosa. A comparison of proximal gastric biopsy samples of gastroenterostomy patients and control group patients is given in Table 4.

Discussion

Hp is responsible for the etiology of gastric cancer (9,10). Cell damage and Hp infection are influential in the development of malignancy in patients undergoing gastroenterostomy (11). Therefore, Hp eradication is important in patients undergoing gastroenterostomy. The prevalence of Hp was 38% in patients who underwent gastroenterostomy for peptic ulcers and 60% (p=0.015) in the control group (12). In our country, Hp's frequency in patients undergoing gastroenterostomy has not been sufficiently studied. In our study, we detected Hp positivity rates of 14% and 20% in distal and proximal gastric biopsy specimens in gastroenterostomy patients, respectively, and 60% and 62% in distal and proximal gastric biopsy specimens in the control group (p<0.01). The lower rates of Hp in gastroenterostomy patients are probably related to the higher pH values of the gastric milieu due to alkaline reflux. Previous studies have pointed out that the risk of developing carcinoma in remnant gastric tissue is related to the fact that gastrectomy is performed before the age of 40 years and to the patients' advanced age (13). In our cases who underwent surgery for adenocarcinoma, two patients showed recurrence at the 2nd and 4th years. Two of our patients with dysplasia had a history of surgery due to peptic ulcers 30 and 45 years ago. Although the number of cases is insufficient, it shows that the risk of developing malignancy in the late period increases in those who underwent surgery for ulcers. Adenocarcinoma should be evaluated for malignancy in the early period because of local recurrence. Hp positivity was lower in gastroenterostomy patients than in non-gastroenterostomy patients. It was concluded that Hp may play an important role in the development of gastric lesions in patients undergoing gastroenterostomy (14). Dysplasia and adenocarcinoma were significantly more common in gastroenterostomy patients than in the control group (5.5%-0) (p<0.02). In the distal biopsy samples, dysplasia and adenocarcinoma were detected in four patients with gastroenterostomy, but none in the control group. The more frequent occurrence of dysplasia and adenocarcinoma in distal biopsy specimens can be explained by their proximity to the primary operation site and increased exposure to enterogastric reflux. Although there was no significant difference between the distal and proximal gastric biopsy samples of patients with gastroenterostomy and the control group in terms of the frequency of intestinal metaplasia, it was concluded that a significant increase in the incidence of intestinal metaplasia could be detected with a larger sample size (p=0.054 vs. p=0.5).

Distal and proximal gastric biopsy specimens showed a high rate of atrophic gastritis compared with the control group (p<0.01). We did not find a significant difference between patients with gastroenterostomy and control group in terms of

Table 3. Comparison of distal gastric biopsy samples of gastroenterostomy and control group patients

	Gastroenterostomy	Control	p
Helicobacter pylori	10 (14.3%)	30 (60%)	<0.001
Intestinal metaplasia	22 (31.4%)	8 (16%)	0.054
Activity	32 (48.6%)	25 (50%)	0.6
Chronic inflammation	58 (82.9%)	46 (92%)	0.1
Atrophic gastritis	42 (60%)	15 (30%)	0.01
Dysplasia-adenocarcinoma	4 (5.5%)	0	0.02

Table 4. Comparison of proximal gastric biopsy samples from gastroenterostomy patients and control group

	Gastroenterostomy	Control	p
Helicobacter pylori	14 (20%)	31 (62%)	0.001
Intestinal metaplasia	13 (18.6%)	7 (14%)	0.5
Activity	31 (44.3%)	12 (24%)	0.02
Chronic inflammation	34 (48.6%)	25 (50%)	0.8
Atrophic gastritis	61 (88.4%)	44 (88%)	0.9
Dysplasia	1 (1.4%)*	1 (2%)	0.6

*: Neuroendocrine tumor

chronic inflammation and activity values. In our study, the small number of patients with R-Y was a limiting factor in comparison among patients who underwent gastroenterostomy. However, in our study, the pathologic examination of patients with gastroenterostomy separately for both distal and proximal gastric mucosa made it possible to evaluate in detail this group of patients with increased frequency of precancerous lesions.

Study Limitations

We think that increasing the number of patients with gastroenterostomy and duration of time after surgery will show us more powerful and correct numbers in accordance with risk factors for gastric malignancies and premalignancies.

Conclusion

This study showed that the frequency of enterogastric reflux increased in patients who underwent gastroenterostomy and, correspondingly, decreased Hp's frequency. The incidence of atrophic gastritis and dysplasia, which are precancerous gastric lesions, is significantly higher in patients undergoing gastroenterostomy. In addition, the frequency of intestinal metaplasia in the distal gastric mucosa is increasing although the difference is not statistically significant.

Considering these results, because enterogastric reflux and Hp have a synergistic damaging effect on the gastric mucosa, we recommend that patients with gastroenterostomy should be tested for Hp, and if they test positive, they should undergo eradication treatment. In addition, biopsies should be taken from the distal remnant gastric mucosa close to the stoma line.

Ethics

Ethics Committee Approval: Ethical approval for the study was obtained from the Clinical Ethics Committee of Türkiye Yüksek İhtisas Hospital (decision number: 242, date: 04.08.2010).

Informed Consent: Informed consent was obtained.

Authorship Contributions

Surgical and Medical Practices: S.S., B.Ö., Concept: S.S., B.Ö., Design: S.S., B.Ö., Data Collection or Processing: S.S., Analysis or Interpretation: S.S., B.Ö., Literature Search: S.S., Writing: S.S.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Pazzi P, Scalia S, Stabellini G, Trevisani L, Alvisi V, Guarneri M. Bile reflux gastritis in patients without prior gastric surgery:therapeutic effects of ursodeoxycholic asid. Current Therapeutic Research 1989;45:476-487.
2. Dixon MF, Neville PM, Mapstone NP, Moayyedi P, Axon AT. Bile reflux gastritis and Barrett's oesophagus: further evidence of a role for duodenogastro-oesophageal reflux? Gut 2001;49:359-363.
3. Freedman J, Ye W, Näslund E, Lagergren J. Association between cholecystectomy and adenocarcinoma of the esophagus. Gastroenterology 2001;121:548-553.
4. Schweizer W, Blunschi T, Gertsch P, Blumgart LH. Postoperativer Verlauf nach Magenresektionen: ein Vergleich von Billroth I, Billroth II und Resektion mit Roux-Y-Rekonstruktion [Postoperative course following stomach resection: a comparison of Billroth I, Billroth II and Roux-en-Y resection-reconstruction]. Schweiz Med Wochenschr 1990;120:521-528.
5. Rugge M, Correa P, Dixon MF, Fiocca R, Hattori T, Lechago J, Leandro G, Price AB, Sipponen P, Solcia E, Watanabe H, Genta RM. Gastric mucosal atrophy: interobserver consistency using new criteria for classification and grading. Aliment Pharmacol Ther 2002;16:1249-1259.
6. Abe H, Murakami K, Satoh S, Sato R, Kodama M, Arita T, Fujioka T. Influence of bile reflux and Helicobacter pylori infection on gastritis in the remnant gastric mucosa after distal gastrectomy. J Gastroenterol 2005;40:563-569.
7. Safatle-Ribeiro AV, Ribeiro Júnior U, Reynolds JC, Gama-Rodrigues JJ, Iriya K, Kim R, Bakker A, Swalsky PA, Pinotti HW, Finkelstein SD. Morphologic, histologic, and molecular similarities between adenocarcinomas arising in the gastric stump and the intact stomach. Cancer 1996;78:2288-2299.
8. Bahnacy A, Kupcsulik P, Elés Z, Flautner L. Occurrence and significance of Helicobacter pylori infection after gastric surgery. Acta Chir Hung 1996;35:201-207.
9. The EUROGAST Study Group. An international association between Helicobacter pylori infection and gastric cancer. The EUROGAST Study Group. Lancet 1993;341:1359-1363.
10. Lynch D A F, Mapstone NP, Clarke A M T, Jackson P, Dixon MF, Quirke P, Cell proliferation in Helicobacter pylori associated gastritis and the effect of eradication therapy. Gut 1993;34 (suppl 1): W12.
11. Lynch DA, Mapstone NP, Clarke AM, Jackson P, Dixon MF, Quirke P, Axon AT. Cell proliferation in the gastric corpus in Helicobacter pylori associated gastritis and after gastric resection. Gut l995;36:351-353.
12. Schilling D, Adamek HE, Wilke J, Schauwecker P, Martin WR, Arnold JC, Benz C, Labenz J, Riemann JF. Prevalence and clinical importance of Helicobacter pylori infection in patients after partial gastric resection for peptic ulcer disease. A prospective evaluation of Helicobacter pylori infection on 50 resected patients compared with matched nonresected controls. Z Gastroenterol 1999;37:127-132.
13. Wieman TJ, Max MH, Voyles CR, Barrows GH. Diversion of duodenal contents: its effect on the production of experimental gastric cancer. Arch Surg 1980;115:959-961.
14. Giuliani A, Caporale A, Demoro M, Benvenuto E, Scarpini M, Spada S, Angelico F. Gastric cancer precursor lesions and Helicobacter pylori infection in patients with partial gastrectomy for peptic ulcer. World J Surg 2005;29:1127-1130.

ORIGINAL RESEARCH

DOI: 10.4274/ejgg.galenos.2023.2023-8-3
Eur J Geriatr Gerontol 2024;6(1):58-64

Polypharmacy-related Orthostatic Intolerance Syndrome in Community-dwelling Older Adults

Arzu Okyar Baş, Yelda Öztürk, Merve Güner, Serdar Ceylan, Zeynep Kahyaoğlu, Süheyla Çöteli, Meltem Koca, Mert Eşme, Cafer Balcı, Burcu Balam Doğu, Mustafa Cankurtaran, Meltem Gülhan Halil

Hacettepe University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, Ankara, Turkey

Abstract

Objective: Polypharmacy (PP) is associated with various adverse outcomes in older adults. Although few studies have shown an association between PP and orthostatic blood pressure changes (OBPCs), its relationship with orthostatic intolerance syndrome (OIS), which describes a group of signs and symptoms triggered by standing up straight with or without OBPCs, is not known. Therefore, we assessed the association between PP and OIS in the geriatric population.

Materials and Methods: Ninety-nine geriatric outpatients were enrolled in the study. In addition to comprehensive geriatric assessment, frailty evaluation (modified fried frailty index), OBPC evaluations [active standing test (AST)], and OIS questioning both experienced in the last three months (self-reported OIS) and symptoms emerged during the AST were performed. PP was defined as using >4 drugs.

Results: The participants' median age was 74 and ranged from 69.5 to 79.0 years, and 66.7% (n=66) of them were female. Patients were split into Non-OIS and OIS groups based on self-reported OIS, with 51 (51.5%) and 48 (48.5%) patients in each group, respectively. The frequency of PP was higher in the OIS group ($p<0.05$). In the regression analysis, OIS was significantly related to PP independent of age, sex, malnutrition, and frailty (odds ratio: 0.353, 95% confidence interval: 0.13-0.92, $p=0.033$). In addition, the number of drugs used was correlated with the total number of OIS symptoms ($r=0.204$, $p=0.042$).

Conclusion: This is the first study to show the link between PP and OIS. Further research is required to verify our results.

Keywords: Orthostatic intolerance, polypharmacy, older adults, geriatric, orthostatic blood pressure changes

Introduction

The increased multimorbidity burden in older adults leads to the prescription of multiple drugs and, ultimately, the development of polypharmacy (PP). Although no consensus on the definition of PP is available, it generally refers to the use of five or more drugs (1). Moreover, PP has been associated with many other geriatric syndromes, such as falls, disabilities, and poor physical performance (2,3).

Orthostatic blood pressure changes (OBPCs), namely orthostatic hypotension (OH), orthostatic hypertension, and orthostatic intolerance syndrome (OIS), are also prevalent issues among older adults (4). OIS is a group of symptoms caused by orthostatic position changes with or without OBPCs. These symptoms, which occur frequently, repeatedly, or persistently, are categorized primarily under seven headings: lightheadedness, exercise intolerance, tremulousness, generalized weakness, palpitations, blurred vision, and fatigue (4). Because of at least one of these symptoms, individuals with OIS have difficulty maintaining a standing position.

OIS is a cluster of symptoms resulting from transient cerebral hypoperfusion upon standing (5) and is related to various adverse outcomes such as depression, decreased quality of life, frailty, and falls (5-7). Although the underlying mechanism of OIS is still unclear, the main pathology is alterations in cerebral blood

Address for Correspondence: Arzu Okyar Baş, Hacettepe University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, Ankara, Turkey
Phone: +90 506 563 07 65 **E-mail:** arzu0506@hotmail.com **ORCID:** orcid.org/0000-0002-1518-5939

Received: 14.08.2023 **Accepted:** 23.11.2023

Cite this article as: Okyar Baş A, Öztürk Y, Güner M, Ceylan S, Kahyaoğlu Z, Çöteli S, Koca M, Eşme M, Balcı C, Doğu BB, Cankurtaran M, Halil MG. Polypharmacy-related Orthostatic Intolerance Syndrome in Community-dwelling Older Adults. Eur J Geriatr Gerontol 2024;6(1):58-64

flow and central or peripheral cardiovascular regulation control. Various factors contributed to the development of OBPCS and OIS (8). Psychotropic medications and drugs with cardiovascular effects are one of the main factors related to OIS (8,9). Similarly, PP and specific types of drugs, such as antihypertensives and diuretics, are known to be associated with OBPCs, particularly OH (10). Although drugs and PP are considered to be one of the primary causes of OH (11,12), no studies have evaluated the link between PP and OIS.

