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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
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info@ejgg.org

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CONTENTS

EDITORIAL

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Eur J Geriatr Gerontol 2024;6(2):80-90

Healthcare Problems and Possible Solutions in Older Adults in Turkey: Geriatric Syndromes and Chronic Diseases

Mehmet Akif Karan[1,2], İlhan Satman[2,3], Teslime Atlı[4], Gülistan Bahat Öztürk[1], Mustafa Cankurtaran[5], Deniz Suna Erdinçler[6], Meltem Halil[5]

[1]İstanbul University, İstanbul Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, İstanbul, Turkey
[2]The Turkish Institute of Public Health and Chronic Disease (TÜHKE), The Health Institutes of Türkiye (TUSEB), İstanbul, Turkey
[3]İstanbul University, İstanbul Faculty of Medicine, Department of Internal Medicine, Division of Endocrinology and Metabolism, İstanbul, Turkey
[4]Medline Adana Hospital, Clinic of Internal Medicine, Division of Geriatrics, Adana, Turkey
[5]Hacettepe University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, Ankara, Turkey
[6]İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, İstanbul, Turkey

Introduction

The increasing number and proportion of the older adult population and its effects on health, social, cultural, and economic fields in Turkey necessitate changes and regulations in policies and actions for older adults' health and care. This study is organized with reference to the vision of the Turkish Institute of Public Health and Chronic Disease (TÜHKE), an official organ of the Health Institutes of Türkiye (TUSEB), and in accordance with the tasks designated in the eleventh development plan (1). In this report, a contemporary approach to older adults' health and diseases in the country is discussed by identifying current situations, barriers, and suggested solutions to existing problems (2). A large study group consisting of 147 representatives from a wide range of public institutions and private sectors dealing with the health of older adults, including the Ministry of Health, the Ministry of Labor and Social Security, the Ministry of Family and Social Services, the TUSEB, the World Health Organization (WHO)-Turkey, the Red Crescent-Turkey, 25 universities, and 19 professional associations, helped in the preparation of this report. Here, the issues covered in this report are summarized along with the main landscapes.

Population Growth

Population growth all over the world and the decrease in mortality along with declining birth rates lead to an increase in life expectancy and the proportion of older adults in society. Such problems that we have encountered in recent years, such as the aging of the population much faster than expected, the transition from a large family to a nuclear family, the increase in urbanization rates along the transition from an agricultural to an industrial society, and the acceleration of the technological revolution, all highlight the health and care problems of older adults. Aging is a global phenomenon. Not only developed countries, but also developing countries are aging. It is estimated that by 2025, two out of three older adults in the world will live in less developed countries (3). WHO defines biological aging as "a condition in which the gradual accumulation of molecular and cellular damage results in a decrease in a physiological reserve capacity, and an individual capacity in general, finally preceding to many diseases and increased risk of death". The generally accepted age threshold is usually 65 years (4).

The percentage of population aged 65 years and over in Turkey was 3.9% in 1935, 3.3% in 1950, and 5.7% in 2000; it reached 9.7% in 2021, accounting for 8,245,124 people (5). It is predicted that this rate will be 11.0% in 2025, 16.3% in 2040, and 25.6% in 2080 (Figure 1). Similarly, the life expectancy at birth was 78 years in the 2013-2015 period, it increased to 78.6 years in the 2017-2019 period (6). This rate is higher than that in upper-middle-income countries (74 years) and worldwide (72.7 years). According to the 2017-2019 life table data, the average

Address for Correspondence: Mehmet Akif Karan, İstanbul University, İstanbul Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, İstanbul, Turkey; The Turkish Institute of Public Health and Chronic Disease (TÜHKE), The Health Institutes of Türkiye (TUSEB), İstanbul, Turkey
Phone: +90 532 674 34 09 **E-mail:** m.akifkaran@gmail.com **ORCID:** orcid.org/0000-0002-9080-404X
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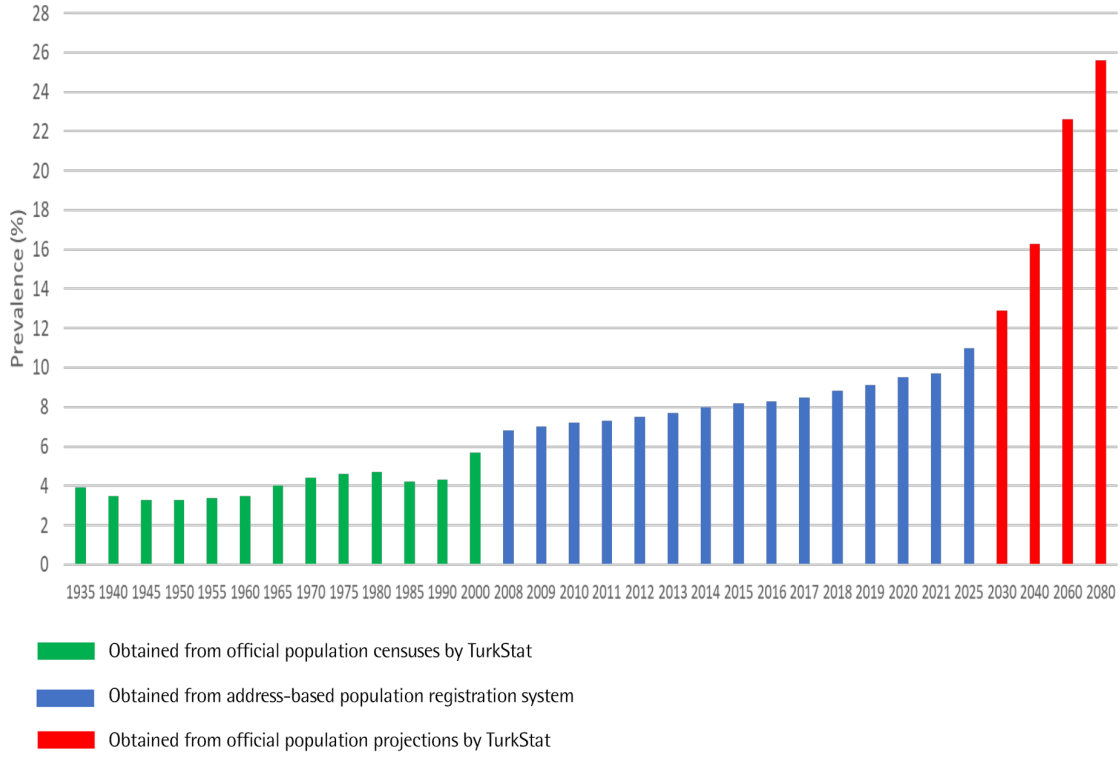

Figure 1. Population growth in 65+ years in Turkey

life expectancy of a 65-year-old person is 18 years (16.3 years for men; and 19.6 years for women). Meanwhile, the older adult dependency ratio (the number of older adults per 100 people of working age) was 7.1% in 1990, 8.8% in 2000, and 12.6% in 2017; it increased to 14.3% in 2021, which is at the level of the world average (5).

