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The impact of undernutrition on the association between hypomagnesemia and dynapenia in older women

Ozcan Uzun[1], Cihan Heybeli[2], Lee Smith[3], Nicola Veronese[4], Masoud Rahmati[5,6,7], Andre Hajek[8] and Pinar Soysal[9*]

Abstract

Objectives To determine the association between hypomagnesemia and dynapenia in older women with different nutritional status.

Methods This cross-sectional study included older women who attended one outpatient geriatric clinic. Undernutrition was defined according to the Mini Nutritional Assessment score (MNA) (< 23,5), and handgrip strength of < 16 kg on dynamometer was defined as dynapenia. The association between hypomagnesemia (serum magnesium < 1.7 mg/dL) and dynapenia was determined by logistic regression analysis.

Results Among the 933 older women (mean age 81 ± 8), the prevalences of undernutrition and hypomagnesemia were 61% and 15%, respectively. The risk of hypomagnesemia increased with each step of decline in nutritional status, and undernutrition was associated with hypomagnesemia (OR 1.64, 95% CI 1.11–2.43, $p = 0.013$) In the entire cohort, hypomagnesemia was associated with dynapenia (OR 2.01, 95% CI 1.35-3.00, $p = 0.001$). In well-nourished patients, hypomagnesemia was not associated with dynapenia, even when unadjusted. However, in the undernourished group, hypomagnesemia was associated with dynapenia after adjusting for age, diabetes mellitus, hypertension, coronary heart disease, Barthel and Lawton scores, polypharmacy, glomerular filtration rate, serum albumin, hemoglobin, and MNA score (OR 2.95, 95% CI 1.04–8.32, $p = 0.040$). The coexistence of hypomagnesemia and undernutrition (versus neither of them) was significantly associated with dynapenia (OR 4.44, 95% CI 2.67–7.41, $p < 0.001$).

Conclusion The prevalence of hypomagnesemia increases with worsening nutritional status. Hypomagnesemia is associated with dynapenia in older women who are undernourished, even after adjusting for nutritional status, but not in those who are well nourished. The coexistence of undernutrition and hypomagnesemia increase the risk of dynapenia substantially.

Highligths

- The prevalence of hypomagnesemia increases with worsening of nutritional status.

*Correspondence:
Pinar Soysal
psoysal@bezmialem.edu.tr

Full list of author information is available at the end of the article

- The relationship between hypomagnesemia and dynapenia varies according to nutritional status; hypomagnesemia is associated with an increased risk of dynapenia in undernourished patients but not in their well-nourished counterparts.
- In the presence of malnutrition, the level of magnesium should also be assessed, and both malnutrition and hypomagnesemia should be treated.

Keywords Aged, Hypomagnesemia, Magnesium, Malnutrition, Sarcopenia

Introduction

Magnesium is one of the major intracellular cations and has been recognized as a cofactor of over 300 enzymatic reactions [1]. Magnesium plays crucial roles in all components of intrinsic capacity [2], which is defined by the World Health Organization as five steps: locomotor, vitality, sensory, cognitive, and psychological [3]. Magnesium insufficiency is common in the general population, but older adults are particularly at risk because of factors including inadequate dietary intake, decreased absorption, increased excretion, drug exposure, diarrhea, and vomiting [4]. Deficiency of magnesium is associated with neurologic, neuromuscular, and cardiovascular problems and may lead to other electrolyte imbalances, including hypokalemia and hypocalcemia [5].