Therefore, we assessed the association between PP and OIS in older individuals.

Materials and Methods

Study Design

This study has a cross-sectional design. Participants admitted to the geriatric outpatient clinic for three months were evaluated. After performing exclusion criteria (i.e., neurodegenerative diseases and any types of dementia, severe edema, decompensated hepatic or cardiac insufficiency, dehydration or anemia, systemic atrophies, any condition causing immobility such as amputation and stroke, demyelinating diseases, valve stenosis, delirium, and patients who were receiving any active treatment for cancer diagnosis, who were not in remission, or terminal-stage patients), 99 geriatric patients were recruited. In addition to demographic data of the individuals (age and sex), chronic diseases. Patients with a history of fall in the previous year were defined as falling in the previous year. Medications, number of drugs, and PP (defined as using ≥5 drugs) were also assessed. Hacettepe University Non-Invasive Clinical Research Ethics Committee approved the study (decision number: 2023/06-19, date: 04.04.2023). A signed informed consent form was obtained from all patients who agreed to participate in the study.

Comprehensive Geriatric Assessment

In line with an objective comprehensive geriatric assessment (CGA), Katz basic and Lawton Brody instrumental activity of daily living (IADL) activities scales, Yesevage geriatric depression scale (YGDS), mini-mental state examination (MMSE) and mini-nutritional assessment-short form (MNA-SF) and were used. The Katz ADL scale (for basic ADL) and Lawton Brody scale (for IADL) were used to evaluate the participants' functional status, with the score decreasing as dependence increased (13-15). Nutritional screening was performed via MNA-SF. Scores ≤7 points refer to malnutrition (16,17). In addition, scores of more than 5 points in YGDS have been defined as positive for depression screening. Clinical assessments were performed to confirm the diagnosis of depression (18). The modified fried frailty index (FFI), which consisted of five criteria (i.e., weight loss, burnout, loss of strength, limitation in physical activity, and slow gait speed), was used to evaluate frailty status. Patients were defined as non-frail (0 points), prefrail (1-2 points), and frail (3-5 points) according to FFI scores (19,20).

Since questioning self-reported OIS depends on normal remembering function, we performed a detailed cognitive assessment. We excluded patients with dementia. According to current recommendations from the National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association and the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders criteria, patients were evaluated via cognitive assessment with a detailed history, cognitive tests, and neuroimaging when needed (21,22). For dementia screening and as a part of the CGA, we used the MMSE test, which also has Turkish validation (23,24). Although a study conducted in older Turkish adults suggested that an MMSE score <22 distinguishes dementia from mild cognitive impairment (25), we evaluated patients with a clinical suspicion of dementia according to clinical assessment, even if the MMSE score was not <22. In summary, after performing the assessments above, patients with no suspicion regarding cognitive functions were defined as having normal cognition and were included in the study.

Orthostatic Status Evaluation

To assess OBPCs, the active standing test (AST) was used. The initial blood pressure reading was acquired using a digital automatic blood pressure measurement instrument (CONTEC ABPM 50®) after the patient lay still on the examination bed for 20 min. The patients were then lifted into an upright position, and measurements were taken from the same arm at the first, third, fifth, and tenth minutes. Symptoms throughout the test were noted, and for OBPC assessment, the data gained from each minute of measurement were assessed. OH is described as a systolic blood pressure drop of at least 20 mmHg or a diastolic blood pressure drop of at least 10 mmHg. Orthostatic hypertension was defined as an increase in systolic or diastolic blood pressure of at least 20 mmHg.

Regarding the presence of OIS, the patients were questioned. We followed the 2017 American College of Cardiology/American Heart Association/Heart Rhythm Society Guidelines to define OIS (4). OIS was described in this recommendation as a group of symptoms that appear in response to a change in the orthostatic position. Patients were questioned with the following questions to assess OIS: "Have you ever experienced one of the following symptoms when you stood up from a sitting or lying position during the last three months?"

1- Lightheadedness

2- Palpitations (tachycardia)

3- Tremulousness

4- Generalized weakness

5- Blurred vision

6- Exercise intolerance (having trouble when exercising)

7- Fatigue

One or more symptoms were required for OIS diagnosis. Patients were also evaluated for the aforementioned symptoms that occurred during AST, and this data is also presented in the results and tables.

Statistics

Version 22.0 of SPSS was used for analysis. The normality of the distribution of the variables was tested using both graphical (histogram, probability graph) and statistical approaches. The number of cases and percentages were reported for nominal variables, whereas the mean and standard deviation were used to define continuous variables with a normal distribution (ND). Variables without ND are given as median [interquartile range (IQR)]. To compare median values across groups, we used the Mann-Whitney U test. Chi-square or Fisher exact tests were used to compare the data for categorical variables, with Bonferroni correction applied where appropriate. Independent factors linked with OIS were analyzed using a multivariate logistic regression model with the enter method. Before performing a multivariate logistic regression analysis, univariate analysis was performed, and confounders with a p-value of <0.05 in the univariate analysis [i.e., age, sex, malnutrition (MNA-SF scores), frailty (FFI score), and PP] were included in the multivariate logistic regression model. Using the Hosmer-Lemeshow goodness-of-fit statistic, the model fit was evaluated. For each predictor, we calculated odds ratios (OR) and 95% confidence intervals (CI). In addition, the Spearman correlation test was used to determine the relationship between each measurement and the total number of OIS symptoms. A p-value of 0.05 was considered statistically significant.

Results

Ninety-nine community-dwelling older adults were enrolled in the study. The median (IQR) age of participants was 74 (69.5-79.0) years, and 66.7% (n=66) were female. According to self-reported OIS, patients were divided into Non-OIS and OIS groups, with 51 (51.5%) and 48 (48.5%) patients in each group, respectively. Although no significant difference was observed between groups according to OH and hypertension in the AST, the frequency of OIS that occurred during the test was also higher in the OIS group (p=0.004). In the OIS group, the MNA-SF scores were lower, and the number of drugs and the frequencies of frailty and falling in the previous year were significantly higher. In addition, the frequency of PP in the whole group was 58.6% (n=58) and was significantly higher in the OIS group (p=0.016). There were no significant differences between the groups regarding age, sex, chronic diseases, and other CGA parameters (p>0.05) (Table 1).

Table 1. Demographical characteristics and comprehensive geriatric assessment according to the presence of orthostatic intolerance

	Non-OIS group n= 51 (51.5%)	OIS group n=48 (48.5%)	p
Age, median (IQR)	72 (68-79)	74 (70-79)	0.219
Female sex, n (%)	30 (58.8)	36 (75.0)	0.088
BMI, median (IQR)	30.1 (27.1-32.9)	30.5 (26.6-35.6)	0.701
Hypertension, n (%)	31 (60.8)	33 (68.8)	0.694
Diabetes mellitus, n (%)	21 (41.2)	17 (35.4)	0.556
Cancer, n (%)	2 (3.9)	7 (14.6)	0.065
Depression, n (%)	5 (9.8)	9 (18.8)	0.202
Cardiovascular diseases, n (%)	7 (13.7)	11 (22.9)	0.236
Cerebrovascular disease, n (%)	5 (10.0)	4 (8.3)	0.775
Renal diseases, n (%)	2 (3.9)	2 (4.2)	0.951
Falling in the previous year, n (%)	10 (20.0)	19 (36.9)	0.034
Basic ADLs, median (IQR)	6 (5.0-6.0)	6 (5.0-6.0)	0.063
Instrumental ADLs, median (IQR)	8 (7.0-8.0)	7 (5.0-8.0)	0.094
MMSE, median (IQR)	26 (23.0-29.0)	25 (21.0-28.0)	0.339
Yesevage scores, median (IQR)	2 (0.0-3.0)	3 (1.0-9.0)	0.059
MNA-SF scores, median (IQR)	13 (10.0-14.0)	10 (8.0-13.0)	0.004
Number of drugs, median (IQR)	4 (2.0-6.0)	6 (4.0-7.0)	0.005
Polypharmacy, n (%)	24 (47.1)	34 (70.8)	0.016
Frailty via FFI, n (%)	34 (66.7)	47 (96.9)	<0.001
Orthostatic hypotension, n (%)	11 (21.6)	13 (27.1)	0.522
Orthostatic hypertension, n (%)	10 (19.6)	8 (16.7)	0.705
Symptoms occurred during the test, n (%)	3 (5.9)	13 (27.1)	0.004

BMI: Body mass index, ADL: Activity of daily living, MMSE: Mini-mental state examination, MNA-SF: Mini-nutiritional assessment-short form, FFI: Fried frailty index, OIS: Orthostatic intolerance syndrome, IQR: Interquartile range

After univariate analysis, which was performed to determine the confounders related to OIS with a p-value of <0.05, age, sex, malnutrition (MNA-SF scores), frailty (FFI score), and PP were included in the multivariate logistic regression model. Regression analysis was used to assess the independent factors related to OIS. According to the multivariate logistic regression analysis, OIS was significantly related to PP regardless of age, sex, malnutrition, and frailty (OR: 0.353, 95% CI: 0.13-0.92, p=0.033) (Table 2).

In addition, in the correlation analysis of the total number of OIS symptoms experienced in the last three months and other parameters, besides the MNA-SF and FFI scores, the number of drugs used was also correlated to the total number of OIS symptoms (r=0.204, p=0.042) (Table 3).

To evaluate the diagnostic accuracy of the number of drugs for predicting OI, the receiver operating characteristic curves were analyzed. Using more than four drugs daily was the cutoff for OIS prediction (area under the curve: 0.665, 95% CI: 0.558-0.771, p=0.005) (Figure 1).

Discussion

This study, which was designed to investigate whether PP is related to OIS regardless of the medication type, revealed that PP is related to OIS regardless of confounders with well-established relationships with OIS (i.e., age, sex, frailty, and malnutrition). Furthermore, our results revealed that using more than four drugs daily may accurately predict OIS.

The prevalence of PP and OIS varies in the geriatric population. The prevalence of PP changes according to the cut-off drug numbers used and the environment where the study was conducted. In a study on Turkish geriatric female patients, PP was defined as using ≥5 drugs, and the prevalence of PP was 47.6% (26). Furthermore, a large sampled study that included

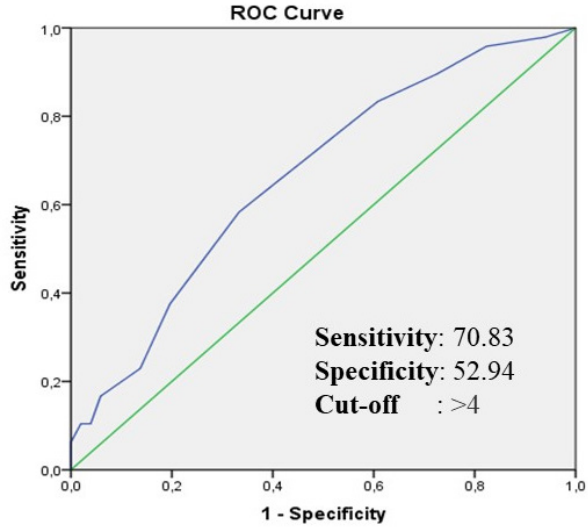

Figure 1. ROC curves demonstrating the accuracy of the predictive value of number of drugs used in determining orthostatic intolerance

AUC: 0.665, 95% CI: 0.558-0.771, p=0.005

ROC: Receiver operating characteristic, AUC: Area under the curve, CI: Confidence interval

Table 2. Logistic regression analysis of independent factors associated with orthostatic intolerance

	Presence of orthostatic intolerance*	
	OR (95% CI)	p
Polypharmacy	0.353 (0.13-0.92)	0.033
Frailty	1.590 (1.09-2.31)	0.015

*Variables included in the multivariate logistic regression analysis: age, sex, malnutrition (mini-nutiritional assessment short form scores), frailty (fried frailty index score) and polypharmacy
OR: Odds ratio, CI: Confidence interval

Table 3. Correlation analysis of the total number of orthostatic intolerance symptoms experienced in the last three months and other parameters

	Total number of orthostatic intolerance symptoms	
	r	p
Age	0.083	0.414
Basic ADLs	-0.189	0.066
Instrumental ADLs	-0.154	0.126
MMSE	-0.124	0.245
Yesevage score	0.130	0.220
MNA-SF score	-0.345	0.001
Fried frailty index score	0.462	<0.001
Number of drugs	0.204	0.042

ADL: Activity of daily living, MMSE: Mini-mental state examination, MNA-SF: Mini-nutiritional assessment-short form

17 European countries revealed that 32.1% of older adults take five or more medications daily (27). Studies in higher-income countries have reported higher PP prevalence (28). Our results demonstrated that the frequency of PP was 58.6%. Because our main aim was not to evaluate the prevalence and the sample size was relatively limited, the prevalence may be slightly higher than that reported in the literature. Unlike the many studies on PP prevalence, there are limited data on OIS prevalence in geriatric patients. Studies on OIS prevalence were often evaluated depending on OH occurrence, ranging between 24-100% (29). We evaluated self-reported OIS and OIS during the AST, and the prevalences were 48.5% and %16.2, respectively. Because there are scant and conflicting data on the link between OH and OI in the geriatric population (29), the prevalence of OIS defined solely based on symptoms during the OH evaluation may have overlooked the actual OIS prevalence. The higher prevalence of self-reported OIS than the symptoms in the test in our results may also support that hypothesis.