Aging: A Natural Consequence of Life

Aging is not a disease; nevertheless, the frequency and number of diseases increase during this period. Among the characteristic problems of the older adult population, the higher rate of disability, being unable to practice their profession, excess of women, individualization, increased number of people living alone, loss of social status, poverty, and inequality are the most prominent ones (7,8). Unfortunately, older people are commonly portrayed as unaware of the world, unable to communicate, frail, dependent, and thought of as a burden to society. This prejudice against older adults and aging is defined as "age discrimination" and poses a substantial threat (9,10).

Practitioners dealing with older people should be well trained on physiologic and psychologic alterations with aging, communication with older adults, difficulties in history taking and physical examination, preventive medicine practices, healthy and successful aging, different presentations of diseases in older adults, management of chronic diseases and geriatric syndromes, multimorbidity, drug metabolism in older adults, short- and long-term care, palliative care and treatment, and terminal patient management (11-16). Interdisciplinary teamwork should be given immense importance to provide effective and productive service to older adults; besides the physicians, other medical professionals, including geriatric nurses, nutritionists, and dietitians, physiotherapists, occupational therapists, ergo therapists, psychologists, gerontologists, and social workers, should be employed in appropriate numbers.

At this point, it is necessary to clarify the concepts of "geriatrics" and "gerontology", which are often confused in non-medical settings as both are in the same field focused on older adults. They serve different functions but also complement each other. Geriatrics is referred to as old age medicine; it is one of the subspecialties in internal medicine, and it focuses on the care and treatment of older persons, including clinical examination, diagnosis, therapy, and follow-up tasks related to all health problems and diseases of people aged 65 and over (13,17). However, "gerontology" is a multidisciplinary field of study and practice that encompasses the physical, mental, and social aspects of aging (18,19).

In Turkey, the number of geriatricians and geriatrics fellows is around 150; however, the actual need should be more than three thousand according to scientific standards (4,13). Enabling the geriatricians to serve in compliance with their profession; giving authorization to geriatricians for reimbursement of

some crucial drugs, which are frequently used in the treatment of commonly encountered diseases and syndromes in older adults by the Social Security Institution; promoting the entire health professionals dealing with older adults on issues such as education, social rights, and an effective working atmosphere will not only contribute to a better quality of life for older adults but will also have a positive impact on health expenditures in the long run, owing to its cost-effectiveness (20-22).

Preventive Medicine in Geriatrics

Screening tests are performed for the early diagnosis of diseases and prevention of complications in older adults (23-26). Life expectancy, skills to perform the test, and personal preferences should be considered when planning screening tests; the benefit-hazard balance should be established by taking into account the possible damages of the tests. In our country, screening policies for breast, prostate, colon, and cervix cancers in older adults and lung cancer in the risk group have been determined. Screening for diseases that increase with age (diabetes, hypertension, osteoporosis, thyroid dysfunctions, etc.) should be pursued. Immunization programs for older adults (influenza, pneumococcal pneumonia, herpes zoster vaccine, tetanus-diphtheria-pertussis vaccine, and coronavirus disease-2019 (COVID-19) vaccine] are applied meticulously in Turkey (27-30). Older people should perform 150-300 minutes of aerobic activity per week. As their physical condition allows, it is beneficial to perform moderate-to-vigorous aerobic exercise for 75-150 minutes per week (31,32).

Geriatric syndromes should be included in the scope of health care provided to older adult individuals in primary settings (23,24,33,34); training and follow-up materials are available so that screening and follow-up on this subject can be performed by family physicians (22-24). Access to services should be facilitated by giving priority to older adults or, if there is no accompanying person, providing personnel to help in secondary and tertiary care outpatient services. It is necessary to increase awareness of health literacy and provide access to e-health applications for older adults (9,10,35,36). A safe home environment should be created to prevent falls, especially among frail older individuals (37-39). Social support is critically important for older adults (36). It is necessary to ensure compliance with society by disseminating life-long learning model practices, and to contribute to intergenerational communications and thus help preserve the mental health of advanced aged people through volunteering projects and social projects that enable them to communicate with young people (9,19,40). It should be strived to create a positive old age perception in society. There should be necessary regulations for older adults to protect their life standards and enable them to work on their medical condition.

The essential aim of geriatric medicine is for the individual to become self-sufficient and self-confident in terms of physical, mental, and cognitive capacity until advanced age, to become independent, and to be "vigorously healthy" (41-43). Frailty is a syndrome with multiple causes that occurs as a result of age-related loss of physiological reserves, insufficient response to internal and external stress factors, and decreased adaptation capacity (39). Frailty may increase the risk of medical complications, delirium and falls, hospitalization, admission to nursing homes, and mortality (25,37,38,44). Appropriate screening tests should be routinely performed to identify frailty. Interventions such as physical exercise, regulation of nutrition, combating polypharmacy, and cognitive training programs should be applied for the prevention or regression of the disease (32,45-47).

Geriatric Syndromes

Low body mass index in older adults is a much more important risk factor than obesity (48). Malnutrition in older adults is caused by inadequate food intake, loss of appetite, inflammatory processes associated with chronic diseases, and sarcopenia (49-51). Malnutrition is a pathological condition that causes a noticeable deterioration in body size, composition, and function as a result of low or high-energy intake of protein and other nutrients and reduces survival (49). The awareness level and knowledge of all physicians and healthcare workers, especially those working in long-term care facilities, such as nursing homes, residential care homes, and hospitals, should be increased. The daily energy requirement is 25-30 kcal/kg for a healthy older adult with practically normal physical activity; the daily protein requirement is 1.0-1.2 g/kg (47,52). In malnutrition, trauma, and medical conditions requiring surgical intervention and hospitalization, protein requirement increases significantly (1.2-1.5 g/kg/day) depending on the severity of the medical condition (2,52,53). The daily fluid requirement can be estimated as 30 mL/kg (53).

Sarcopenia is the deterioration of the individual's mobility, independence in daily life activities, and physical performance as a result of decreased muscle mass, muscle strength, and physical performance (34). Early diagnosis of sarcopenia is crucial because its prevalence increases with advanced age and causes mortality, falls, functional loss, hospitalization, long-term hospital stay, decreased quality of life, and increased frailty (54,55). The prevalence of sarcopenia among older adults living in the community is between 10% and 20% (2,34). The cornerstones of sarcopenia treatment are nutritional support, physical activity, and vitamin D supplementation. It is necessary to raise awareness among health professionals and the society regarding malnutrition and sarcopenia in older adults and increase preventive and therapeutic practices (52,53).

Falls pose an important public healthcare problem in the older adult population because of their medical, social, and economic consequences (37). Approximately 20% of post-fall hip fractures

are lost within a year or result in dependence, loss of autonomy, confusion, immobilization, depression, and fear of falling (2). "The risk of falling" should be determined in all individuals over 65 years of age who apply for any reason; problems should be treated, and risk should be reduced by creating a safe environment (37).