Muscle health is closely related to magnesium stores [6],, and skeletal muscle health is essential for human functionality, mobility, and overall well-being [7]. Muscle strength in older adults significantly affects their overall health status and quality of life. As people age, muscle strength declines more rapidly than muscle mass, and it is not caused by neurological or muscular diseases. This condition is known as dynapenia [8]. This decline results in movement restrictions, increased dependency, and potential deterioration in emotional and mental health, ultimately leading to higher morbidity and mortality rates [9]. Inadequate magnesium levels can have a negative impact on muscle strength by reducing mitochondrial efficiency, decreasing energy production, and increasing reactive oxygen species. Reactive oxygen species can subsequently cause structural and functional damage to vital molecules, including DNA and proteins, all of which are associated with ageing [10]. Magnesium plays a crucial role in mitochondrial functions, including the electron transport chain, oxygen detoxification, and the production of ATP, which acts as the primary energy currency in cells, driving numerous physiological functions [11]. Given that both magnesium deficiency and sarcopenia (loss of skeletal muscle mass) are more common in the aging population and that magnesium plays a central role in muscle ATP production, impaired magnesium status may be a contributing factor to sarcopenia observed later in life. Previous studies have demonstrated that magnesium supplementation may be associated with improvement of sarcopenia among older adults [12, 13]. However, malnutrition is also a common geriatric syndrome which is related to sarcopenia [14], and how much of the association between magnesium deficit and sarcopenia can be explained by undernutrition is completely unknown. Moreover, only older females were included in the present study because of hormonal, socioeconomic and anthropometric differences between the sexes that may affect the development, of both dynapenia and geriatric syndromes. Therefore, the aim of this study was to determine the association between hypomagnesemia and dynapenia in older women with different nutritional states.

Methods

This cross-sectional study included patients from a single geriatric outpatient clinic in Turkey. All patients were ≥ 60 years old. The majority of our cohort included female patients, and cut off level for the definition of dynapenia based on handgrip strength differs between females and males. For these reasons, we included only female patients to study in a more homogeneous cohort. In total, data from 1821 patients admitted to one outpatient geriatric clinic and who underwent comprehensive geriatric assessment (CGA) between November 2016 and May 2024 were retrospectively reviewed. Data were obtained from electronic medical records and patient files. This study conformed to the Declaration of Helsinki and was approved by Bezmialem Vakıf University Ethics Committee (IRB code: 54022451-050.05.04-; 25.08.2020). Written informed consent was provided by each participant, their caregivers, relatives, or a legal guardian before participating in the study.

Inclusion and exclusion criteria

Patients who underwent CGA and laboratory work-up on the same day were included in the study. Patients with the following conditions were excluded: severe dementia; severe visual or hearing impairment that prevents communication and understanding commands during the examination; refusal to participate in the examination; fatal illness, life-threatening illness in the last 6 months, or those who have been hospitalized for a major surgery; the presence of an acute health problem (such as infection, acute kidney failure, delirium, stroke); and severe chronic renal impairment defined as an estimated glomerular filtration rate (eGFR) below 30 mL/min/1.73 m^2. A total of 371 male patients, 357 patients without

magnesium values, 84 patients with severe chronic kidney disease (CKD), 50 patients without MNA, and 26 patients with hypermagnesemia were excluded from the study. Patients with severe CKD were excluded since these patients frequently suffer from malnutrition and frailty due to factors specific to CKD [15]. Additionally, patients with severe CKD less frequently have hypomagnesemia due to reduced excretion of the ion.

Patient characteristics Age, years of education, number of medications, body mass index, and comorbidities, including hypertension, diabetes mellitus, ischemic heart disease, and cerebrovascular diseases (history of of stroke syndromes without sequelae), were recorded. A geriatrician interviewed the family members or people who lived with each patient with dementia to obtain information on demographic characteristics, the presence of comorbidities, as well as to perform CGA. Comorbid diseases were recorded according to medical history obtained via anamnesis.

Laboratory measurements

At the geriatric clinic, blood samples were taken at a fasting state and during the same visit with CGA. During the routine evaluation for comprehensive geriatric evaluation, 15 cc of blood is taken for biochemistry, hormone, vitamin D and full blood count analysis. This was part of the routine of our outpatient clinic for comprehensive geriatric assessment, and no specific intervention was made solely for this study. Blood was drawn by the nurses of center laboratory. Laboratory tests included hemoglobin, serum albumin, glucose, urea, creatinine, Vitamin D, sodium, potassium, LDL-cholesterol, HDL-cholesterol, and triglycerides. Glomerular filtration rate was estimated using serum creatinine levels according to the Chronic Kidney Disease Epidemiology Collaboration formula. A serum magnesium level of <1.7 mg/dL was defined as hypomagnesemia and a level of >2.4 mg/dL was defined as hypermagnesemia [16].