OIS is associated with many factors, such as long-term bed rest, chronic diseases (diabetes mellitus, Parkinson's disease, multiple sclerosis, etc.), and drugs, particularly diuretics and those with psychotropic effects (8,30-32). In addition to the well-known relationship between OIS and drugs, drugs also have a well-established relationship with OBPCs. A meta-analysis of 27,079 individuals from 69 studies, compared with placebo, beta-blockers, tricyclic antidepressants, alpha-blockers, antipsychotics, and sodium glucose co-transporter 2 inhibitors, showed a higher risk of OH. Although the above study was not designed to assess the link between OH and PP, the authors revealed that patients with PP may be at the greatest risk of drug-induced OH (10). In the study conducted by Samajdar et al. (33), geriatric patients were evaluated in terms of cardiac autonomic dysfunction via the Valsalva ratio, the presence of OH, the rise in diastolic blood pressure following an isometric hand-grip exercise, and heart rate variability, and the results showed that PP was significantly related to cardiac autonomic neuropathy. Cardiovascular autonomic dysfunction is also strongly associated with OIS (34,35). The underpinning pathway of the relationship between OIS and PP shown in our study may be cardiovascular autonomic dysfunction associated with both OIS and PP.

In previous studies, OIS and PP were related to various geriatric syndromes. Although OH is a major risk factor for falls in older adults, limited data have shown that OIS is associated with falls (36,37). Similar to OH, PP is strongly related to fall risk in the geriatric population (38). Moreover, interventions on PP and OH are recommended to prevent falls in older adults (37). Malnutrition and frailty are other common geriatric syndromes associated with PP and OBPCs, including OIS (7,39-41). In line with the current evidence, our results revealed that falls, frailty, and malnutrition are more likely in patients with OIS, and the number of OIS symptoms experienced in the last three months correlated with malnutrition and frailty. Moreover, when adjusted for independent factors that are both related to PP and OIS (i.e., age, sex, frailty, and malnutrition), a significant relationship between OIS and PP remained. This finding may indicate that there may be a strong and distinct pathway, such as exaggerated autonomic dysfunction, in the underlying mechanism for the independent relationship between these two entities. In addition to reviewing the drug groups for the prevention/treatment of OIS, reviewing the number of drugs may also work in geriatric patients.

Study Limitations

There are also some limitations in this study. The relatively small sample size was the major limitation. In addition, the small sample size may also make it unable to evaluate the effect of individual drug groups on the relationship between PP and OIS. Because FFI primarily assesses the physical domain of frailty, using only FFI for frailty assessment may be a limitation.

Conclusion

In conclusion, to the best of our knowledge, this is the first study showing that the number of drugs and multiple drug usage, namely PP, is associated with a higher frequency of OIS in the geriatric population. Larger sampled studies, including multidimensional frailty assessment and more detailed drug group analysis, are warranted to support our findings.

Ethics

Ethics Committee Approval: Hacettepe University Non-Invasive Clinical Research Ethics Committee approved the study (decision number: 2023/06-19, date: 04.04.2023).

Informed Consent: Informed consent was obtained.

Authorship Contributions

Surgical and Medical Practices: A.O.B., M.G., S.C., Z.K., S.Ç., M.C., M.G.H., Concept: A.O.B., Y.Ö., M.G., S.C., S.Ç., C.B., B.B.D., M.G.H., Design: A.O.B., Y.Ö., B.B.D., M.G.H., Data Collection or Processing: A.O.B., M.G., S.C., Z.K., S.Ç., M.K., M.G.H., Analysis or Interpretation: A.O.B., Y.Ö., M.G., S.C., M.K., M.E., C.B., B.B.D., M.C., M.G.H., Literature Search: A.O.B., Y.Ö., M.K., M.E., C.B., B.B.D., M.G.H., Writing: A.O.B., M.E., C.B., M.G.H.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. BMC Geriatr 2017;17:230.
2. Fried TR, O'Leary J, Towle V, Goldstein MK, Trentalange M, Martin DK. Health outcomes associated with polypharmacy in community-dwelling older adults: a systematic review. J Am Geriatr Soc 2014;62:2261-2272.

3. Ozkok S, Aydin CO, Sacar DE, Catikkas NM, Erdogan T, Kilic C, Karan MA, Bahat G. Associations between polypharmacy and physical performance measures in older adults. Arch Gerontol Geriatr 2022;98:104553.
4. Shen WK, Sheldon RS, Benditt DG, Cohen MI, Forman DE, Goldberger ZD, Grubb BP, Hamdan MH, Krahn AD, Link MS, Olshansky B, Raj SR, Sandhu RK, Sorajja D, Sun BC, Yancy CW. 2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Circulation 2017;136:25-59.
5. Novak V, Spies JM, Novak P, McPhee BR, Rummans TA, Low PA. Hypocapnia and cerebral hypoperfusion in orthostatic intolerance. Stroke 1998;29:1876-1881.
6. Moon J, Kim DY, Byun JI, Sunwoo JS, Lim JA, Kim TJ, Shin JW, Lee WJ, Lee HS, Jun JS, Park KI, Jung KH, Lee ST, Jung KY, Chu K, Lee SK. Orthostatic intolerance symptoms are associated with depression and diminished quality of life in patients with postural tachycardia syndrome. Health Qual Life Outcomes 2016;14:144.
7. Okyar Baş A, Güner Oytun M, Kahyaoğlu Z, Çöteli S, Ceylan S, Boğa İ, Doğu BB, Cankurtaran M, Halil MG. Orthostatic intolerance: a frailty marker for older adults. Eur Geriatr Med Jun 2022;13:675-684.
8. Goswami N, Blaber AP, Hinghofer-Szalkay H, Montani JP. Orthostatic Intolerance in Older Persons: Etiology and Countermeasures. Front Physiol 2017;8:803.
9. Luciano GL, Brennan MJ, Rothberg MB. Postprandial hypotension. Am J Med 2010;123:281.
10. Bhanu C, Nimmons D, Petersen I, Orlu M, Davis D, Hussain H, Magammanage S, Walters K. Drug-induced orthostatic hypotension: A systematic review and meta-analysis of randomised controlled trials. PLoS Med 2021;18:e1003821.
11. Dani M, Taraborrelli P, Panagopoulos D, Dirksen A, Torocastro M, Sutton R, Lim PB. New horizons in the ageing autonomic nervous system: orthostatic hypotension and supine hypertension. Age Ageing 2022;51:150.
12. Walston J, Hadley EC, Ferrucci L, Guralnik JM, Newman AB, Studenski SA, Ershler WB, Harris T, Fried LP. Research agenda for frailty in older adults: toward a better understanding of physiology and etiology: summary from the American Geriatrics Society/National Institute on Aging Research Conference on Frailty in Older Adults. J Am Geriatr Soc 2006;54:991-1001.
13. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969;9:179-186.
14. Arik G, Varan HD, Yavuz BB, Karabulut E, Kara O, Kilic MK, Kizilarslanoglu MC, Sumer F, Kuyumcu ME, Yesil Y, Halil M, Cankurtaran M. Validation of Katz index of independence in activities of daily living in Turkish older adults. Arch Gerontol Geriatr 2015;61:344-350.
15. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of Illness in the aged. The index of ADL: A standardized measure of biological and psychosocial function. JAMA 1963;185:914-919.
16. Guigoz Y, Lauque S, Vellas BJ. Identifying the elderly at risk for malnutrition. The Mini Nutritional Assessment. Clin Geriatr Med 2002;18:737-757.
17. Sarikaya D, Halil M, Kuyumcu ME, Kilic MK, Yesil Y, Kara O, Ozturk S, Gungor E, Karabulut E, Balam Yavuz B, Cankurtaran M, Ariogul S. Mini nutritional assessment test long and short form are valid screening tools in Turkish older adults. Arch Gerontol Geriatr 2015;61:56-60.
18. Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey M, Leirer VO. Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res 1982;17:37-49.
19. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA; Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:146-156.
20. Varan HD, Deniz O, Çöteli S, Doğrul RT, Kızılarslanoğlu MC, Göker B. Validity and reliability of Fried frailty phenotype in Turkish population. Turk J Med Sci 2022;52:524-527.
21. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology 1984;34:939-944.
22. Association AP. Diagnostic and statistical manual of mental disorders: DSM-5. American psychiatric association; 2013.
23. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-198.
24. Güngen C, Ertan T, Eker E, Yaşar R, Engin F. Standardize Mini Mental test'in türk toplumunda hafif demans tanisinda geçerlik ve güvenilirliği [Reliability and validity of the standardized Mini Mental State Examination in the diagnosis of mild dementia in Turkish population]. Turk Psikiyatri Derg 2002;13:273-281.
25. Varan HD, Kizilarslanoglu MC, Balci C, Deniz O, Coteli S, Dogrul RT, Aycicek GS, Kilic MK, O'Caoimh R, Molloy DW, Svendrovski A, Halil M, Cankurtaran M, Goker B, Yavuz BB. Comparison of the Accuracy of Short Cognitive Screens Among Adults With Cognitive Complaints in Turkey. Alzheimer Dis Assoc Disord 2020;34:350-356.
26. Bahat G, Tufan F, Bahat Z, Tufan A, Aydin Y, Akpinar TS, Nadir S, Erten N, Karan MA. Comorbidities, polypharmacy, functionality and nutritional status in Turkish community-dwelling female elderly. Aging Clin Exp Res 2014;26:255-259.
27. Midão L, Giardini A, Menditto E, Kardas P, Costa E. Polypharmacy prevalence among older adults based on the survey of health, ageing and retirement in Europe. Arch Gerontol Geriatr 2018;78:213-220.
28. Young EH, Pan S, Yap AG, Reveles KR, Bhakta K. Polypharmacy prevalence in older adults seen in United States physician offices from 2009 to 2016. PLoS One 2021;16:e0255642.
29. Christopoulos EM, Tran J, Hillebrand SL, Lange PW, Iseli RK, Meskers CGM, Maier AB. Initial orthostatic hypotension and orthostatic intolerance symptom prevalence in older adults: A systematic review. Int J Cardiol Hypertens 2021;8:100071.
30. Eguchi K, Pickering TG, Ishikawa J, Hoshide S, Komori T, Tomizawa H, Shimada K, Kario K. Severe orthostatic hypotension with diabetic autonomic neuropathy successfully treated with a beta(1)-blocker: a case report. J Hum Hypertens 2006;20:801-803.
31. Pintér A, Cseh D, Sárközi A, Illigens BM, Siepmann T. Autonomic Dysregulation in Multiple Sclerosis. Int J Mol Sci 2015;16:16920-16952.
32. Bae HJ, Lim JH, Cheon SM. Orthostatic hypotension and cognitive impairment in de novo patients with Parkinson's disease. J Mov Disord 2014;7:102-104.
33. Samajdar SS, Das S, Sarkar S, Mukherjee S, Pathak A, Stålsby Lundborg C, Saha I, Tripathi SK, Pal J, Chatterjee N, Joshi SR. Association between Polypharmacy and Cardiovascular Autonomic Function among Elderly Patients in an Urban Municipality Area of Kolkata, India: A Record-Based Cross-Sectional Study. Geriatrics (Basel) 2022;7:136.
34. Flachenecker P, Wolf A, Krauser M, Hartung HP, Reiners K. Cardiovascular autonomic dysfunction in multiple sclerosis: correlation with orthostatic intolerance. J Neurol 1999;246:578-586.
35. Grubb BP, Karas B. Clinical disorders of the autonomic nervous system associated with orthostatic intolerance: an overview of classification, clinical evaluation, and management. Pacing Clin Electrophysiol 1999;22:798-810.
36. Goswami N. Falls and fall-prevention in older persons: geriatrics meets spaceflight! Front Physiol 2017;8:603.
37. Montero-Odasso M, van der Velde N, Martin FC, Petrovic M, Tan MP, Ryg J, Aguilar-Navarro S, Alexander NB, Becker C, Blain H, Bourke R, Cameron

ID, Camicioli R, Clemson L, Close J, Delbaere K, Duan L, Duque G, Dyer SM, Freiberger E, Ganz DA, Gómez F, Hausdorff JM, Hogan DB, Hunter SMW, Jauregui JR, Kamkar N, Kenny RA, Lamb SE, Latham NK, Lipsitz LA, Liu-Ambrose T, Logan P, Lord SR, Mallet L, Marsh D, Milisen K, Moctezuma-Gallegos R, Morris ME, Nieuwboer A, Perracini MR, Pieruccini-Faria F, Pighills A, Said C, Sejdic E, Sherrington C, Skelton DA, Dsouza S, Speechley M, Stark S, Todd C, Troen BR, van der Cammen T, Verghese J, Vlaeyen E, Watt JA, Masud T; Task Force on Global Guidelines for Falls in Older Adults. World guidelines for falls prevention and management for older adults: a global initiative. Age Ageing 2022;51:205.

38. van der Velde N, Seppala LJ, Hartikainen S, Kamkar N, Mallet L, Masud T, Montero-Odasso M, van Poelgeest EP, Thomsen K, Ryg J, Petrovic M; EuGMS Task, Finish Group on Fall-risk-increasing drugs. European position paper on polypharmacy and fall-risk-increasing drugs recommendations in the World Guidelines for Falls Prevention and Management: implications and implementation. Eur Geriatr Med 2023;14:649-658.
39. Z Zhang Q, Shen S, Guan H, Zhang J, Chen X. Orthostatic hypotension is associated with malnutrition diagnosed by GLIM in elderly hypertensive patients. BMC Geriatr 2022;22:866.
40. Zanetti M, Veronese N, Riso S, Boccardi V, Bolli C, Cintoni M, Francesco VD, Mazza L, Onfiani G, Zenaro D, Pilotto A. Polypharmacy and malnutrition in older people: A narrative review. Nutrition 2023;115:112134.
41. Debain A, Loosveldt FA, Knoop V, Costenoble A, Lieten S, Petrovic M, Bautmans I; Gerontopole Brussels Study Group. Frail older adults are more likely to have autonomic dysfunction: A systematic review and meta-analysis. Ageing Res Rev 2023;87:101925.