Multiple or inappropriate drug use is an important problem in older adults. In our country, the rate of use of 5 or more types of drugs is more than 50% among individuals aged 65 years and older who apply to outpatient clinics (46). Age-related physiological changes affect drug metabolism. Polypharmacy and inappropriate drug use have many negative consequences, such as drug-drug interactions, drug side effects, morbidity, mortality, hospitalization rates, treatment costs, and increased drug non-compliance. To combat polypharmacy and inappropriate drug use, training programs to raise awareness among society and healthcare workers should be promoted, and information technologies should be used to support physicians and pharmacists (45,46). Physicians are eager to intensify medications, whereas they largely ignore the deintensification of diabetes management. According to a large multicentral cross-sectional study of older patients with type 2 diabetes performed in Turkey, one in ten older adults was overtreated, while one in four required modifications of their current antihyperglycemic and antihypertensive treatments (56). These results warrant reinforced measures to improve the care of older adults with type 2 diabetes and hypertension. For this purpose in our country, "Turkey inappropriate drug use criteria (TIME criteria)" has been established under the leadership of the Academic Geriatrics Association, and with the wide participation of expert faculty members, the developed application can be used on all smartphones (57).

Urinary incontinence negatively affects individuals' quality of life as a result of decreased participation in physical activities, social isolation, and increased stress levels (58,59). Correctable and reversible causes of urinary incontinence in older adults should be investigated and treated.

Dementia syndrome is a condition in which cognitive function is impaired as a result of damage to the central nervous system in adults, and this deterioration affects daily life activities (60). The prevalence of dementia is 1-2% at the age of 65 years, and this rate doubles every six years of life (2). Dementia is the fifth most common cause of death worldwide, and the expenses spent on patients are approaching 1 trillion dollars annually (2). The most common cause of dementia is Alzheimer's disease (61). In patients with dementia, reversible causes such as delirium and depression, medical diseases, normal pressure hydrocephalus, and brain tumors should be investigated (60,62,63). Reasons that increase the risk of dementia, such as low education level, hypertension, diabetes mellitus, hearing loss, obesity, smoking, depression, physical inactivity, low social interaction, excessive alcohol consumption, and head trauma, should be addressed (2,64). Most people with dementia also have other diseases. Post-diagnostic care, physical and mental health, social care, and support programs should be developed. With special interventions and support for caregiver family members, the quality of life of patients and caregivers can be enhanced, and costs can be reduced.

Depression is a mood disorder in which an individual feels collapsed or unwilling/unhappy for most of the day for a minimum of two weeks, additionally, thoughts of guilt and valuelessness, such psychological symptoms as death wish or plan, or physical symptoms such as loss of concentration and appetite, sleep disorders, exhaustion, and weakness (62). Suicide attempts, an important complication of depression, are more common in older adults (65). The prevalence of geriatric depression in our country is between 16-45% (2). It is necessary to raise awareness of depression among older adults and explain to the public that depression in old age is not a normal situation. Depression prevention, screening, diagnosis, treatment, and follow-up processes should be developed. Physicians' knowledge of geriatric psychiatry should be increased through postgraduate training; topics such as the different presentations of psychiatric syndromes in older adults, older adults-specific treatment methods, and pharmacological treatment should be included in these trainings. "Geriatric psychiatry" should be organized as a subspecialty area. Regulations should be made in the Health Practice Communiqué so that physicians treating geriatric patients can prescribe appropriate anti-depressant medications.

Delirium is a syndrome that progresses with deterioration in attention and awareness, usually emerges within hours and days, tends to rapidly emerge and fluctuate during the day compared with the previous attention/awareness level of the person (66,67). Delirium is observed in 50% of hospitalized older adults, and approximately 60% of cases are omitted (2). Delirium may be the first and only manifestation of serious illness in older adults. Conversely, situations that increase and facilitate the tendency toward delirium should be recognized and corrected. Delirium may cause prolonged hospital stay; increased risk of complications, falls, and pressure ulcers; transfer to nursing homes; increased incidence of dementia, mortality, and healthcare costs. Delirium may lead to a decrease in the quality of life, cognitive function, and functionality of patients and their relatives (2,68). The awareness level and knowledge of all physicians and healthcare workers, especially those working in healthcare institutions and hospitals, should be increased.

Pressure sores and ulcers are the result of localized tissue damage to the skin and/or subcutaneous tissue caused by pressure or shearing forces. Pressure injuries have negative

effects on the physical, functional, and social well-being of older adults and significantly increase health costs. Risk factors include functional limitation, impaired mobilization, fecal and urinary incontinence, impaired sensory perception, decreased level of consciousness, malnutrition, age 75 years and older, presence of comorbid conditions, lack of family and social support, and skin wetness. Prevention of pressure sores is easier and more important than treatment; repositioning, skin care, nutritional status, and disease treatment are the main preventive approaches (68). Prevention of pressure ulcers is a quality indicator of health. Particularly, insufficient care while turning the patient or changing the bed sheets or the patient's clothes can cause pressure on the skin by friction and shear forces (2,69,70). In addition to the employees of the inpatient institutions, the knowledge of the members of the home care team should be increased.

Chronic Diseases

One of the main fields of geriatrics is the diagnosis and treatment of chronic diseases and the approach to multimorbid older adults (46). The prevalence of multimorbidity is less than 2% among those under the age of 35 years, and it reaches 46% among those 65 years and older in Turkey (2). In particular, the prevalence of hypertension, diabetes, coronary artery disease, atrial fibrillation, chronic kidney disease, cerebrovascular disease, dyslipidemia, Parkinson's disease, chronic obstructive pulmonary disease, depression, and cancer is higher in older adults than in the general population (71-80) (Table 1). In addition, approximately, 25% of adults aged over 65 years experience pain and loss of function due to osteoarthritis. It is estimated that one out of three females and one out of five males aged over 50 years will experience an osteoporosis-related fracture in the rest of their lives (79).

The most common cancers in older adults are breast, cervical, and corpus uteri cancer in women; prostate cancer, colon-rectal, and non-Hodgkin lymphoma in men (2). The first three cancer types that cause the most death in the world are lung and bronchial cancers, liver, and stomach in men; breast, lung, and colorectal cancers in women. In contrast, lung, stomach, and lymphoma in men; and lung, breast, and lymphoma in women are the most common causes of death from cancers in Turkey (80,81).

Prevention and Early Diagnosis of Chronic Diseases

Physiological and functional status varies greatly among older adults. This heterogeneity means that both preventive and therapeutic decisions must be based on individual needs. Age alone may not be the main determinant of interventions (4,14,82). All treatments should aim to preserve function and maximize quality of life. The concept of latency is important in screening and other preventive measures. With the occult blood test in stool, the risk of death in only one out of 1000 people screened in 10 years can be prevented for colorectal cancer. If an individual's life expectancy is five years, then this screening is unlikely to provide any benefit. For this reason, each patient should be evaluated individually, and the screening process should be decided (83-86). Preventive medicine practices are classified into three levels: primary, secondary, and tertiary.