Comprehensive Geriatric Assessment measures included the following:

- **Dementia**: The diagnosis of dementia was based on the Diagnostic and Statistical Manual of Mental Disorders–- Fifth Edition diagnostic criteria [17].
- **Mini-Nutritional Risk Assessment Score (MNA)**: The MNA test includes simple measurements and 18 questions that can be completed in less than 10 min: anthropometric measurements (four items related to body mass index, weight loss, brachial circumference, and calf circumference); global assessment (six questions about lifestyle, medication, and mobility); dietary habits and subjective assessment (eight questions about number of meals, food and fluid intake, and autonomy of feeding, self perception of health, and nutrition) [18]. Of the total score of 30, a score of lower than 23.5 is defined as undernutrition. MNA was validated to screen malnutrition for Turkish geriatric patients in 2015 [19].
- **Frailty**: Frailty was evaluated according to the Fried's criteria [20], and was defined as in the presence of three or more of the following: unintentional weight loss (10 lbs in past year), self-reported exhaustion, weakness (grip strength), slow walking speed, and low physical activity.
- **Risk of falling**: The risk of falling was determined based on the Tinetti Scale, which comprises 28 points (maximum balance score 16, and maximum walking score 12). A score below 19 denotes a high risk of falling [21].
- **Dependency**: Barthel Basic Daily Living Activity Scale (BADL) score was evaluated out of 100 points. Lower scores indicate greater dependence on activities of daily living [22]. On the Lawton Instrumental Activities of Daily Living Scale (IADL), patients who do not need any help are assigned 8 points [23]. BADL and IADL scores were used as continuous variable.
- **Polypharmacy**: Chronic exposure to ≥ 5 drugs in an outpatient clinic is defined as polypharmacy [24].
- **Dynapenia**: Handgrip strength was assessed three times for each hand using the Jamar hand-held hydraulic dynamometer (Jamar hand dynamometer; Sammons Preston, Inc., Bolingbrook, IL, USA). Patiens were standing with their arms parallel to their trunk and were asked to squeeze the dynamometer at maximum strength. The maximum handgrip strength was recorded. The entire cohort included female patients; thus, a maximal handgrip strength of <16 kg was recorded as dynapenia [25].

Statistical analysis

Normality tests were evaluated using the Kolmogorov-Smirnov tests. Continuous variables with skewed distribution are presented as medians with interquartile ranges, and variables with normal distribution are expressed as means with standard deviations. Qualitative variables are presented as counts and percentages. Chi-square or Fisher's exact test was used to compare proportions. Means of the hypomagnesemia and normomagnesemia groups were compared using the Mann–Whitney U test. Logistic regression analysis was performed to identify associations between hypomagnesemia, undernutrition, and dynapenia. Results are expressed as odds ratios (ORs) and 95% confidence intervals. Statistical analysis was performed using SPSS 22.0

version (IBM SPSS, Chicago, IL). A P value of < 0.05 was considered statistically significant.

Results

The mean age was 81 ± 8 years. One hundred forty (15%) patients had hypomagnesemia. The percentages of patients in the well-nourished, at risk of malnutrition, and malnourished groups were 39%, 42%, and 19%, respectively. Overall, the undernourished group comprised 61% of the cohort. Hypomagnesemia was present in 12%, 16%, and 20% of well-nourished (MNA scores > 23.5, at risk of malnutrition (MNA scores: 17-23.5), and malnourished patients (MNA scores < 17), respectively ($p = 0.021$). Undernutrition was associated with hypomagnesemia (OR 1.64, 95% CI 1.11–2.43, $p = 0.013$).