ORIGINAL RESEARCH

DOI: 10.4274/ejgg.galenos.2023.2023-9-6

Eur J Geriatr Gerontol 2024;6(1):65-72

Polypharmacy and Falls-risk-increasing Drugs in Community-dwelling Older Adults

Sibel Akın[1], Nurdan Şentürk Durmuş[1], Tuba Soysal[1], Firuzan Fırat Özer[1], Bilge Müge Gökçekuyu[1], Gözde Ertürk Zararsız[2]

[1]Erciyes University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, Kayseri, Turkey
[2]phD, Erciyes University Faculty of Medicine, Department of Biostatistics, Kayseri, Turkey

Abstract

Objective: To evaluate the relationship between polypharmacy and the risk of recurrent falls and to assess the fall risk with different pharmacological groups of drugs.

Materials and Methods: In this cross-sectional study, falls risk-increasing drugs were defined as cardiovascular drugs, analgesics, central nervous system drugs, endocrine drugs, and others. Falls were evaluated according to their presence during the past 12 months. Two or more falls were recorded as recurrent fallers.

Results: Five hundred and eighteen participants had a mean age of 71.9 years (7.5) and 71.0% were female. While 87 (51.4%) participants fell once, 82 (48.5%) participants reported recurrent falls. Two hundred and eighty-eight (55.6%) participants had polypharmacy. The percentage of patients who used at least one potentially inappropriate mediation on admission, as defined by the Beers criteria, was 155 (29.9%). The determinants of the risk of recurrent falls were older age and use of angiotensin-converting enzyme inhibitors (ACE-I) [odds ratio (OR) 1.05: 95% confidence interval (CI) 1.00-1.09 and OR 4.04: 95% CI 1.70-9.60, respectively]. Low handgrip strength (HGS) increased the risk of falls approximately 1.7 times (OR 1.69 95% CI 1.11-2.58).

Conclusion: Although the polypharmacy rate of the participants was high, there was no significant relationship between polypharmacy and falling. However, we found low HGS, a component of sarcopenia, as a risk factor for falls, and use of ACE-I and older were risk factors for recurrent falls.

Keywords: Falls risk-increasing drugs, handgrip, older adults, polypharmacy, recurrent falls

Introduction

Polypharmacy is widespread in older adults because of comorbidities. One of the most important reasons why polypharmacy is seen in older adults is that; aging increases the incidence of chronic diseases (1). Changes in the pharmacokinetics and pharmacodynamics of drugs in older age lead older adults to be more susceptible to drug-induced adverse events (2,3). Decrease in total skeletal muscle and body water and increase in body fat with aging are associated with more frequent pharmacokinetic changes. In addition, decreased renal function in older adults affects drug clearance (2,3). An increase in the volume of distribution of lipid-soluble drugs and decreased clearance may increase the half-life of the drug and prolong its effect in older people. Polypharmacy is associated with an increased risk of poor outcomes such as frailty, disability, cognitive impairment, falls, hospitalizations, and mortality (2,4).

Falls frequently result from a combination of risk factors such as muscle weakness and frailty, vision and balance problems, cognitive impairment, polypharmacy, depression, and environmental hazards (4-6). Approximately 1/3 of older adults fall each year, and recurrent falls are seen in half of these the following year (5). Conditions associated with recurrent falling include a history of falling in the previous year, older age, sex,

Address for Correspondence: Sibel Akın, Erciyes University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, Kayseri, Turkey
Phone: +90 352 207 66 66 **E-mail:** sibelyanmaz@gmail.com **ORCID:** orcid.org/0000-0002-6139-7254

Received: 22.09.2023 **Accepted:** 14.12.2023

Cite this article as: Akın S, Şentürk Durmuş N, Soysal T, Fırat Özer F, Gökçekuyu BM, Ertürk Zararsız G. Polypharmacy and Falls-risk-increasing Drugs in Community-dwelling Older Adults. Eur J Geriatr Gerontol 2024;6(1):65-72

malnutrition, dependency, sleeping problems, use of walkers, balance problems, fear of falls, polypharmacy, the presence of potentially inappropriate medications (PIM), and some types of drug classes (5,7,8). Data from several studies suggest that oral antidiabetics, antipsychotics, antidepressants, benzodiazepines, beta-blockers, pain relief drugs, analgesics, antiparkinsonian, antiacids, and neuroleptic drugs are related to recurrent falling (5,9-13). More recently, contradictory findings have emerged that polypharmacy itself is not a risk factor for falling unless a fall-risk-increasing drug (FRID) is part of the drug regimen (3,14). Much uncertainty still exists regarding the relationship between polypharmacy, types of drugs, and falls. Thus, the present study aims to assess the associations among falls, recurrent falls, FRIDs, polypharmacy, and PIM in community-dwelling older adults in Turkey, thereby contributing to this controversial issue with data from Turkey.

Materials and Methods

This cross-sectional study was conducted in a tertiary geriatric outpatient clinic between January 2020 and February 2021 with participants >60 years. The exclusion criterion was being diagnosed with dementia. Patient information regarding age, sex, comorbidities, and the number of drugs used was recorded. Patients' self-reports were used for drug recording and were additionally controlled from the national medulla system (in Turkey). Polypharmacy was defined as the regular use of four or more drugs (1). Eyedrops, inhalers, and topical drugs were not recorded as a part of the total number of drugs. All participants provided written informed consent, and the Erciyes University Local Ethics Committee approved the study (decision number: 2019/136, date: 20.02.2019).

FRIDs were identified from previous systematic reviews and meta-analyses as cardiovascular drugs, analgesics, central nervous system drugs, endocrine drugs, and other drugs. Falls were evaluated according to their presence during the past 12 months. A fall was defined as an unexpected event in which a person came to rest on the ground or at a lower level. Persons who stated that they fell according to this definition were considered fallers. Two or more falls were recorded as recurrent fallers. Functional capacity was evaluated by the activities of daily living (ADL) (bathing or showering, dressing, moving from bed to chair, carrying out personal toileting, urine or bowel continence, and eating) (15) and the instrumental ADL (IADL) (preparing food, telephone, doing laundry, shopping, housekeeping, using transportation, handling finances, handling drugs) (16). Frailty was defined on the basis of the fatigue, resistance, ambulation, illnesses, and weight loss scale (17). Muscle strength was assessed by handgrip strength (HGS) using a dynamometer (Takei TKK 5401 Digital Handgrip Dynamometer, Niigata City, Japan). Low muscle strength was defined by HGS <30 kg and HGS <20 kg, for males and females, respectively (18). The Tinetti (19) assessment tool was used to determine the risk of falls in older adults (<19= high fall risk, 19-24= medium fall risk, and 25-28= low fall risk). Lying and standing tensions were measured and recorded under the outpatient clinic's control of all participants. A drop in blood pressure of at least 20 mmHg for systolic blood pressure and at least 10 mmHg for diastolic blood pressure within 3 min of standing up was accepted as the presence of orthostatic hypotension (20). The 2019 Updated American Geriatrics Society Beers Criteria (2) was used to screen for PIM.

Statistics

The histogram and q-q plots were examined. The normality of the data was tested using the Shapiro-Wilk test. The Levene test was used to test the homogeneity of variance. Pearson's chi-squared or Fisher's exact test was used to compare differences between groups for categorical variables. The Mann-Whitney U test was used to compare continuous variables. To investigate the effect of variables in estimating the number of drugs used for fallers and recurrent fallers in geriatric patients, binary logistic regression analysis models were constructed. Age- and sex-adjusted multiple logistic regression models were adjusted. Univariate and multiple binary logistic regression analyses were performed in the faller/non-faller and recurrent faller/non-recurrent faller groups.

The Wald statistic was used as a criterion for selecting models. Goodness-of-fit tests were performed using the Hosmer-Lemeshow test. Odds ratios were calculated with 95% confidence intervals. To control for multiple testing, the calculated p-values were adjusted using the Benjamini-Hochberg procedure. All analyses were performed using TURCOSA (Turcosa Analytics Ltd. Co., www.turcosa.com.tr); p-values below 0.050 were considered statistically significant.

Results

Of the 518 participants with a mean age of 71.9±7.5 years, 71.0% were female. The mean number of comorbidities was 2.81±1.57 (0-9). Seventy percent (386) patients had diabetes mellitus and 67.8% (233) had hypertension. The most commonly used drugs were, in descending order, diuretics (40.7%), angiotensin receptor blockers (ARBs) (29.3%), biguanides (28.8%), proton pump inhibitors (PPIs) (27.4%), acetyl salicylic acid (ASA) (26.8%), beta-blockers (23.2%), insulin (22.4%), calcium channel blockers (21.8%), and angiotensin-converting enzyme inhibitors (ACE-I) (20.7%). Approximately half of the patients (288) had polypharmacy. The percentage of patients using at least one PIM on admission according to the Beers criteria was 29.1% (151). The most commonly prescribed PIMs on admission were PPIs, 9.8% (51); non-steroidal anti-inflammatory drugs (NSAIDs), 8.7% (45); and antidepressants, 3.7% (19). Differences between participants are highlighted in Table 1.

Table 1. Baseline characteristic of participants based on polypharmacy

Variables	<4 drugs n=230	≥4 drugs n=288	p
Age, years	70.0 (65.8-75.0)	72.0 (67.0-78.0)	**0.027**
Sex, female	162 (44.0)	206 (56.0)	0.819
Years of education	5.0 (0-5.0)	1.0 (0-5.0)	0.392
Number of drugs	2.0 (1.0-2.3)	3.00 (2.0-4.0)	**<0.001**
PIMs n (%) Beers criteria	57 (24.8)	94 (32.6)	0.051
PIMs			
PPI	24 (42.1)	27 (28.7)	0.094
NSAIDs	16 (28.1)	29 (30.9)	0.717
Antidepressant	7 (12.3)	12 (12.8)	0.930
ADLs	1 (0.4)	16 (5.6)	**0.001**
IADLs	32 (15.6)	67 (25.8)	**0.008**
Comorbidities			
Hypertension	115 (50.0)	239 (81.9)	**<0.001**
Diabetes mellitus	59 (25.7)	174 (60.4)	**<0.001**
Stroke	8 (3.5)	23 (8.0)	**0.027**
Cardiac problems	18 (7.8)	66 (22.9)	**<0.001**
History of falls			
Non-faller	153 (66.5)	196 (68.1)	
One-faller	45 (19.6)	42 (14.6)	0.235
Recurrent fallers	32 (13.9)	50 (61.0)	
FRAIL score	1.0 (1.0-2.0)	2.0 (1.0-3.0)	**<0.001**
FRAIL			
Non-FRAIL	189 (82.2)	183 (63.5)	**<0.001**
FRAIL	41 (28.1)	105 (36.5)	
Physical performance			
TUG	9.2 (7.0-12.1)	10.0 (7.0-13.0)	0.103
Low handgrip strength	99 (46.7)	152 (59.6)	**0.005**
Blood pressure			
SBP	130.0 (115.0-140.0)	80.0 (70.0-90.0)	0.047
DBP	80.0 (70.0-90.0)	80.0 (70.0-82.5)	0.709
OH	36 (20.6)	46 (23.2)	0.535
Tinetti fall risk			
Low fall risk	176 (80.7)	173 (64.6)	
Medium fall risk	24 (11.0)	50 (18.7)	**<0.001**
High fall risk	18 (8.3)	45 (16.8)	

Low handgrip strength was <20 kg for women and <30 kg for men. Tinetti 25-28= low fall risk, 19-24= medium fall risk, <19= high fall risk values are expressed as n (%) or median (1st-3rd quartiles). Adjusted p-values are calculated using Benjamini-Hochberg procedure and significant adjusted p-values are shown in bold. ADL: Activities of daily living, DBP: Diastolic blood pressure, IADL: Instrumental activities of daily living, NSAID: Non-steroidal anti-inflammatory drug, OH: Orthostatic hypotension, PIM: Potentially inappropriate medication, PPI: Proton pump inhibitor, SBP: Systolic blood pressure, TUG: Timed Up & Go test, FRAIL: Fatigue, resistance, ambulation, illnesses, and weight loss

Falling was reported by 32.6% (169/518) of the participants, 51.4% (87) of the participants fell once, and 48.5% (82) reported recurrent falls. No significant differences were found between sex and single faller (p=0.152), and recurrent faller (p=0.397). The chi-square test did not show any significant differences between polypharmacy and one fall (p=0.711) and recurrent falls (p=0.098). No statistically significant difference could be observed between PIM and single-faller (p=0.072) and recurrent fallers (p=0.963). The relationship between the drug groups and fallers and recurrent fallers is shown in Table 2. There was no evidence that drug groups have an influence on falling. The results shown in Table 2 indicate that recurrent falls were significantly higher in those using ACE-I, ARB, and pregabalin (p=0.002, 0.038 and 0.024 respectively).