Primary prevention: It covers the preventive medicine practices applied to prevent disease occurrence in asymptomatic people. For example, immunization, recommendations for diet and exercise to prevent cardiovascular diseases, and quitting smoking and alcohol (29,43,87-89).

Secondary prevention: It includes preventive medicine practices that seek to detect diseases in the asymptomatic period and prevent disease progression with treatment. For example; blood pressure measurement (90) and blood glucose measurement (91), cancer screening (80,92-95), bone mineral densitometry measurement (96,97), screening for mild cognitive impairment (98,99), screening for impaired visual acuity for early diagnosis of age-related macular degeneration (100), and treatment of hyper/dyslipidemia (101,102).

Table 1. Commonly encountered chronic diseases in older adults in Turkey

Chronic disease	Prevalence (%)	Age group (years)
Hypertension	74	60-69
	79	70-79
	83	≥80
Diabetes	34.7	≥65
Coronary artery disease and/or stroke	22	≥65
Atrial fibrillation	2	60-69
	2.5	≥70
Chronic kidney disease	15.7	≥18
	32.7	60-69
	41.3	70-79
	54.7	≥80
Cerebrovascular disease	6	65-74
	M: 9, F: 11	≥75
Hyperlipidemia	M: 20, F: 34	65-74
	M: 18, F: 26	≥75
Parkinson disease	1.9	≥65
Dementia	4.8	≥65
Chronic obstructive lung disease	M: 13, F: 12	65-74
	M: 17, F: 15	≥75
Any cancer	3	≥65

M: Male, F: Female

Tertiary prevention: It comprises preventive medicine practices targeting to reduce the complications of diseases and prevent the progression of the disease. For example; such as eye examination in patients with diabetes for retinopathy and albuminuria measurement for nephropathy (103).

Functional decline and loss of independence are not inevitable consequences of aging. Given the prevalence and impact of chronic noncommunicable diseases among older patients, evidence-based interventions to address these issues are increasingly important to maximize life expectancy and quality of life in older adults (104).

Intervention, Treatment, and Care

The targets and treatment of chronic diseases are different in frailing and conditioned or vigorously healthy older adult individuals (104). Considering the life expectancy of older adults with chronic diseases, interactions among drugs, side effect profiles, and multimorbidity, follow-up, and treatment specific to each chronic disease should be based on evidence-based guidelines and updated when necessary (57,102,103,105). Older adults should be screened for chronic diseases in primary care, and diagnosis and treatment should be arranged in secondary and, when necessary, tertiary health institutions; follow-up should be undertaken by primary health care institutions as much as possible, and cooperation and coordination between the institutions should be ensured.

According to the definition of the WHO, rehabilitation is "a set of interventions designed to optimize the functionality and reduce disability of individuals in various health states who interact with their environment". Rehabilitation includes medical, psychological, social, and vocational services (4,22,106). Most of those benefiting from rehabilitation services in Turkey are older people.

Long-term care services include all services that provide support to people who have difficulty in maintaining their basic life activities independently because of a lack of or decrease in physical, functional, or mental capacity. The status of family members who play a critical role in home care is often ignored. Long-term care facilities, such as nursing homes, care and rehabilitation centers, and home care services for adults and persons with a disability in Turkey. Local authorities (municipalities), on the other hand, usually provide services such as maintenance, repair, and cleaning services, participation in social activities, etc., under the name of domestic care. To achieve good care service, it is necessary to monitor compliance with quality standards, management, and strategic planning at all levels. Older adult care insurance should be implemented as a financing model.

With the aging of the population, the emergence of various physiological alterations in the human body, variability in drug metabolism, different manifestations, and disease course have led to the need to solve the problems of older adults in a single center by allocating sufficient time (7,11,12,57,79,104). The interdisciplinary team consists of geriatricians, nurses, gerontologists, dieticians, psychologists, social workers, physiotherapists, occupational therapists, and pharmacologists/pharmacists. Moreover, if necessary, other members, such as podologists, optometrists, audiologists, language-speech therapists, dentists, and spiritual support teams, should be incorporated into the team (13,107-110). The legislative regulations should be established to enable the interdisciplinary team members to serve as full-time employees in the same institution, in a united structure, in compliance with their job definition and specialty. It is also necessary to create legislation to pay for every service provided by team members. Assigning older adult care technicians to the interdisciplinary team may contribute to these services.

The mortality rate of COVID-19 was particularly high in frail older adults with low functional reserve and high morbidity (111,112). This experience helped us establish preparedness plans for future pandemics and unexpected critical conditions. To prevent falls and long periods of inactivity, it would be beneficial to offer informative brochures or digital platforms that will provide physical mobility during and after the quarantine period for such conditions for the use of older adults. To meet the basic needs of older adults who are isolated from society and stay at home during the quarantine, loyalty social support teams, municipalities, volunteers, and headmen should be made visible, and older adults should be informed about the existence of these services. Establishment of different communication and support lines for older adults; social and spiritual support mechanisms and formation of teams; and provision of delayed/skipped routine health check-ups and care services should be presented. COVID-19 in older adults may not be recognized because of atypical symptoms such as falling, cognitive fluctuations, and behavioral changes (112). The clinician following the patient should decide on the treatment of older adult patients according to the general condition of the patient, presence and condition of underlying diseases, laboratory values, oxygen demand, and presence of other concomitant infections (113). The side effects of COVID-19 medications should be considered in older adult patients; such health problems as life-threatening cardiac arrhythmias and liver and kidney dysfunctions should be taken into account. Malnutrition and sarcopenia are the causes of infection with severe acute respiratory syndrome coronavirus 2, and they may also result in the fatal course of the disease. A precision diet, exercise, and physical activity program customized according to the individual's needs should be organized (54,114-116). Tele-rehabilitation applications and studies should be initiated to provide the physiotherapy and rehabilitation services at home to older adults who have had

COVID-19 infection at home or have been discharged from the hospital and have post-COVID-19 syndrome (111).

Due to the challenges and tough life standards, immigrants are expected to have signs of social, physiological, and psychological aging well before the age of 65. Turkey, with more than 4 million immigrants, has become "the top-ranked country with the highest number of refugees in the world" Syrians registered in Turkey can benefit from all health services free of charge. Migrants and asylum seekers are provided with health services in immigrant health centers, foreign nationals outpatient clinics, and voluntary health facilities, psycho-social support, counseling, rehabilitation, and various support services for older adults in temporary accommodation centers (117). Those who require care must apply to the official geriatric care institutions. Not being able to participate in the labor force among immigrants is the most important risk factor for social exclusion (118). Public service announcements, increased translation services, and cultural sensitivity training of health personnel will benefit health levels. These measures will enable older adult immigrants and asylum refugees to access health services (117,119). To ensure intercultural cohesion, content that encourages social cohesion and multiculturalism should be prepared in the media, in schools, parks, mosques, and other communal living spaces in areas where immigrants are predominantly living. Furthermore, awareness should be raised about problems that can cause discrimination and xenophobia (118,120).