Table 1 presents the characteristics of patients with and without hypomagnesemia. Patients with hypomagnesemia were older (82 versus 80), and had higher prevalences of diabetes mellitus (69% versus 29%), hypertension (80% versus 69%), and coronary heart disease (22% versus 12%, $p < 0.05$). Regarding laboratory workup, patients with hypomagnesemia had lower hemoglobin, serum albumin, and glomerular filtration rate ($p < 0.05$). Most comprehensive geriatric assessment measures were less favorable in the hypomagnesemia group. These patients were more likely to be dependent according to the scores of Barthel basic activities of daily living and Lawton instrumental activities of daily living ($p < 0.05$). Additionally, the frequency of undernutrition, dynapenia, and polypharmacy was more prevalent in the hypomagnesemia group ($p < 0.05$).

Dynapenia was present in 515 (58%) patients. In the entire cohort, hypomagnesemia was associated with dynapenia (OR 2.01, 95% CI 1.35-3.00, $p = 0.001$). This significance remained after adjusting for age, but not after adjustments for comorbidities and geriatric syndromes (Table 2). Patients were divided into two groups according to nutritional category. In well-nourished patients, hypomagnesemia was not associated with dynapenia, even when unadjusted. In the undernutrition group however, hypomagnesemia was associated with dynapenia after adjustments for age, diabetes mellitus, hypertension, coronary heart disease, Barthel and Lawton scores, polypharmacy, glomerular filtration rate, serum albumin, and hemoglobin (OR 3.15, 95% CI 1.12–8.89, $p = 0.003$). This association remained significant even after adjusted for the previously mentioned factors plus the MNA score (OR 2.95, 95% CI 1.04–8.32, $p = 0.040$).

Table 3 presents the associations between hypomagnesemia and undernutrition and their coexistence with

Table 1 Demographics, laboratory workup, and comprehensive geriatric assessment of patients with hypomagnesemia versus normomagnesemia

	Hypomagnesemia ($n = 140$)	Normomagnesemia ($n = 778$)	*P*
Age, years, mean ± SD	82.1 ± 7.3	80.4 ± 7.9	**0.026**
Education, years, median (IQR)	4.0 (0.0–5.0)	5.0 (0.0–6.0)	0.195
Body mass index (kg/m^2)	30.4 ± 5.7	29.7 ± 5.8	0.137
Diabetes mellitus	96 (69%)	222 (29%)	**< 0.001**
Hypertension	112 (80%)	534 (69%)	**0.007**
Dementia	61 (44%)	288 (37%)	0.141
Coronary heart disease	31 (22%)	91 (12%)	**0.001**
Cerebrovascular diseases	15 (11%)	78 (10%)	0.790
Hemoglobin, g/dl, mean ± SD	11.8 ± 1.4	12.4 ± 1.6	**< 0.001**
GFR, ml/min/1.73 m^2, median (IQR)	57.0 (47.0–70.0)	67.0 (51.0–78.0)	**0.001**
Serum albumin, g/dl, mean ± SD	4.1 ± 0.5	4.2 ± 0.4	**0.015**
CRP, (mg/L), median (IQR)	5.0 (0.5–16.2)	2.0 (0.4–6.9)	**0.001**
Serum ferritin, ng/mL, median (IQR)	46.9 (22.5-101.4)	51.9 (27.4–97.3)	0.585
Vitamin D level (ng/ml), median (IQR)	23.5 (17.1–30.9)	22.9 (14.2–32.0)	0.303
Folate, ng/ml, median (IQR)	6.6 (4.7–9.8)	7.0 (5.2–9.7)	0.494
Vitamin B12, pg/ml, median (IQR)	395.0 (277.0-556.0)	387.5 (273.0-600.5)	0.796
Lawton index, median (IQR)	5 (2–8)	7 (3–8)	**0.003**
Barthel index, median (IQR)	78.0 (55.0–90.0)	85.0 (68.0–95.0)	**0.003**
MNA score, mean ± SD	20.5 ± 5.3	21.2 ± 5.1	**0.003**
Undernutrition	99 (70%)	463(60%)	**0.012**
Dynapenia	99 (70%)	416 (56%)	**0.004**
Polypharmacy	116 (83%)	519 (67%)	**< 0.001**
Frailty	74 (53%)	352 (45%)	0.096
Risks of falls *	60 (44%)	267 (37%)	0.083

*Risks of falls were based on Tinetti scale. GFR: glomerular filtration rate, IQR: interquartile range (25-75%), MNA: Mini Nutritional Risk Assessment, SD: standard deviation.