The Hosmer-Lemeshow test applied to each final model showed x^2=4.80, p=0.779 for recurrent fallers, x^2=4.59, p=0.802 for fallers. These results demonstrate the appropriateness of the multiple binary logistic regression model constructed for the prediction of clinical outcomes in older adults. From the data presented in Table 3, having a low HGS increased the risk of falling by approximately 1.7-fold (OR 1.69: 95% CI 1.11-2.58, p=0.022). Further analysis showed that older age and use of ACE-I were linked to the risk of recurrent falls (OR 1.05: 95% CI 1.00-1.09 and OR 4.04: 95% CI 1.70-9.60, p=0.031 and 0.006, respectively) (Table 4).

Table 2. Comparison of drugs between fallers vs. non-fallers and recurrent fallers vs. non-recurrent fallers

Variables	Faller n=169	Non-fallers n=349	p	Recurrent fallers n=87	Non-recurrent fallers n=82	p
Endocrine drugs						
Thyroid drugs	23 (13.6)	62 (17.8)	0.231	8 (9.8)	15 (17.2)	0.156
Antidiabetic drugs						
Insulin	35 (20.7)	81 (23.2)	0.522	20 (24.4)	15 (17.2)	0.252
Biguanides	46 (30.9)	103 (29.5)	0.589	24 (29.3)	22 (25.3)	0.561
Sulfonylureas	3 (1.8)	8 (2.3)	0.462	2 (2.4)	1 (1.1)	0.478
DPP4I	25 (14.8)	50 (14.3)	0.888	16 (19.5)	9 (10.3)	0.093
Other antidiabetics	1 (0.6)	7 (2.0)	0.221	0 (0.0)	1 (1.1)	0.515
Analgesics						
NSAIDS	19 (11.2)	39 (11.2)	0.982	12 (14.6)	7 (8.0)	0.174
CNS medicines						
Antidepressants						
SSRI	10 (5.9)	13 (3.7)		8 (9.8)	2 (2.3)	
SNRI	18 (10.7)	38 (11.0)	0.525	6 (7.3)	12 (13.8)	0.060
Antiparkinsonians	13 (7.7)	16 (4.4)	0.149	6 (7.3)	7 (8.0)	0.859
Benzodiazepines	2 (1.2)	3 (0.9)	0.526	2 (2.4)	0 (0.0)	0.234
Antipsychotics	6 (3.6)	15 (4.3)	0.686	3 (3.7)	3 (3.4)	0.941
Cardiovascular drugs						
α-blockers	8 (95.3)	15 (4.3)	0.821	3 (3.7)	5 (5.7)	0.523
β-blockers	37 (21.9)	83 (23.8)	0.633	18 (22.0)	19 (21.8)	0.986
ACE-inhibitors	35 (20.7)	72 (20.6)	0.983	25 (30.5)	10 (11.5)	**0.002**
ARB	43 (25.4)	109 (31.2)	0.175	15 (18.3)	28 (32.2)	**0.038**
Calcium channel blockers	34 (20.1)	79 (22.6)	0.515	14 (17.1)	20 (23.0)	0.338
Diuretics	62 (36.7)	149 (42.7)	0.192	29 (35.4)	33 (37.9)	0.729
ASA	48 (28.4)	91 (26.1)	0.575	29 (35.4)	19 (21.8)	**0.061**
Drugs other than fall risk-increasing drugs						
H2RA	0 (0.0)	2 (0.6)	0.324	-	-	-
PPI	45 (26.6)	97 (27.8)	0.780	26 (31.7)	19 (21.8)	0.147
Dyslipidemic drugs	16 (9.5)	43 (12.3)	0.338	8 (9.8)	8 (9.8)	0.901
Steroids	2 (1.2)	15 (4.3)	**0.047**	4 (2.4)	0 (0.0)	0.234
Pregabalin	8 (4.7)	16 (4.6)	0.940	7 (8.5)	1 (1.1)	**0.024**
Gabapentin	7 (4.1)	17 (4.9)	0.711	5 (6.1)	2 (2.3)	0.198
Piracetam	12 (7.1)	13 (3.7)	0.093	9 (11.0)	3 (3.4)	0.074

Descriptive statistics is n (%). Adjusted p-values are calculated using Benjamini-Hochberg procedure and significant adjusted p-values are shown in bold. ACE: Angiotension converting enzyme, ARB: Angiotension receptor blocker, ASA: Acetyl salicylic acid, CNS: Central nervous system, DPP4I: Dipeptidyl peptidase 4 inhibitor, H2RA: Histamine 2 receptor blocker, NSAID: Non-steoridal anti-inflammatory drug, PPI: Proton pump inhibitor, SSRI: Selective serotonin reuptake inhibitor, SNRI: Selective noradrenalin reuptake inhibitor

Discussion

To our knowledge, this is the first study to evaluate the associations between falls, recurrent falls, FRID, polypharmacy, and PIM use in community-dwelling older adults. Studies investigating the association between recurrent falls and polypharmacy are limited. In the present study, 55.6% of older adults had polypharmacy and 29.1% of participants had taken at least one PIM. Thirty-two percent of older adults had fallen at least once in the previous year, and approximately half reported recurrent falls. The most important result was that having low HGS increased the risk of falling, and older age and using ACE-I increased the risk of recurrent falls.

The fall rate in this study (32%) was lower than that in several other studies in older adults, which reported fall rates of 13.1-41.8% and recurrent fall rates of 13.1-86.9% (5,21). These studies included either unhealthy populations (e.g., people with chronic stroke) or different populations (e.g., home care patients). However, polypharmacy was not correlated with falling or recurrent falling.

Consistent with the literature, this research found that the polypharmacy prevalence was 55.6 (2,4,6,21). Different types of drugs have been reported as the most commonly used in previous studies (6,21). In this study, the most commonly used drugs were diuretics, ARBs, biguandides, PPIs, and ASA. Differences in preferred drugs between populations and the lack of standardization in drug selection worldwide may explain this.

Studies have shown that polypharmacy is an independent risk factor for falls. Drugs are significant risk factors for falls, and discontinuing drugs that increase the risk of falling is an

Table 3. Univariate and multiple binary logistic regression analysis in estimating faller in older adults

	Crude model		Adjusted model		Multiple model	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Sex	1.35 (0.89-2.05)	0.152	-	-	1.59 (0.98-2.56)	0.058
Age	1.01 (0.98-1.04)	0.312	-	-	-	-
Number of comorbidities	1.07 (0.95-1.20)	0.236	1.06 (0.95-1.20)	0.292	-	-
Number of medications	0.99 (0.93-1.06)	0.853	0.99 (0.92-1.05)	0.720	-	-
Polypharmacy	0.93 (0.64-1.35)	0.711	0.91 (0.62-1.31)	0.603	-	-
Number of PIMs	0.96 (0.50-1.83)	0.893	1.07 (0.55-2.07)	0.842	-	-
Antihypertensive drugs usage	0.71 (0.48-1.05)	0.088	0.64 (0.43-0.96)	**0.032**	0.66 (0.42-1.03)	0.070
ACE-I	1.00 (0.64-1.58)	0.983	1.00 (0.63-1.58)	0.992	-	-
ARB	0.75 (0.50-1.14)	0.176	0.70 (0.46-1.07)	0.097	-	-
KATZ-ADL	2.40 (0.91-6.33)	0.077	2.16 (0.80-5.82)	0.129	-	-
IADL	1.51 (0.95-2.40)	0.082	1.43 (0.86-2.38)	0.165	-	-
FRAIL	1.49 (0.99-2.21)	0.052	1.38 (0.91-2.09)	0.124	-	-
Low handgrip strength	1.52 (1.03-2.25)	**0.036**	1.43 (0.95-2.16)	0.088	1.69 (1.11-2.58)	**0.015**

Adjusted models are controlled for age and sex. Adjusted p-values are calculated using Benjamini-Hochberg procedure and significant adjusted p-values are shown in bold. ACE: Angiotension converting enzyme, PIM: Potentially inappropriate medication, ARB: Angiotension receptor blocker, ADL: Activities of daily living, IADL: Instrumental activities of daily living, FRAIL: Fatigue, resistance, ambulation, illnesses, and weight loss, OR: Odds ratio, CI: Confidence interval

Table 4. Univariate and multiple binary logistic regression analysis in estimating recurrent faller in older adults

	Crude model		Adjusted model		Multiple model	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Sex	1.35 (0.67-2.74)	0.398	-	-	-	-
Age	1.04 (0.99-1.08)	0.074	-	-	1.05 (1.00-1.09)	**0.031**
Number of comorbidities	1.00 (0.84-1.20)	0.941	1.00 (0.84-1.20)	0.942	-	-
Number of drugs	1.08 (0.97-1.21)	0.160	1.08 (0.96-1.20)	0.192	-	-
Polypharmacy	1.67 (0.91-3.08)	0.099	1.60 (0.86-2.97)	0.135	-	-
Number of PIMs	1.22 (0.44-3.37)	0.904	0.95 (0.50-1.82)	0.876	-	-
Antihypertensive drugs usage	1.17 (0.63-2.19)	0.618	1.11 (0.58-2.12)	0.756	-	-
ACE-I	3.38 (1.50-7.59)	**0.003**	3.38 (1.49-7.69)	**0.004**	4.04 (1.70-9.60)	**0.002**
ARB	0.47 (0.23-0.97)	**0.040**	0.44 (0.21-0.94)	**0.034**	-	-
KATZ-ADL	0.51 (0.12-2.21)	0.356	0.36 (0.08-1.60)	0.179	-	-
IADL	1.18 (0.56-2.48)	0.656	0.88 (0.38-2.01)	0.762	-	-
FRAIL	1.37 (0.55-1.96)	0.911	0.86 (0.44-1.68)	0.668	-	-
Low handgrip strength	1.88 (0.97-3.62)	0.060	1.60 (0.80-3.18)	0.182	-	-

Adjusted models are controlled for age and sex. Adjusted p-values are calculated using Benjamini-Hochberg procedure and significant adjusted p-values are shown in bold. ACE: Angiotension converting enzyme, PIM: Potentially inappropriate medication, ARB: Angiotension receptor blocker, ADL: Activities of daily living, IADL: Instrumental activities of daily living, FRAIL: Fatigue, resistance, ambulation, illnesses, and weight loss, OR: Odds ratio, CI: Confidence interval

effective intervention to prevent falls (6,14,22). In 13 of the 19 meta-analysed studies, polypharmacy was not associated with falling (3). As shown in other meta-analyses (23), polypharmacy did not appear to be a risk factor for falls in our study. Although the relationship between polypharmacy and falls is debated, the relationship between recurrent falls and polypharmacy has been shown in many studies. In our study, the rate of recurrent falls was higher than that reported in few other studies (48.5% vs. 12.2% and 28%) (12.2% and 28% vs. 48.5%) (5,7). This study was unable to demonstrate that polypharmacy and recurrent falls were related.

Some studies have found that PIM use leading to falls was more important in increasing the risk of falls than the number of drugs used by older adult patients (24,25). Some studies have found no association between falls and PIM use (21,25). One study found no difference in falls between patients who used PIM, which increases the risk of falls, and those who did not (25). Eleven types of drugs (ibuprofen, gabapentin, sertraline, zolpidem) were identified as PIM in a study of 99 participants. However, no association was reported between PIM and falls or recurrent falls. No association was observed between recurrent falls and polypharmacy (21). Atak et al. (4) reported that 28.8%

of participants used PIM, which increased the risk of falling according to the Beers criteria. The risks associated with PIM were associated with the number of drugs used and the number of comorbidities, but no analysis of FRIDs was performed in this study (4). In the present study, only 29.1% of patients were found to have a PIM, despite the high rate of polypharmacy. Between the presence of PIM and the types of drugs according to the Beers criteria and falls and recurrent falls, no significant correlation was found.

Drug classes that have been associated with an increased risk of falls include the following: antihypertensive agents, sedatives and hypnotics, neuroleptics and antipsychotics, antidepressants, benzodiazepine, and NSAIDs. In the studies conducted, a direct relationship between some drug groups and falls was observed. A two-way relationship was found between FRID and polypharmacy in one study (22). Although the prevalence of FRIDs was higher in patients with polypharmacy, polypharmacy was also more common in patients with FRIDs (22). Using FRIDs increases the risk of falls (26).

When we looked at the specific drug groups, NSAIDs, benzodiazepines, antidepressants, hypnotics, opioids, and antihypertensive drugs were associated with falls in some studies (3,27). However, nine of 13 studies showed no association between NSAID use and falls (28). In a meta-analysis, opioid and antiepileptic usage were significantly associated with an increased risk of falling. However, NSAIDs, PPIs, anti-dementia drugs, antiparkinsonian drugs, and analgesics were not associated with falling (14). Lawson et al. (21) reported that no significant relationship was observed between 23 drug types and falls.

Antipsychotic, antidepressant, analgesic, antiparkinsonian, nasal, and ophthalmic drugs have been associated with recurrent falls (8). Formiga et al. (9) found that people with recurrent falls were more likely to have polypharmacy and to use neuroleptic drugs. One study showed that the use of psychoactive drugs, defined as PIM according to the Beers criteria, increased the risk of falling by up to 20% (29). Anderson and Lane (7) found an association between the use of antidepressants and recurrent falls among drugs including antipsychotics, anti-anxiety agents, antidepressants, and diuretics. A study of community-dwelling older adults showed an association between recurrent falls and selective serotonin reuptake inhibitor use, moderate dose, and short duration (30). A meta-analysis also found that the use of psychotropic drugs increased the risk of falling in some studies, and not others (3). To our surprise, we did not find an association between the use of benzodiazepines, antipsychotics, antidepressants, and NSAIDs and recurrent falls. The reason for this may be the restriction on the use of hypnotic drugs and on the prescribing of these drugs imposed on individual doctors in Turkey by the Ministry of Health. It may also be that participants were unaware that they could take NSAIDs without a prescription; non-prescription drugs are not part of the medulla system; therefore, these drugs were not included. We found that only ACE-I use was associated with an increased risk of recurrent falls. Antihypertensive drugs cause falls through several mechanisms. They increase the risk of falls due to sudden falls in blood pressure, orthostatic hypotension, and electrolyte disturbances (31).