Technological Solutions

It has become necessary to use technological applications to reduce health expenditures. Digital literacy should also be disseminated to older adults. Tele-medicine enables patients with financial and transportation restrictions to access health services and also saves time. Tele-medicine, tele-nursing, and tele-rehabilitation services should be disseminated. In this context, technologies such as image-based, sensor-based, virtual reality-based, and robotic applications are used for tele-monitoring and evaluation, physiotherapy and rehabilitation practice, tele-conference/tele-education, and tele-consultation/tele-counselling (35,36,121). With the use of information and communication technologies (ICT) in older adults, it is possible to reduce the number of physician visits, prevent re-admissions to the hospital, and prevent the emergence of adverse conditions with patient and caregiver education. Moreover, ICT helps monitor patients' vital symptoms, enables healthcare professionals to intervene when needed, and eases access to care services (2). With wearable technological devices, the lives of older adults become easier, quality of life increases, physical, mental, and social capacities are improved, and real-time health monitoring can be performed (121). These technologies may help prevent the disappearance of patients with cognitive disorders. Furthermore, the technology may help in areas such as monitoring falls, cardiovascular functions, tremors, hearing and vision losses, pressure ulcers, respiratory functions, balance problems, diabetes, skeletal and muscle problems, mouth and dental problems, and stool and urine controls.

"Smart homes" are residences that are equipped with a high-tech network connected to sensors and indoor devices. They can remotely monitor, access, and control devices and applications and provide services to meet the needs of residents (2). Effective and useful for monitoring physiological and functional parameters, providing a safe environment and reducing risks, following up and helping when necessary; facilitating social interactions as well as cognitive and sensory support.

While designing "the elder-friendly cities", exterior spaces and buildings, transportation, residences, social participation, inclusion in social life, and society's respect for older adults, fulfilling their civic duty and participating in the workforce, information and communication, community support, and health services are prioritized (109,122,123). "The elderly-friendly hospitals" are healthcare institutions that provide services to older individuals in the most appropriate manner and aim to provide a physical environment and service processes compatible with the needs of older adults and their families (109,124,125). Elderly-friendly cities and hospitals that support active aging should be developed and augmented in Turkey (110).

In our country, the awareness of healthcare professionals and other stakeholders involved in innovation processes is insufficient. Uncertainties about intellectual property rights and lack of support during certification and clinical trials are the leading issues. In addition, there are many other problems and obstacles such as the inadequacy of policies, infrastructure, and resources that encourage and facilitate the innovation process; insufficient cooperation networks with institutions and organizations in different fields; the absence of health-oriented innovation centers; and the lack of models that support and provide attractive guiding processes to provide motivation. Health innovation models and policies unique to the country should be developed; health-oriented innovation models to participate in all processes should be established; and integrated cooperation platforms where all stakeholders are involved should be created. Priority should be considered in resources as well as targets; innovation should be planned and supported according to the manpower infrastructure in the country and the strategic needs of the market, and the investment-production-market relationship should be brought into functionality.

Conclusion

In conclusion, life expectancy in Turkey is increasing and the number of older adults is rising faster than expected. The

aging of society should be the main denominator in all areas, especially health and care services, economic, social, political, etc. Policies should be established based on this situation, which has not been experienced before, and solutions should be developed for existing and potential problems. Individuals at younger ages should be educated about active and healthy aging. To increase the knowledge and skills of healthcare professionals regarding older adults' health and care, education should be continued after graduation as before graduation. We should always take into account that effective and high-quality health and care services can be provided to our older adults not only by physicians but also by the interdisciplinary teamwork of all health professionals and with the support and interest of society.

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Keywords: Chronic diseases, geriatric syndromes, geriatrics, healthy aging, older adults

Authorship Contributions

Concept: M.A.K., İ.S., Design: M.A.K., İ.S., Analysis or Interpretation: M.A.K., İ.S., T.A., G.B.Ö., M.C., D.S.E., M.H., Literature Search: M.A.K., İ.S., T.A., G.B.Ö., M.C., D.S.E., M.H., Writing: M.A.K., İ.S.

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ORIGINAL RESEARCH

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Self-efficacy and Optimism in Frail Older Men Without Functional Disability Attending Geriatric Outpatient Clinic: A Case-control Study

Doaa Ageez[1,2], Heba El-Sobky[2], Nessma Mohammad[1], Doha Rasheedy[1], Heba Shaltoot[1]

[1]Ain Shams University Faculty of Medicine, Department of Geriatrics, Cairo, Egypt

[2]Mansoura University Faculty of Medicine, Department of Geriatrics, Mansoura, Egypt

Abstract

Objective: Psychological frailty, including cognitive, mood, and motivational components, is an important predictor of overall well-being. Therefore, there is an increasing scientific interest in studying different determinants of psychological frailty. Unfortunately, the psychological components of frailty are not fully evaluated and currently, there is currently no consensus on the proper assessment or intervention. This study evaluated optimism and self-efficacy among frail older men without functional disability.

Materials and Methods: A case-control study. Seventy older men ≥60 years were divided into frail and non-frail groups. The self-efficacy scale (SES) and revised life orientation test (R-LOT) were applied for all participants, in addition to the comprehensive geriatric assessment, to determine other factors affecting physical frailty.

Results: Those with physical frailty had lower self-efficacy and optimism scores. R-LOT and SES had moderate diagnostic accuracy in predicting frailty; the area under the curve for both tools were 0.75 and 0.71, respectively.

Conclusion: There is an association between poor general self-efficacy, low optimism, and frailty among older men. Thus, the importance of addressing the psychological determinants of frailty is on par with that of addressing the physical components. Integrating the SES and R-LOT scales into the comprehensive assessment of older men with physical frailty can improve the assessment of psychological resilience, ultimately promoting their well-being and quality of life.

Keywords: Frailty, optimism, revised life orientation test, self-efficacy, self-efficacy scale

Introduction

Frailty is a growing global health challenge that affects healthcare systems worldwide. The prevalence of frailty is exponentially rising due to graying of the population (1).

Frailty is a condition of reduced resilience due to dysregulated homeostasis that increases vulnerability to stressors and delays recovery (2), leading to many adverse outcomes, including dependence, falls, long-term institutionalization, hospitalization, and increased mortality (3).

Frailty is a multifaceted concept that extends beyond physical decline, encompassing a spectrum of deficits in cognitive, social, and psychological domains (4). Recently, psychological frailty was described as a multi-component concept that includes mood, cognitive, mental, and fatigue-associated problems (5).

Psychological resilience, optimism, and self-efficacy are interrelated constructs that play a crucial role in the ability to positively adapt to stressors (4,5).