Table 2 Association between hypomagnesemia and dynapenia in well-nourished and undernourished patient groups

Models	Overall					Well-nourished					Undernourished				
	β	Std err	OR	95% CI	p value	β	Std err	OR	95% CI	p value	β	Std err	OR	95% CI	p value
Unadjusted	0.700	0.203	2.01	1.35-3.00	**0.001**	0.163	0.337	1.18	0.61–2.28	0.627	0.887	0.280	2.43	1.40–4.20	**0.002**
Model 1	0.569	0.217	1.77	1.16–2.70	**0.009**	0.066	0.363	1.07	0.52–2.18	0.857	0.782	0.291	2.19	1.24–3.87	**0.007**
Model 2	0.434	0.247	1.54	0.95–2.51	0.080	-0.84	0.400	0.83	0.38–1.82	0.645	0.906	0.333	2.47	1.29–4.76	**0.007**
Model 3	0.320	0.346	1.38	0.70–2.72	0.356	-0.504	0.545	0.60	0.21–1.76	0.355	1.148	0.529	3.15	1.12–8.89	**0.03**
Model 4	0.322	0.349	1.38	0.70–2.74	0.356	-0.542	0.551	0.58	0.20–1.71	0.325	1.083	0.528	2.95	1.04–8.32	**0.040**

Model 1 adjusted for age. Model 2 adjusted for age, diabetes mellitus, hypertension, coronary heart disease, Bartel and Lawton scores, polypharmacy. Model 3 adjusted for age, diabetes mellitus, hypertension, coronary heart disease, Bartel and Lawton scores, polypharmacy, glomerular filtration rate, serum albumin, CRP and hemoglobin. Model 4 adjusted for factors in model 3 plus MNA score.

dynapenia. As previously stated, there was no significant association between hypomagnesemia and dynapenia among well-nourished patients. Undernutrition was significantly associated with dynapenia among patients with normal serum magnesium levels (OR 1.83, 95% CI 1.50–2.23, $p < 0.001$). The coexistence of hypomagnesemia and undernutrition (versus neither of them) was significantly associated with dynapenia (OR 4.44, 95% CI 2.67–7.41, $p < 0.001$).

Discussion

Although that many studies have shown the benefits of oral magnesium supplementation on physical functions [12, 26], the significance of hypomagnesemia on patient outcomes is unknown. Since 99% of the ion resides inside the cell, some researchers suggested that serum levels may not clearly indicate the overall body magnesium status [11], and a direct correlation may not exist between serum magnesium levels and patient outcomes. In this study, we have shown a significant association between hypomagnesemia and dynapenia among older women but only in those who were undernourished. The same association could not be observed among well-nourished counterparts even when unadjusted.

Insufficiency or deficiency of an element in the setting of undernutrition is not unexpected, and hypomagnesemia is generally accepted to be a result of malnutrition [27]. However, previous studies did not focus on the relationship between nutritional status and serum magnesium levels, and there are no data about such a relationship. One of the important findings of our study was that the prevalence of hypomagnesemia increased as the nutritional status of the patient decreased. The prevalence of undernutrition was significantly higher in patients with hypomagnesemia versus normomagnesemia (70% versus 60%). Although this is not surprising, to our knowledge, this is the first study to demonstrate such an increase in the prevalence of hypomagnesemia according to each step of the decline in nutritional status.