Our study showed a strong relationship between low HGS and recurrent falls, which is a sarcopenia criteria affecting muscle strength in falling. In line with other studies (26,32), we showed in this study that older age was associated with an increase in recurrent falls. Older people are known to be more prone to falls, recurrent falls, and fall injuries (9). To date, many studies have shown an association between falling and walking speed (6,32). The relationship between muscle strength and falling has only been investigated in a few studies. In some of these trials, individuals who fell repeatedly had low HGS levels, as in our study (32). It is a well-known fact that sarcopenia increases the risk of falling and that people with a low HGS are likely to be sarcopenic (18).

Study Limitations

In our study, there were some limitations. A limitation of this study was the lack of an investigation of drug interactions. Although some drugs may not increase the risk of a fall on their own, they may significantly increase the risk of a fall because of their cumulative effects when used together with drugs from another group. It is unfortunate that the study did not include the use of over-the-counter medicines, nasal medicines, ophthalmic medicines, and herbal medicines. By including only outpatients, the study population may be healthier than the community older adult population. In addition, the study was designed as a cross-sectional study, which may have limited its ability to show a causal relationship between the risk factors for fall and recurrent falls.

Conclusion

The results of this study did not confirm the findings of previous studies linking certain classes of drugs to the risk of falling in older adults. Drugs are a known risk factor for falls. However, it is important to consider the reason for taking a drug before deciding to stop or withdraw a drug for fall prevention because the condition that the drug is being used to treat may itself be a risk factor for falls. Therefore, each drug should be considered individually, and the benefits and risks of stopping or continuing the drug should be carefully weighed. This study may not have been able to prove the association between certain groups of drugs and falls and recurrent falls, as other studies have done. However, low HGS, a component of sarcopenia, is a risk factor

for falls. This once again highlights the importance of screening and detecting sarcopenia in the geriatric population.

Ethics

Ethics Committee Approval: This study was approved by the Erciyes University Ethics Committee (decision number: 2019/136, date: 20.02.2019).

Informed Consent: Informed consent was obtained from all participants.

Authorship Contributions

Surgical and Medical Practices: S.A., Concept: S.A., N.Ş.D., T.S., F.F.Ö., B.M.G., G.E.Z., Design: S.A., N.Ş.D., Data Collection or Processing: S.A., N.Ş.D., T.S., F.F.Ö., B.M.G., G.E.Z., Analysis or Interpretation: S.A., N.Ş.D., G.E.Z., Literature Search: S.A., N.Ş.D., T.S., F.F.Ö., B.M.G., Writing: S.A., N.Ş.D., G.E.Z.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. BMC Geriatr 2017;17:230.
2. By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc 2019;67:674-694.
3. Park H, Satoh H, Miki A, Urushihara H, Sawada Y. Medications associated with falls in older people: systematic review of publications from a recent 5-year period. Eur J Clin Pharmacol 2015;71:1429-1440.
4. Atak BM, Aktas G, Duman TT, Kurtkulagi O, Bilgin S, Kahveci G, Demirkol ME. Inappropriate medication use in older adults according to Beers Criteria in a Tertiary Referral Hospital, in Bolu, Turkey. Russian Open Medical Journal 2021;10:211.
5. Alenazi AM, Alshehri MM, Alothman S, Rucker J, Dunning K, D'Silva LJ, Kluding PM. Functional Reach, Depression Scores, and Number of Medications Are Associated With Number of Falls in People With Chronic Stroke. PM R 2018;10:806-816.
6. Dhalwani NN, Fahami R, Sathanapally H, Seidu S, Davies MJ, Khunti K. Association between polypharmacy and falls in older adults: a longitudinal study from England. BMJ Open 2017;7:e016358-e.
7. Anderson LK, Lane K. Characteristics of falls and recurrent falls in residents of an aging in place community: A case-control study. Appl Nurs Res 2020;51:151190.
8. Askari M, Eslami S, Scheffer AC, Medlock S, de Rooij SE, van der Velde N, Abu-Hanna A. Different risk-increasing drugs in recurrent versus single fallers: are recurrent fallers a distinct population? Drugs Aging 2013;30:845-851.
9. Formiga F, Navarro M, Duaso E, Chivite D, Ruiz D, Perez-Castejon JM, Lopez-Soto A, Pujol R. Factors associated with hip fracture-related falls among patients with a history of recurrent falling. Bone 2008;43:941-944.
10. Lee JS, Kwok T, Leung PC, Woo J. Medical illnesses are more important than medications as risk factors of falls in older community dwellers? A cross-sectional study. Age Ageing 2006;35:246-251.
11. Seppala LJ, Petrovic M, Ryg J, Bahat G, Topinkova E, Szczerbińska K, van der Cammen TJM, Hartikainen S, Ilhan B, Landi F, Morrissey Y, Mair A, Gutiérrez-Valencia M, Emmelot-Vonk MH, Mora MÁC, Denkinger M, Crome P, Jackson SHD, Correa-Pérez A, Knol W, Soulis G, Gudmundsson A, Ziere G, Wehling M, O'Mahony D, Cherubini A, van der Velde N. STOPPFall (Screening Tool of Older Persons Prescriptions in older adults with high fall risk): a Delphi study by the EuGMS Task and Finish Group on Fall-Risk-Increasing Drugs. Age Ageing 2021;50:1189-1199.
12. Bahat G, Ilhan B, Erdogan T, Oren MM, Karan MA, Burkhardt H, Denkinger M, Garfinkel D, Cruz-Jentoft AJ, Morrissey Y, Onder G, Pazan F, Tommelein E, Topinkova E, van der Velde N, Petrovic M. International Validation of the Turkish Inappropriate Medication Use in the Elderly (TIME) Criteria Set: A Delphi Panel Study. Drugs Aging 2021;38:513-521.
13. Bahat G, Ilhan B, Erdogan T, Halil M, Savas S, Ulger Z, Akyuz F, Bilge AK, Cakir S, Demirkan K, Erelel M, Guler K, Hanagasi H, Izgi B, Kadioglu A, Karan A, Kulaksizoglu IB, Mert A, Ozturk S, Satman I, Sever MS, Tukek T, Uresin Y, Yalcin O, Yesilot N, Oren MM, Karan MA. Turkish inappropriate medication use in the elderly (TIME) criteria to improve prescribing in older adults: TIME-to-STOP/TIME-to-START. Eur Geriatr Med 2020;11:491-498.
14. Seppala LJ, van de Glind EMM, Daams JG, Ploegmakers KJ, de Vries M, Wermelink AMAT, van der Velde N; EUGMS Task and Finish Group on Fall-Risk-Increasing Drugs. Fall-Risk-Increasing Drugs: A Systematic Review and Meta-analysis: III. Others. J Am Med Dir Assoc 2018;19:372.e1-e8.
15. Katz S, Downs TD, Cash HR, Grotz RC. Progress in development of the index of ADL. The Gerontologist 1970;10:20-30.
16. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. The Gerontologist 1969;9:179-186.
17. Morley JE, Malmstrom TK, Miller DK. A simple frailty questionnaire (FRAIL) predicts outcomes in middle aged African Americans. J Nutr Health Aging 2012;16:601-608.
18. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, Schneider SM, Sieber CC, Topinkova E, Vandewoude M, Visser M, Zamboni M; Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48:16-31.
19. Tinetti ME. Performance-oriented assessment of mobility problems in elderly patients. J Am Geriatr Soc 1986;34:119-126.
20. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. The Consensus Committee of the American Autonomic Society and the American Academy of Neurology. Neurology 1996;46:1470.
21. Lawson K, Vinluan CM, Oganesyan A, Gonzalez EC, Loya A, Strate JJ. A retrospective analysis of prescription medications as it correlates to falls for older adults. Pharm Pract (Granada) 2018;16:1283.
22. Correa-Pérez A, Delgado-Silveira E, Martín-Aragón S, Rojo-Sanchís AM, Cruz-Jentoft AJ. Fall-risk increasing drugs and prevalence of polypharmacy in older patients discharged from an Orthogeriatric Unit after a hip fracture. Aging Clin Exp Res 2019;31:969-975.
23. Richardson K, Bennett K, Kenny RA. Polypharmacy including falls risk-increasing medications and subsequent falls in community-dwelling middle-aged and older adults. Age Ageing 2015;44:90-96.
24. Beer C, Hyde Z, Almeida OP, Norman P, Hankey GJ, Yeap BB, Flicker L. Quality use of medicines and health outcomes among a cohort of community dwelling older men: an observational study. Br J Clin Pharmacol 2011;71:592-599.
25. Bor A, Matuz M, Csatordai M, Szalai G, Bálint A, Benkő R, Soós G, Doró P. Medication use and risk of falls among nursing home residents: a retrospective cohort study. Int J Clin Pharm 2017;39:408-415.

26. Musich S, Wang SS, Ruiz J, Hawkins K, Wicker E. Falls-Related Drug Use and Risk of Falls Among Older Adults: A Study in a US Medicare Population. Drugs Aging 2017;34:555-565.

27. Ryynänen OP, Kivelä SL, Honkanen R, Laippala P, Saano V. Medications and chronic diseases as risk factors for falling injuries in the elderly. Scand J Soc Med 1993;21:264-271.

28. Hegeman J, van den Bemt BJF, Duysens J, van Limbeek J. NSAIDs and the risk of accidental falls in the elderly: a systematic review. Drug Saf 2009;32:489-498.

29. Agashivala N, Wu WK. Agashivala N, Wu WK. Effects of potentially inappropriate psychoactive medications on falls in US nursing home residents: analysis of the 2004 National Nursing Home Survey database. Drugs Aging 2009;26:853-860.

30. Marcum ZA, Perera S, Thorpe JM, Switzer GE, Castle NG, Strotmeyer ES, Simonsick EM, Ayonayon HN, Phillips CL, Rubin S, Zucker-Levin AR, Bauer DC, Shorr RI, Kang Y, Gray SL, Hanlon JT; Health ABC Study. Antidepressant Use and Recurrent Falls in Community-Dwelling Older Adults: Findings From the Health ABC Study. Ann Pharmacother 2016;50:525-533.

31. Shimbo D, Barrett Bowling C, Levitan EB, Deng L, Sim JJ, Huang L, Reynolds K, Muntner P. Short-Term Risk of Serious Fall Injuries in Older Adults Initiating and Intensifying Treatment With Antihypertensive Medication. Circ Cardiovasc Qual Outcomes 2016;9:222-229.

32. Zia A, Kamaruzzaman SB, Tan MP. The consumption of two or more fall risk-increasing drugs rather than polypharmacy is associated with falls. Geriatr Gerontol Int 2017;17:463-470.

CASE REPORT

DOI: 10.4274/ejgg.galenos.2023.2023-2-1
Eur J Geriatr Gerontol 2024;6(1):73-75

Diagnostic Challenge of an Advanced Stage Dementia Case

Emin Taşkıran

Isparta City Hospital, Clinic of Geriatrics, Isparta, Turkey

Abstract

A 63-year old male was brought to the geriatric outpatient unit by his wife with a complaint of progressive loss of movement skill and intellectual capacity over the last 3 years. He was a farmer and began to have difficulties in multilevel tasks. Sleeping problems started to occur. Also, he was agitated most of the time and even used violence against his wife. At presentation to the geriatric outpatient unit, he was in a wheelchair and dependent on his wife during all daily living activities. He was bedridden and incontinent. He had muscle stiffness. He had 14 points on the Glasgow Coma scale. His eyes were open spontaneously but did not obey commands. Cranial nerve reflexes were intact. His neurological examination did not reveal any specific findings for a previous stroke or meningitis. A cranial magnetic resonance imaging scan revealed an atrophic cortex of the cerebrum with ischemic gliosis fields in the periventricular white matter. In the light of all findings, major neurocognitive disorder with Lewy body diagnosis was made according to the diagnostic and statistical manual of mental disorders-5 diagnostic criteria. Dementia related to Parkinson's disease (PD) and supranuclear palsy were other relevant diseases for differential diagnosis. In this case, the movement disorder developed after psychotic symptoms and memory impairment. This is contrary to dementia related to PD. At presentation, cranial nerve examination was normal, unlike supranuclear palsy in this case. Rivastigmine 10 cm^2 transdermal patch once a day and levadopa-benserazid 50-12.5 mg three times a day prescribed.

Keywords: Advanced stage dementia, clinical geriatrics, cognitive disorders, dementia with lewy body, geriatric psychiatry

Introduction

A case with advanced stage dementia usually exhibits similar symptoms and findings without any specific sign of the underlying primary cause of dementia. Currently, physicians tend to diagnose and treat most advanced dementia cases as cerebrovascular dementia or Alzheimer's disease because they are the main causes of late-onset dementia. The diagnosis of the underlying cause mostly depends on the history taken from the relatives of the patient. The history may reveal the primary symptom, age at which the symptoms begin, and predisposing factors for dementia. Thus, a correct history of the patient is essential for a correct diagnosis. Dementia with Lewy body (DLB) is an early-onset, progressive, and relatively rare disease with confounding symptoms that may lead to a possible misdiagnosis as a psychotic disorder. In this case report, a retrograde diagnosis of an advanced stage dementia case of disorder with Lewy body is presented.