Address for Correspondence: Doaa Ageez, Ain Shams University Faculty of Medicine, Department of Geriatrics, Cairo, Egypt; Mansoura University Faculty of Medicine, Department of Geriatrics, Mansoura, Egypt

Phone: +20 127 376 09 80 **E-mail:** doaaageez1995@hotmail.com **ORCID:** orcid.org/0009-0005-6683-3894

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Optimism as a cognitive construct is defined as positive expectations regarding future outcomes (6). Older adults with higher levels of optimism have a longer lifespan (7), as they are more likely to embrace healthier lifestyles, such as participating in regular physical activity, eating a healthy diet, and smoking cessation (8).

Self-efficacy is defined as having the confidence of being able to accomplish a specific behavior to achieve specific performance expectations (9). Self-efficacy is flexible and responsive to change; thus, it can be effectively targeted in healthcare-related interventions. Augmenting self-efficacy promotes health behaviors such as physical exercise and maintaining a healthy diet (10). The impact of physical frailty on optimism and self-efficacy remains an area of limited research. These psychological factors should be examined for their potential role in patient-centered interventions. Therefore, this study quantified the effect of frailty on self-efficacy and optimism in older men.

Materials and Methods

A case-control study was conducted on 70 older men aged 60 years, and above recruited from the geriatric outpatient clinic at Mansoura University Hospital, Mansoura, Egypt, between August 2022 and March 2023. A sample size of 35 cases and 35 controls achieves a power of 80% according to Doba et al. (11). We used a purposive random sampling. The frailty status was rated according to the modifications of Fried criteria adopted by Avila-Funes et al. (12). The score ≥3 was considered frail. Those who scored 0 were non-frail (robust) individuals. Exclusion criteria: individuals categorized as pre-frail, patients with acute or chronic conditions that could interfere with the initial assessment or communication, patients with functional disabilities who need aid in one or more of the basic activities of daily living (ADL) (13), and patients with a diagnosis of dementia or depression.

Data Collection and Assessment Tools

The older men attending the clinic underwent comprehensive geriatric assessment and were assessed for eligibility through the following:

- Proper history taking.
- Mini nutritional assessment (MNA) (14) to evaluate the risk of malnutrition. The participants were rated malnourished if scored less than 17, at risk of malnutrition with scores between 17 and 23.5, and well-nourished with scores ≥24.
- The Arabic version of the mini-mental state examination (15,16): excludes patients with dementia. The interpretation of results was performed according to the normal reference values adjusted for age and education (17).
- The Arabic version of the geriatric depression scale (GDS) (18,19): those who scored five or more indicated potential depression, and accordingly, they were excluded from the study (20).
- ADL (21), and instrumental ADL (IADL) (22): those with ADL <6 were excluded based on the presence of physical disability.

The participants were assigned to either the frail group or the non-frail group using the physical frailty phenotype (PFP) (23), according to the modifications made by Avila-Funes et al. (12). The PFP includes five criteria: slowness, unintentional weight loss, weakness, low physical activity, and exhaustion.

Both groups underwent: optimism assessment using the Arabic version of the revised life orientation test (R-LOT) (24). The R-LOT is a self-report measure that assesses motivation and the participant's expectations regarding future outcomes. This is a 10-item questionnaire consisting of direct-scored, reverse-scored, and filler items. Scores ranging from 0 to 13 indicated low optimism, 14 to 18 indicated moderate optimism, and 19 to 24 indicated high optimism.

Self-efficacy was assessed using the Arabic version (25) of the general efficacy scale (26). It is a self-report tool that assesses confidence in the ability to face challenges. It consists of 10 items rated according to a 4-point Likert scale ranging from 1 "not at all true" to 4 "exactly true". The overall score ranges from 10 to 40. Higher scores (≥29) indicate high self-efficacy, whereas lower scores (<29) indicate low self-efficacy.

The study methodology was revised and approved by the Research Ethics Committee at the Faculty of Medicine, Ain Shams University (approval number: FMASU MS 490/2022, date: 9.8.2022). All study participants were interviewed during clinic visits. We respected confidentiality and obtained their informed written consent for participation.

Statistics

Collected data were encoded, tabulated, and statistically analysed using IBM Statistical Package for Social Sciences (SPSS) statistics software version 28.0 (IBM Corp., Chicago, USA, 2021. Quantitative data were described as mean ± standard deviation and compared using an independent t-test for two independent groups and an ANOVA test for three independent groups. Qualitative data were described as numbers and percentages and compared using the chi-square test or Fisher's Exact test. The receiver operating characteristic curve was used to evaluate the performance of self-efficacy scale (SES) and R-LOT for diagnosing physical frailty. A $p<0.050$ was considered significant.

Results

Seventy older men were enrolled in this study; they were evenly divided between the frail and non-frail groups. The

sociodemographic variables were matched between the two groups.

Compared with the robust group, the frail group reported an increased prevalence of sleep problems, social inactivity, and higher chronic pain levels. In addition, MNA and IADL scores were notably lower, malnutrition was more prevalent, GDS scores were significantly higher, and there was a significantly higher number of comorbid conditions. Moreover, body mass index (BMI) was significantly lower in the frail group (Table 1).

Self-efficacy, measured by SES, had a mean score of 25.3±5 among frail group and 28.1±4.6% in the robust group, whereas optimism, measured by R-LOT, had a mean score of 12.7±3.3 in

Table 1. Sociodemographic and clinical characteristics of the study groups

Variables		Frail group (total=35)	Control group (total =35)	p
Age (years)	Mean ± SD	69.1±5.1	67.7±4.0	^0.195
Education	Educated	13 (37.1%)	13 (37.1%)	#0.999
	Illiterate	22 (62.9%)	22 (62.9%)	
Caregiver	Family	35 (100.0%)	33 (94.3%)	§0.493
	Paid	0 (0.0%)	2 (5.7%)	
Marital status	Married	28 (80.0%)	31 (88.6%)	#0.324
	Unmarried	7 (20.0%)	4 (11.4%)	
Living arrangement	Alone	3 (8.6%)	4 (11.4%)	§0.999
	With spouse	32 (91.4%)	31 (88.6%)	
Presence of social events in the last 6 months		14 (40.0%)	9 (25.7%)	#0.203
Presence of economic problems		25 (71.4%)	21 (60.0%)	#0.314
Smoking	None	9 (25.7%)	14 (40.0%)	#0.203
	Current/ex	26 (74.3%)	21 (60.0%)	
BMI (kg/m²)		19.4±3.7	21.5±2.8	^0.010
Sleep problems		28 (80.0%)	12 (34.3%)	#<0.001
Lack of social activities		25 (71.4%)	12 (34.3%)	#0.002
Pain	None	12 (34.3%)	20 (57.1%)	#0.015
	Mild	14 (40.0%)	14 (40.0%)	
	Moderate	8 (25.7%)	1 (2.9%)	
MNA	Mean ± SD	20.9±3.5	23.9±3.0	^<0.001
Nutritional status	Normal	11 (31.4%)	27 (77.1%)	#<0.001
	At risk/malnourished	24 (68.6%)	8 (22.9%)	
MMSE		26.5±2.2	27.1±2.0	^0.230
GDS		3.4±0.8	1.6±1.3	^<0.001
IADL		4.7±0.9	7.7±0.7	^<0.001
DM		20 (57.1%)	10 (28.6%)	#0.016
Hypertension		16 (45.7%)	12 (34.3%)	#0.329
IHD		14 (40.0%)	14 (40.0%)	#0.999
Stroke		3 (8.6%)	1 (2.9%)	§0.614
CKD		6 (17.1%)	5 (14.3%)	#0.743
CLD		16 (45.7%)	11 (31.4%)	#0.220
COPD		10 (28.6%)	5 (14.3%)	#0.145
Anaemia		9 (25.7%)	6 (17.1%)	#0.382
Thyroid		2 (5.7%)	2 (5.7%)	#0.999
Number of comorbidities		2.7±1.4	1.9±1.1	^0.004
Number of medications		5.1±3.0	4.8±1.8	^0.56