Although many studies have examined the relationship between nutrition and aging, many have focused on the prevention of diseases such as type 2 diabetes, cardiovascular disease, Alzheimer's disease, and cancer [28–31]. Very few studies have examined the importance and role of nutrition, with a particular focus on micronutrients in older adults. In this context, it is of considerable importance to measure and monitor serum electrolyte levels that are not routinely recorded, such as magnesium, as it plays crucial roles in physiology [32]. Although hypomagnesemia due to dietary deficiency is rare and renal adaptation to magnesiim conservation is high, the recommended daily intake is low [6], and there are few studies examining magnesium levels according to nutritional status [33].

Table 3 Associations between hypomagnesemia and undernutrition and their coexistence with dynapenia

Hypomagnesemia[1]					Undernutrition[2]					Both[3]			
β	Std err	OR	95% CI	p value	β	Std err	OR	95% CI	p value	β	Std err	OR	95% CI	p value
0.163	0.337	1.18	0.61–2.28	0.627	0.626	0.163	1.83	1.50–2.23	**<0.001**	1.755	0.285	4.44	2.67–7.41	**<0.001**

1Hypomagnesemia versus no hypomagnesemia among patients with well-nutrition (unadjusted)

2Undernourished versus well-nourished patients with normal magnesium levels (unadjusted)

3Hypomagnesemia plus undernutrition vs. normal serum magnesium and normal nutrition (unadjusted)

The significant association between hypomagnesemia and dynapenia in the undernourished cohort was independent of many other factors, including the MNA score, suggesting that the association is not related to other nutritional deficiencies that can be co-incidentally observed with hypomagnesemia. This may mean that improvement in overall nutrition without an increase in serum magnesium levels among patients with hypomagnesemia may not be associated with an optimal improvement in dynapenia. Since hypomagnesemia is not associated with dynapenia in the well-nourished group, correction of hypomagnesemia without improvement in nutritional status may not help in the treatment of muscle problems. Additionally, the coexistence of undernutrition and hypomagnesemia was associated with an increased odds of dynapenia compared to the absence of either condition. Compared with well-nourished patients with normal serum magnesium levels, patients with undernutrition who had normal serum magnesium levels had an odds of 1.83 of having dynapenia. Compared to the former group, in patients with undernutrition plus hypomagnesemia the odds of dynapenia increased to 4.44. Independent correlation was shown between serum magnesium levels and muscle performance among older adults [10]. Another study found associations between low serum magnesium levels and frailty, basic activities of daily living, gait, and balance [34]. Further studies confirmed benefits from oral magnesium supplementation. In a study by Veronese et al., [12] it was found that older women who received oral magnesium oxide for 12 weeks experienced improvement in short physical performance battery, chair stand time, and 4-m walking speed. Another cross-sectional study confirmed the benefit of oral magnesium supplementation in terms of improvement of sarcopenia among older adults [13]. Our study is among the first to investigate the association between serum magnesium levels and dynapenia. Moreover, we confirmed the role of nutrition in this association.

The frequency of hypomagnesemia is high among older adults and may change according to the setting. Chronic magnesium deficiency is common among the aging population, often due to reduced dietary magnesium intake and decreased intestinal absorption [11]. There is a relationship between hypomagnesemia and the increase in aging-related diseases and polypharmacy [6]. Diuretics, antiepileptic drugs, antibiotics, antihistamines, proton pump inhibitors, antacids, H2 blockers, and calcineurin inhibitors contribute to magnesium deficiency [35]. Factors such as deterioration of oral health with aging, decreased sense of smell and taste, visual and hearing impairment, and anorexia associated with depression affect dietary intake by decreasing appetite [36]. Additional factors include financial constraints, reduced physical activity, and the development of sarcopenia, which

can lead to self-sufficently [36]. Given its widespread effects and physiological roles, it is reasonable to correct serum magnesium levels. Struijk et al. showed that adequate dietary magnesium intake was associated with a 16% lower risk of developing frailty through its role in muscle function in older women [37], highlighting magnesium as an essential element for physical integrity in the older population.