Case Report

A 63-year-old male was brought to the geriatric outpatient unit by his wife with a complaint of progressive loss of movement skill and intellectual capacity over the last 3 years. Anamnesis was learned from his wife. She told that after an event that had led to deep sadness for him, he started to have paranoid thoughts like feeling hostile towards himself from his wife or relatives as well as a loss of concentration at work. He was a farmer and began to have difficulties in multilevel tasks. Sleeping problems started to occur. Also, he was agitated most of the time and even used violence against his wife. He was sometimes alert and sometimes sleepy during the day. At that

Address for Correspondence: Emin Taşkıran, Isparta City Hospital, Clinic of Geriatrics, Isparta, Turkey
Phone: +90 530 067 09 80 **E-mail:** emintaskiran@yahoo.com **ORCID:** orcid.org/0000-0002-4709-4222
Received: 06.02.2023 **Accepted:** 11.08.2023
Cite this article as: Taşkıran E. Diagnostic Challenge of an Advanced Stage Dementia Case. Eur J Geriatr Gerontol 2024;6(1):73-75

time, he did not have any comorbidities. He was examined by a psychiatrist and diagnosed with late-life schizophrenia. Antipsychotic drugs were prescribed. These medications helped him settle down. However, in a 3-year period, he started to have difficulties in moving progressively, resulting in a bedridden situation. There was no anything remarkable in his medical and familial history. At presentation to the geriatric outpatient unit, he was in a wheelchair and dependent on his wife during all daily living activities. He was bedridden and incontinent. He had muscle stiffness. He was on levetiracetam 500 mg twice a day.

On physical examination, blood pressure was 120/65 mmHg, body temperature was 36.7 0C, and respiratory rate was 10 beats/min. He had 14 points on the Glasgow Coma scale. His eyes were open spontaneously but did not obey commands. He was not answering any questions but turning his head toward his voice. His eye movements were normal and preserved in all ways. Cranial nerve reflexes were intact. He could swallow liquid and semi-liquid food. He was localizing a painful stimulus on the sternum and was trying to grab the physician's hand. During passive flexion and extension movement of both arms and legs, the cogwheel sign was not observed. Deep tendon reflexes were weak, and Babinski's sign was negative. His neurological examination did not reveal any specific findings for a previous stroke or meningitis. He had a grade 1-2 pressure ulcer on his sacrum. Other systems were normal at the time of examination.

Laboratory findings revealed slight anemia with 11.2 g/dL of hemoglobin and an elevated C-reactive protein level of 20 mg/dL. A cranial magnetic resonance imaging scan was performed, which revealed an atrophic cortex of the cerebrum with ischemic gliosis fields in the periventricular white matter (Figure 1).

Considering all findings, major neurocognitive DLB diagnosis was made according to the diagnostic and statistical manual of mental disorders-5 diagnostic criteria (1). Dementia related to Parkinson's disease (PD) and supra-nuclear palsy were other relevant diseases for differential diagnosis. In this case, the movement disorder developed after psychotic symptoms and memory impairment. This is contrary to dementia related to PD. At presentation, cranial nerve examination was normal, unlike supra-nuclear palsy in this case. Rivastigmine 10cm2 transdermal patch once a day and levadopa-benserazid 50-12.5 mg three times a day prescribed.

At the first month of control, the patient was more mobile in the bed. He was still unable to communicate orally but started to express his wishes and seemed to understand some sentences with a meaningful look. His swallowing ability improved and daytime sleeping reduced. He was taking enteral nutritional products orally. He was still dependent on his wife for all daily life activities. He became an easier patient to take care of his caregiver. Both his and his wife's quality of life improved positively with the help of the current therapy. Patient written consent was obtained to publish.

Discussion

A diagnosis of Lewy body dementia requires a progressive decline in your ability to think, and at least two of the following:

- Fluctuating alertness and thinking function
- Repeated visual hallucinations
- Parkinsonian symptoms
- Rapid eye movement sleep behavior disorder, in which people act out their dreams during sleep

The diagnosis is made clinically. In addition, there are some helpful laboratory and imaging findings such as abnormally low uptake of iodine-123-metaiodobenzylguanidine in myocardial scintigraphy and reduced dopamine transporter uptake in basal ganglia demonstrated by 18F-fluoro-2-deoxy-D-glucose positron emission tomography (2).

DLB usually starts after the age of 50 and rarely starts after 70. The disease can progress to advanced stage dementia in 2 to 8 years. It can be challenging to diagnose DLB at the beginning of the symptoms because these symptoms mimic psychiatric disorders. In many cases, it is diagnosed after the movement disorder begins. The differences between DLB and dementia related to PD are the characteristics and timing of the movement disorder and disease progression. PD starts with

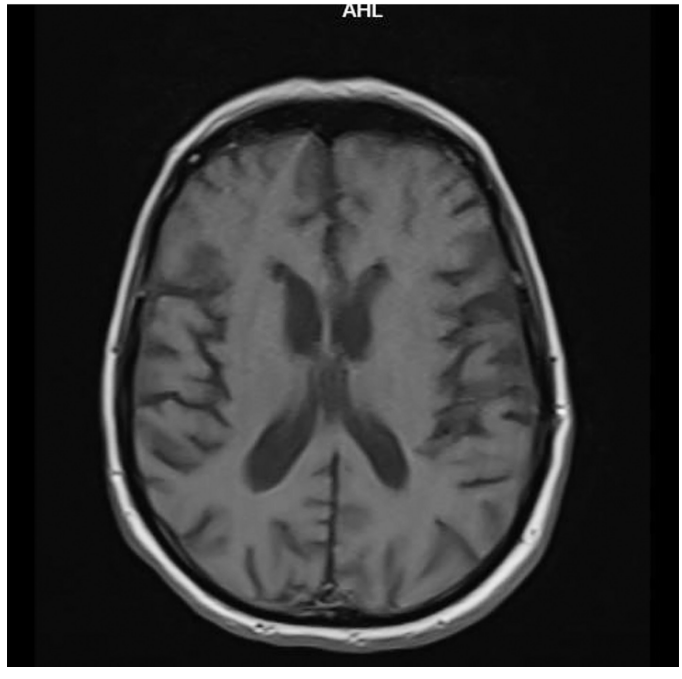

Figure 1. Atrophic cortex of the cerebrum with ischemic gliosis fields in the periventricular white matter

AHL is a sign copied from the imaging system of the hospital. It does not have an importance.

a resting tremor in the unilateral extremity. DLB tremor starts more generally and predominantly affects the lower extremities. DLB's movement disorder progresses more rapidly than PD and poorly improves with levodopa treatment. Dementia develops 6-8 years later after the onset of Parkinson's symptoms. However, dementia develops simultaneously or even before the onset of DLB symptoms. Psychiatric presentation is related to the medications used in PD. On the other hand, paranoia and hallucinations may be very early symptoms of DLB.

DLB is not a curable disease, and treatment options are only used to slow progression and increase patients' quality of life. Treatment options for DLB include cholinesterase inhibitors (rivastigmine, donepezil) and memantine. Cholinesterase inhibitors are effective in reducing daytime sleepiness, hallucinations, and confusion. Memantine helps to reduce the same symptoms by blocking glutamate intake to the neurons. Memantine is added to therapy during moderate or severe dementia. There are some drugs that are used to control some symptoms in DLB. For example, levodopa is used to reduce movement problems and muscle stiffness. However, it may worsen hallucinations. Thus, close monitoring is essential. Antidepressants are used to reduce depressive symptoms and anhedonia. In the case presented above, Rivastigmine patch was chosen because he had difficulty swallowing. In addition, levodopa was started to reduce muscle stiffness (3).

The diagnostic challenge of our case originated from presenting very recently, at advanced stage dementia. At that stage, defining the etiology of dementia becomes difficult, as most cases have similar clinical findings such as being bedridden, having difficulty in swallowing, and lacking orientation or communication skills. In this case, retrospective anamnesis from relatives led us to the correct diagnosis. That case has been treated to have a psychotic disorder for 3 years, which is a long period to diagnose a case with DLB. In such a case, differentiation from psychotic disorders may not be easy and clear. Following up with the patients with the aforementioned symptoms would lead the physician to the correct diagnosis. The quality of care given by relatives may help correct misdiagnosis, as in this case. Similar to our report, Valença et al. (4) reported a misdiagnosed DLB case in 2022. In this report, a 73-year-old man was treated as having refractory depression for 3 years (4). However, some late-life schizophrenia cases might not be differentiated from advanced stage dementia. Shimada et al. (5) reported an 83-year-old woman who had experienced auditory and visual hallucinations since she was 67 years old. She was diagnosed and treated for late onset schizophrenia. However, she started to have cognitive decline and memory impairment with age. They performed a cerebrospinal fluid tau protein measurement and found high levels. That finding led tem to start dementia medications on her (5).

As a result, correctly diagnosing a patient with advanced stage dementia may lead his or her relatives to have true expectations in the future while the disease progresses. Even if the treatment options are very limited and less effective, initiating the correct therapy may improve both the patient's and caregiver's quality of life.

Ethics

Informed Consent: Patient written consent was obtained to publish.

Financial Disclosure: The author declared that this study received no financial support.

References

1 The Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM–5; American Psychiatric Association, 2013)

2. Yamada M, Komatsu J, Nakamura K, Sakai K, Samuraki-Yokohama M, Nakajima K, Yoshita M. Diagnostic Crite-ria for Dementia with Lewy Bodies: Updates and Future Directions. J Mov Disord 2020;13:1-10.

3. Işık AT, Soysal P. Geriatri Pratiğinde Geriatrik Sendromlar. İntertıp yayınevi İzmir 2018:73-135.

4. Valença AM, Studart Leal CC, Oliveira GC, de Moraes TM, Nardi AE, Mendlowicz MV. Case Report: Depression × dementia with Lewy bodies in the elderly: The importance of differential diagnosis. Front Psychiatry 2022;13:1059150.

5. Shimada T, Uehara T, Nagasawa T, Hasegawa M, Maeda Y, Kawasaki Y. A case report of late-onset schizophrenia differentiated from a dementing disorder. Neurocase 2021;27:467-473.

CASE REPORT

DOI: 10.4274/ejgg.galenos.2023.2023-6-4
Eur J Geriatr Gerontol 2024;6(1):76-79

Huge Hepatocellular Carcinoma in a Geriatric Patient with Normal Alfa-feto Protein Levels: A Case Report

Gülru Ulugerger Avcı[1], Bahar Bektan Kanat[1], Rana Berru Durmuş[2], Alper Döventaş[1]

[1]İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, İstanbul, Turkey
[2]İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Internal Medicine, İstanbul, Turkey

Abstract

Hepatocellular carcinoma (HCC) is a common type of liver cancer and is a widespread cause of death from malignancy worldwide. The diagnosis of HCC is made by radiological liver imaging and the presence of serum alfa-fetoprotein. Our patient, a 75-year-old man, had a mass (14x17 cm) in the right liver lobe. Serum alfa-fetoprotein (AFP) was normal. There were no signs of metastasis except for several suspicious subcentimetric lymph nodes. Diagnosis of HCC confirmed by liver biopsy. He was evaluated by a multidisciplinary team. The team favored Yttrium-90 radioembolization treatment. The tumor showed slight regression. However, a new subcentimetric nodule was detected in the posterior segment of the left lower lobe of the lung. Sorafenib was initiated as a salvage drug by medical oncology. In conclusion, this case shows that with HCC can present with normal AFP levels even in advanced diseases. Biomarkers other than AFP are believed to contribute to HCC tumor growth. Moreover, we can infer from this case that the tumor shows less aggression in HCC patients with normal AFP levels. The treatment of HCC should be based on the patient's age and comorbidities.

Keywords: Hepatocellular carcinoma, serum alfa-fetoprotein, geriatric oncology, cancer management, older patient

Introduction

Hepatocellular carcinoma (HCC) is a common type of liver cancer and is a widespread cause of mortality worldwide. Although it is highly prevalent in Asia and Africa, it is the leading cause of death in Europe and America (1,2).

HCC is also one of the most aggressive tumors, causing frequent intrahepatic metastasis and common recurrence after surgery. Cirrhosis represents the greatest risk factor for this malignancy and is the main indicator for screening and surveillance. Extrahepatic metastases to the lungs, brain, bone, and adrenal glands are observed in patients with advanced-stage intrahepatic tumors (3). Vascular invasion and tumor thrombosis are usually detected in most advanced HCC cases (4). In general, the diagnosis of HCC is identified by radiological liver imaging and the presence of serum alfa-fetoprotein (AFP), without the need for biopsy. The management of HCC requires a multidisciplinary approach including surgeons, radiation oncologists, radiologists, pathologists, hepatologists, and medical oncologists. With the advantage of having more than one treatment option for patients with HCC, there is a decision-making approach according to the patient's clinic. Systemic pharmacological therapy options are frequently preferred for older patients with HCC. In recent years, immune checkpoint inhibitors have played an essential role in HCC management. Sorafenib was the first multikinase inhibitor used as a treatment option for HCC for more than ten years. Sorafenib or lenvatinib as first-line therapy and cabozantinib, regorafenib, or ramucirumab as second-line therapy are approved for most patients with HCC receiving current systemic treatment (5).