^:Independent t-test, #:Chi-square test, §:Fisher's exact test, SD: Standard deviation, MNA: Mini nutritional assessment, MMSE: Mini-mental state examination, GDS: Geriatric depression score, IADL: Instrumental activities of daily living, COPD: Chronic obstructive pulmonary disease, CLD: Chronic liver disease, CKD: Chronic kidney disease, IHD: Ischemic heart disease, DM: Diabetes mellitus, BMI: Body mass index

the frail group compared with 16.6±4.4 in the robust group. Both SES and R-LOT scores were significantly lower in the frail group (Table 2). Both R-LOT and SES demonstrated moderate diagnostic accuracy in predicting frailty, with an area under the curve of 0.75 for R-LOT ≤17 and 0.71 for SES ≤30 (refer to Figure 1).

Self-efficacy was significantly lowest in patients with low optimism as measured by R-LOT, with no significant difference between moderate and high grades (Table 3).

There was a positive correlation between SES and R-LOT scores, with (r=0.611, p<0.0001). After adjusting for the following confounding factors (MNA score, presence of chronic pain, sleep problems, and the number of comorbidities), the correlation analysis between SES and R-LOT score was (r=0.518, p=0.003) in the frail group and (r=0.568, p<0.001) in the robust group (Table 4).

Discussion

In this study, health-related factors affecting frailty were evaluated, and the effect of frailty on optimism and self-efficacy was assessed. Both SES and R-LOT scores were significantly lower in the frail group. Moreover, there was a positive correlation between the R-LOT and SES scores. The SES score was significantly lower in patients with low optimism; however, there was no significant difference between moderate and high levels of optimism regarding SES scores. The impact of physical frailty on self-efficacy has attracted increasing attention in the past few years. In addition to its impact on emotional, behavioral, and cognitive performance, self-efficacy also affects the biological responses to stressors, playing an essential role in both mental and physical well-being (27). There was a direct effect of general self-efficacy on frailty in 327 hospitalized older patients aged ≥60 years with chronic medical conditions. However, loneliness played a mediating role in this relationship (27).

Hladek et al. (10), in their study, reported that high self-efficacy was negatively correlated with pre-frailty and frailty. The odds

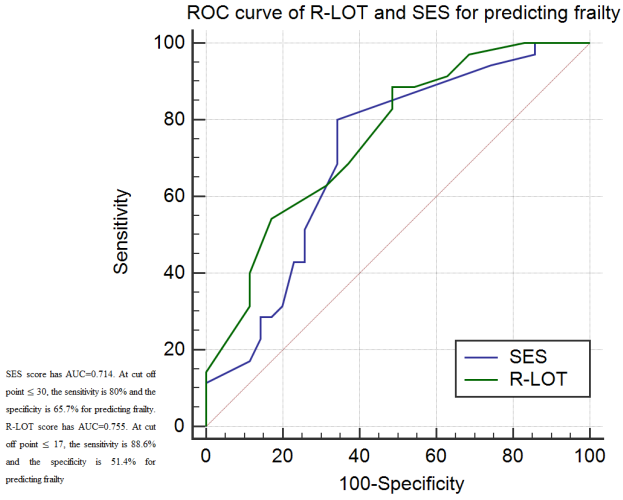

Figure 1. ROC curve for R-LOT and SES in predicting frailty. R-LOT and SES demonstrated moderate diagnostic accuracy in predicting frailty, with an AUC of 0.75 for R-LOT ≤17 with a sensitivity of 88.6% and a specificity of 51.4%, and an AUC of 0.71 for SES ≤30 with a sensitivity of 80% and a specificity of 65.7% for predicting frailty

ROC: Receiver operating characteristics, R-LOT: Revised life orientation test, SES: Self-efficacy scale, AUC: Area under the curve

Table 2. Optimism and self-efficacy among the study groups

Variables		Frail group (total=35)	Control group (total =35)	p
R-LOT score		12.7±3.3	16.6±4.4	ˆ<0.001
R-LOT interpretation	Low optimism	22 (62.9%)	11 (31.4%)	#0.007
	Moderate optimism	10 (28.6%)	11 (31.4%)	
	High optimism	3 (8.6%)	13 (37.2%)	
SES score		25.3±5.0	28.1±4.6	ˆ0.015
SES interpretation	Low	24 (68.6%)	12 (34.3%)	#0.004
	High	11 (31.4%)	23 (65.7%)	

ˆ: Independent t-test, #: Chi-square test, R-LOT: Revised life orientation test, SES: Self-efficacy scale

Table 3. Comparison between cases with low, moderate, and high optimism as measured by R-LOT regarding self-efficacy

Variables		Low optimism (total=22)	Moderate optimism (total=10)	High optimism (total=3)	p
SES score		23.6±5.5	28.3±1.8	27.3±2.9	ˆ0.031
SES interpretation	Low	16 (72.7%)	7 (70.0%)	1 (33.3%)	$0.459
	High	6 (27.3%)	3 (30.0%)	2 (66.7%)	

ˆ: Independent t-test, $: Fisher's exact test, R-LOT: Revised life orientation test, SES: Self-efficacy scale

of frailty decreased by 91% after adjusting for confounding factors (age, comorbidities, and life events). Furthermore, low self-efficacy was an independent predictor of frailty in a linear regression model (11).

In their prospective cohort study, Hladek et al. (28) reported that low general self-efficacy predicted incident frailty during seven years of follow-up. The risk of incident frailty increased by 41% in older adults with low self-efficacy after adjustment for other confounding variables.

Optimism as a psychological construct was associated with the adoption of healthy behaviors. Studies have shown that optimistic adults tend to have enhanced health status and that optimism can benefit those with various chronic medical conditions, including cancer, diabetes, cardiovascular, and neurological diseases (29). In this study, 62.9% of frail men had low optimism levels, whereas only 31.4% of those in the robust group exhibited low levels of optimism. It is well established that optimistic people tend to adapt more effectively to the challenges of aging and life stressors by using coping strategies such as problem-solving, seeking support from others, and reevaluating situations to find more positive views (30).