We recognize the limitations of this study. The cause and effect relationship between hypomagnesemia and dynapenia cannot be determined due to the observational design. We included older, white women from a single center; thus, our results may not be generalizable to other populations. Normal blood magnesium levels are maintained within a narrow range, representing only approximately 0.8% of the body's total magnesium stores; therefore, blood magnesium levels may not accurately reflect the body's overall magnesium status [38]. Several drugs, including diuretics and proton pump inhibitors, can cause magnesium loss and hypomagnesemia; polypharmacy increases the risk of affecting magnesium status. Dynapenia does not indicate sarcopenia; rather, it implies an increased risk. Relatively large sample size, however, provided us to demonstrate clear association between hypomagnesemia and dynapenia, irrespective of numerous factors. This study is the first to demonstrate such an association. Additionally, an increase in the prevalence of hypomagnesemia was observed with each step of decline in the nutritional status.

Conclusion

Hypomagnesemia is associated with dynapenia in older women who are undernourished but not well-nourished. The coexistence of hypomagnesemia and undernutrition substantially increases the risk of dynapenia. Probably, solely correcting hypomagnesemia without treatment of undernutrition would not help improve dynapenia, and overall evaluation of nutrition in the setting of hypomagnesemia appears to be reasonable. The prevalence of hypomagnesemia is closely related to and is increased by each step of decline in the nutritional status. Prospective randomized studies are needed to demonstrate the impact of correcting low serum magnesium levels on improving dynapenia.

Abbreviations

BADL	Barthel Basic Daily Living Activity Scale
CGA	Comprehensive Geriatric Assessment
CKD	Chronic Kidney Disease
eGFR	Estimated Glomerular Filtration Rate
IADL	Lawton Instrumental Activities of Daily Living Scale
MNA	Mini Nutritional Assessment
OR	Odds ratios

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Author contributions

Conceptualization: PS, CH; Data curation: PS, OU, LS, MR, AH, NV; Formal analysis: CH, NV, PS, LS, MR, AH, OU; Investigation: CH, NV, PS, LS, MR, AH, OU; Methodology: CH, PS; Project administration: PS, NV, MR, LS; Resources; Software: PS, OU; Supervision: PS, NV; Validation: All authors; Visualization: All authors; Writing- original draft: CH, OU; Writing- review and editing: PS, LS, MR, AH, NV.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was approved by Bezmialem Vakıf University Ethics Committee (IRB code: 54022451-050.05.04-; 25.08.2020). Written informed consent was obtained from each participant before participation in the study.

Consent for publication

Written informed consent was taken from patients or their caregivers for publication of their data which is anonymised.

Conflict of interest

None.

Research involving human participants and/or animals

The authors certify that the study was performed in accordance with the ethical standards established in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Clinical trial number

Not applicable.

Author details

[1]Yalova Education and Research Hospital, Division of Nephrology, Yalova, Turkey
[2]Division of Nephrology, Dokuz Eylul University Hospital, İzmir, Turkey
[3]Center for Health Performance and Wellbeing, Anglia Ruskin University, Cambridge, UK
[4]Geriatric Unit, Department of Medicine, University of Palermo, Palermo 90127, Italy
[5]CEReSS-Health Service Research and Quality of Life Center, Aix-Marseille University, Marseille, France
[6]Department of Physical Education and Sport Sciences, Faculty of Literature and Human Sciences, Lorestan University, Khoramabad, Iran
[7]Department of Physical Education and Sport Sciences, Faculty of Literature and Humanities, Vali-E-Asr University of Rafsanjan, Rafsanjan, Iran
[8]Department of Health Economics and Health Services Research, University Medical Center Hamburg-Eppendorf, Hamburg Center for Health Economics, Hamburg, Germany
[9]Department of Geriatric Medicine, Faculty of Medicine, Bezmialem Vakif University, Adnan Menderes Bulvarı (Vatan Street, Fatih, Istanbul 34093, Turkey

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