Address for Correspondence: Gülru Ulugerger Avcı, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, İstanbul, Turkey
Phone: +90 212 414 30 00 **E-mail:** gulru83@gmail.com **ORCID:** orcid.org/0000-0002-5661-1738
Received: 30.06.2023 **Accepted:** 03.09.2023

Cite this article as: Ulugerger Avcı G, Kanat Bektan B, Durmuş RB, Döventaş A. Huge Hepatocellular Carcinoma in a Geriatric Patient with Normal Alfa-feto Protein Levels: A Case Report. Eur J Geriatr Gerontol 2024;6(1):76-79

Here we report a patient diagnosed with a massive mass of HCC with imaging and tissue sampling whose serum AFP level was normal and hepatitis markers were negative. He had no prior history of alcohol consumption. Imaging revealed no signs of cirrhosis or metastasis. With this rare case, we aimed to contribute to the diagnosis and treatment management of HCC in older patients in light of current guidelines.

Case Report

A 75-year-old man with a history of pacemaker implantation due to sick sinus syndrome and Parkinson's disease local hospital with difficulty starting urination. An abdominal ultrasound was performed because of his complaints regarding urination. Ultrasound revealed a mass in the right liver lobe of approximately 15.8x12.8 cm with a clear boundary and uneven internal echo mass in the liver. Serum AFP was 1.65 µg/L (normal value <13 µg/L). His routine biochemistry showed no abnormalities. Hepatitis B virus surface antigen was negative. Then, he was referred to our hospital for further investigation and treatment.

Abdominal magnetic resonance imaging revealed a 14x16,5x13 cm lesion in the posterior right lobe of the liver with satellite lesions and a 17x14 mm lesion with significant contrast enhancement and diffusion restriction (Figure 1). Wash-out pattern was not reported. Repeat serum AFP level was 1.84 µg/L (normal value <13 µg/L). Ultrasound-guided liver biopsy was performed, which confirmed a diagnosis of HCC. Because AFP negative, a pathology revision was ordered to exclude the fibrolamellar variant of HCC However, there were no significant features for the particular variant, and genetic testing was negative for both DNAJB1-PRKACA oncogenic driver fusion gene and PRKAR1A abnormalities. Immunophenotype analysis revealed that CK7 and CD68 levels were negative.

Positron emission tomography-computed tomography revealed a 15-cm right hepatic mass with high 2-fluoro-2-deoxy-D-glucose (FDG) metabolism (maximum standardized uptake value =9.69). There was also a 14x18 mm nodular lesion in segment 4A of the liver with no abnormal FDG metabolism, suggesting a benign liver lesion. There were no signs of pathological FDG metabolism apart from several subcentimetric paracealiac lymph nodes suspicious for primary tumor metastasis. The patient was evaluated by a multidisciplinary hepatobiliary surgery team in cooperation with the department of diagnostic radiology, department of medical oncology, and nuclear medicine. The team favored Yttrium-90 radioembolization treatment over surgery because of his comorbidities. Positron emission tomography/computed tomography scan was ordered to assess treatment response. The tumor volume showed slight regression. However, a new subcentrimetric nodule with minimal metabolism was detected in the posterior segment of the lung's left lower lobe, which raised suspicion for metastasis. Based on this evaluation, the patient was transferred to medical oncology for further treatment options. Sorafenib was initiated as a salvage therapy, and the patient is currently followed up at frequent intervals by the medical oncology department. Informed consent was obtained.

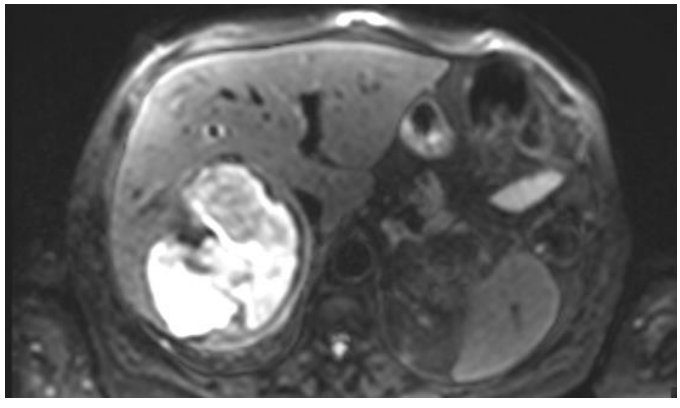

Figure 1. Huge hepatocellular mass in the liver right lobe

Discussion

HCC is a common leading cause of cancer-related death, and its prevalence is increasing worldwide. The age at diagnosis is increasing in adults. Thus, HCC is a rising issue in these vulnerable patients. Therefore, reliable management strategies are required for older patients with HCC.

The major risk factors for developing HCC are viral hepatitis, cirrhosis, obesity, diabetes mellitus, and non-alcoholic steatohepatitis (NASH) (6). It is based on the typical radiological signs in dynamic contrast imaging for diagnosing HCC and uses AFP as a standalone tool.

AFP is routinely used as a tumor marker for screening, diagnosis, and treatment follow-up of HCC. AFP-positive HCC can be easily diagnosed based on typical imaging features and high serum AFP levels. Some studies have shown that AFP is a predictor of tumor development (7).

Most AFP-normal HCCs are also associated with small and early-stage tumors. However, some patients with HCC have normal AFP levels, even in advanced diseases. Some studies have shown that most of these HCC patients with normal AFP levels are associated NASH (8,9). A study found that HCC patients with normal AFP levels were significantly older (10).

It has also been suggested that AFP, as a diagnostic serum tumor marker, has functional roles in HCC and is associated with aggressive HCC behavior, metastasis, and poor prognosis (11). This information shows that our patient with a large liver mass had a normal AFP value and significant metastases. It is also unknown whether large tumors show more significant invasion. In another study, HCC patients with higher serum AFP levels

had a larger tumor size, more frequent hepatic cirrhosis, portal vein thrombosis and metastasis, high Child-Pugh score, and advanced clinical stage (12).

Studies show that many factors other than AFP contribute to increased HCC size. Inflammatory cytokines are hypothesized to be important in HCC growth. Therefore, new biomarkers are required (13). Some studies have focused on DNA, RNA, and protein biomarkers in addition to AFP for HCC diagnosis (14).

Successful HCC management requires a multidisciplinary approach, including surgeons, radiation oncologists, radiologists, pathologists, hepatologists, and medical oncologists (15,16). Geriatric patients with moderate-to-advanced HCC at diagnosis are poorer candidates for surgical resection or transplantation because of comorbid conditions and compromised liver regeneration. In an older patient with multimorbidities, as preferred in our patient, Yttrium-90 radioembolization therapy was the main treatment for HCC. Systemic therapy is considered when extrahepatic nodal or distant metastatic disease is present or if the patient has a tumor burden or other comorbid conditions (17).

The patient profile impacts decision-making regarding the use of different pharmacological options against HCC. Systemic therapy is a part of the standard disease management for patients with advanced HCC. Systemic treatments are frequently preferred for patients with HCC, especially for patients for whom surgery is not possible. Nowadays, immune checkpoint inhibitors have been used to treat HCC Traditionally, the multikinase inhibitor Sorafenib has been one of the most frequently approved agents for over a decade (18). There are studies evaluating immunotherapies in all stages of HCC that could change the management of disease (19).

We demonstrated that many treatment options for older HCC patients, especially pharmacological treatments, are preferred over surgical treatment because of comorbidities and vulnerability.

Conclusion

HCC is a common liver malignancy worldwide, with a high mortality rate. AFP is routinely used as a tumor marker for the diagnosis and follow-up of cancer. However, some patients with HCC have normal AFP levels, even in advanced diseases. Therefore, AFP is not an ideal reliable biomarker, and the diagnosis of HCC relies mainly on imaging. New biomarkers are needed. In addition, in HCC patients with normal AFP, the tumor shows less aggression, as in this case. There are multiple treatment options for patients with HCC. To select the best treatment options for each patient, a multifactorial and multidisciplinary approach must be shaped by the patients' characteristics and the availability of treatment. Radioembolization and systemic pharmacological treatments are appropriate treatment options for patients with liver cancer in older adults.

Considering this case, we aim to contribute to the literature by attracting attention to the diagnostic and therapeutic management of HCC, the latest evidence, and the recommendations in the guidelines for accurate HCC management.

Ethics

Informed Consent: Informed consent was obtained.

Authorship Contributions

Surgical and Medical Practices: G.U.A., Concept: G.U.A., Design: G.U.A., B.B.K., A.D., Data Collection or Processing: G.U.A., B.B.K., R.B.D., Analysis or Interpretation: G.U.A., A.D., Literature Search: B.B.K., R.B.D., Writing: G.U.A., R.B.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Llovet JM, Kelley RK, Villanueva A, Singal AG, Pikarsky E, Roayaie S, Lencioni R, Koike K, Zucman-Rossi J, Finn RS. Hepatocellular carcinoma. Nat Rev Dis Primers 2021;7:6.
2. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136:359-386.
3. Masci G, Magagnoli M, Grimaldi A, Covini G, Carnaghi C, Rimassa L, Santoro A. Metastasis of hepatocellular carcinoma to the heart: a case report and review of the literature. Tumori 2004;90:345-347.
4. Connolly GC, Chen R, Hyrien O, Mantry P, Bozorgzadeh A, Abt P, Khorana AA. Incidence, risk factors and consequences of portal vein and systemic thromboses in hepatocellular carcinoma. Thromb Res 2008;122:299-306.
5. Feng MY, Chan LL, Chan SL. Drug Treatment for Advanced Hepatocellular Carcinoma: First-Line and Beyond. Curr Oncol 2022;29:5489-5507.
6. Bellissimo F, Pinzone MR, Cacopardo B, Nunnari G. Diagnostic and therapeutic management of hepatocellular carcinoma. World J Gastroenterol 2015;21:12003-12021.
7. Turshudzhyan A, Wu GY. Persistently Rising Alpha-fetoprotein in the Diagnosis of Hepatocellular Carcinoma: A Review. J Clin Transl Hepatol 2022;10:159-163.
8. Yasui K, Hashimoto E, Tokushige K, Koike K, Shima T, Kanbara Y, Saibara T, Uto H, Takami S, Kawanaka M, Komorizono Y, Okanoue T; Japan NASH Study Group. Clinical and pathological progression of non-alcoholic steatohepatitis to hepatocellular carcinoma. Hepatol Res 2012;42:767-773.
9. Ascha MS, Hanouneh IA, Lopez R, Tamimi TA, Feldstein AF, Zein NN. The incidence and risk factors of hepatocellular carcinoma in patients with nonalcoholic steatohepatitis. Hepatology 2010;51:1972-1978.
10. Lee CW, Tsai HI, Lee WC, Huang SW, Lin CY, Hsieh YC, Kuo T, Chen CW, Yu MC. Normal Alpha-Fetoprotein Hepatocellular Carcinoma: Are They Really Normal? J Clin Med 2019;8:1736.
11. Parpart S, Roessler S, Dong F, Rao V, Takai A, Ji J, Qin LX, Ye QH, Jia HL, Tang ZY, Wang XW. Modulation of miR-29 expression by α-fetoprotein is linked

to the hepatocellular carcinoma epigenome. Hepatology 2014;60:872-883.

12. Chi X, Jiang L, Yuan Y, Huang X, Yang X, Hochwald S, Liu J, Huang H. A comparison of clinical pathologic characteristics between alpha-fetoprotein negative and positive hepatocellular carcinoma patients from Eastern and Southern China. BMC Gastroenterol 2022;22:202.
13. Carr BI, Akkiz H, Üsküdar O, Yalçın K, Guerra V, Kuran S, Karsaoğullarından Ü, Altıntaş E, Özakyol A, Tokmak S, Ballı T, Yücesoy M, Bahçeci Hİ, Ülkü A, Akçam T, Polat KY, Ekinci N, Şimşek H, Örmeci N, Sonsuz A, Demir M, Kılıç M, Uygun A, Demir A, Delik A, Arslan B, Doran F, Yilmaz S, Tokat Y. HCC with low- and normal-serum alpha-fetoprotein levels. Clin Pract (Lond) 2018;15:453-464.
14. Wang T, Zhang KH. New Blood Biomarkers for the Diagnosis of AFP-Negative Hepatocellular Carcinoma. Front Oncol 2020;10:1316.
15. Gadsden MM, Kaplan DE. Multidisciplinary Approach to HCC Management: How Can This Be Done? Dig Dis Sci 2019;64:968-975.
16. Gish RG, Lencioni R, Di Bisceglie AM, Raoul JL, Mazzaferro V. Role of the multidisciplinary team in the diagnosis and treatment of hepatocellular carcinoma. Expert Rev Gastroenterol Hepatol 2012;6:173-185.
17. Clark T, Maximin S, Meier J, Pokharel S, Bhargava P. Hepatocellular Carcinoma: Review of Epidemiology, Screening, Imaging Diagnosis, Response Assessment, and Treatment. Curr Probl Diagn Radiol 2015;44:479-486.
18. Weinmann A, Galle PR. Role of immunotherapy in the management of hepatocellular carcinoma: current standards and future directions. Curr Oncol 2020;27:152-164.
19. Llovet JM, Castet F, Heikenwalder M, Maini MK, Mazzaferro V, Pinato DJ, Pikarsky E, Zhu AX, Finn RS. Immunotherapies for hepatocellular carcinoma. Nat Rev Clin Oncol 2022;19:151-172.