Similar findings were reported by Kim and Won (31), who found that individuals with frailty exhibited lower levels of optimism than those without frailty. This association persisted after accounting for age, malnutrition, cognitive function, and physical activity. However, this association between frailty and optimism was partially attributed to depression.

Wang et al. (32) reported that a higher level of optimism decreased the odds of frailty. However, after adjusting for age, gender, social factors, self-rated health, smoking, dietary factors, and physical activity, optimism was no longer associated with frailty.

The SES score was significantly lowest in cases with low optimism. This association was anticipated, given the shared conceptual underpinnings of self-efficacy and optimism and their established role in predicting overall well-being (6).

The association between the two constructs was evaluated in relation to academic performance (33), psychological health (34), and inflammatory bowel disease activity (35). However, to date, no study has examined this relationship in frail men. 51.4% of our frail patients were underweight. Our result aligns with the observation made by Xu et al. (36) who found that those with low BMI were more at risk of frailty. Similarly, Wu et al. (37) showed that the incidence of sarcopenia increases with low BMI. According to the Fried criteria of PFP, unintentional weight loss and/or BMI <18 kg/m^2 were addressed as a component of physical frailty (23).

There was an increased prevalence of higher chronic pain among patients. This agrees with other studies in which the prevalence of both frailty and chronic pain was related (38-40).

Sleep problems are another important determinant of frailty. Our study is consistent with Pourmotabbed et al. (41), who found that experiencing daytime sleepiness, breathing sleep

Table 4. Correlations of frailty, R-LOT, and SES scores between the frail and control groups

Variables		Among the frail group			Among the control group	
		Frailty score	R-LOT score	SES score	R-LOT score	SES score
LOT	r	-0.315				
	p	0.084				
SES	r	-0.358	0.518		0.568	
	p	0.048	0.003		0.001	
Age	r	-0.146	0.017	-0.097	0.085	0.181
	p	0.433	0.927	0.604	0.649	0.329
Medications number	r	-0.096	-0.327	-0.223	-0.115	-0.293
	p	0.606	0.073	0.227	0.539	0.110
BMI	r	0.041	0.026	0.124	-0.123	-0.008
	p	0.829	0.890	0.506	0.510	0.965
MMSE	r	-0.182	0.276	0.467	0.177	-0.156
	p	0.327	0.133	0.008	0.341	0.403
GDS	r	-0.044	0.183	-0.232	-0.139	-0.303
	p	0.816	0.324	0.209	0.456	0.098
IADL	r	-0.311	0.053	0.134	0.030	0.120
	p	0.089	0.776	0.472	0.872	0.520

Partial correlation, with control for number of comorbidities, MNA, pain, sleep problems. r: Correlation coefficient, R-LOT: Revised life orientation test, SES: Self-efficacy scale MNA: Mini nutritional assessment, MMSE: Mini-mental state examination, GDS: Geriatric depression score, IADL: Instrumental activities of daily living, BMI: Body mass index

problems, and prolonged sleep latency increased the risk of frailty. In our participants, the lack of social activities was more prevalent among the frail group. This aligns with previous research indicating that the risk of physical frailty was higher in those experiencing social isolation and a sense of loneliness, especially in older men (42,43). We agree with Zhang et al. (44) that malnutrition and high risk of malnutrition were substantially more frequent among the frail group.

Frail were more dependent on IADL compared with the control group. Many researchers have concluded similar results (45,46). Generally, frail older adults are more prone to develop or worsen disabilities in ADL and IADL.

Although older adults with depression (GDS ≥5) were excluded from this study, frail cases scored higher on GDS. Accumulating evidence suggests a reciprocal relationship between depressive symptoms and physical frailty in older adults. They are both common among older adults, and each of them can increase the likelihood of developing the others (47).

The number of comorbidities was higher among frail men. Diabetes mellitus was more prevalent in the frail group (57.1%). This is consistent with previous studies showing an association between multimorbidity and frailty. Indeed, most frail older adults have multiple chronic conditions, but not all multimorbid individuals are frail. Nevertheless, multimorbidity increases the risk of mortality in frail patients (48,49).

Study Limitations

We recognize that our study has certain limitations. The relatively small sample size and the use of a case-control design limit our ability to establish definitive causal relationships. Moreover, the study participants were men and predominantly from the young-old age group; thus, further research is needed to validate these findings in women and older participants. Additionally, inclusion of patients with moderate pain could have biased the results because pain can negatively impact mood and other psychological factors. Future interventional psychological and behavioral studies are needed to determine the potential protective effect of promoting self-efficacy and optimism on frailty.

Conclusion

An association exists between poor general self-efficacy, low optimism, and the presence of frailty among older men. The SES and R-LOT scales were moderately accurate in predicting frailty. Therefore, these scales could be used as part of a comprehensive evaluation of frail older men. Healthcare providers, particularly geriatricians, should address the psychosocial determinants of frailty. Psychological interventions that enhance self-efficacy, optimism, and other aspects of psychological frailty are crucial. These interventions, in addition to managing other factors such as nutrition, physical activity, polypharmacy, depression, sleep problems, social isolation, and traditional medical interventions for physical frailty, could significantly benefit older adults by delaying the onset of frailty and mitigating its negative consequences.

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Ethics

Ethics Committee Approval: The study methodology was revised and approved by the Research Ethics Committee at the Faculty of Medicine, Ain Shams University (approval number: 490/2022, date: 09.08.2022).

Informed Consent: Informed consent was obtained.

Authorship Contributions

Surgical and Medical Practices: D.A., H.E-S., Concept: D.R., H.S., Design: D.R., H.S., Data Collection or Processing: D.A., Analysis or Interpretation: D.A., H.E-S., N.M., D.R., H.S., Literature Search: D.A., H.E-S., N.M., D.R., H.S., Writing: D.A., D.R.

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ORIGINAL RESEARCH

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Validating the Use of Sphygmomanometer for Measuring Hand Grip Strength and Its Association with Functional Dependency in Older Females

Eman Mahmoud Abdelhamid Mohamed Megahed, Sarah Ahmed Hamza, Doha Rasheedy, Khalid Elsayed Elsorady

Ain Shams University Faculty of Medicine, Department of Geriatrics and Gerontology, Cairo, Egypt

Abstract

Objective: With global aging, older adults with functional decline is expected to increase. There is a need for simple and valid tools to assess functional decline that can be applied to different settings. The measurement of hand grip strength (HGS) remains a valuable objective tool that can overcome the barriers of self-reported ones. However, use of dynamometer is greatly limited to specialized geriatrics and rehabilitation services in low-resource countries, creating an increasing demand for alternative devices. The aim was to validate the use of a sphygmomanometer for measuring HGS and to determine its association with functional dependency in older females.

Materials and Methods: This cross-sectional study included 100 females aged ≥60 years, recruited from the outpatient clinics and from the caregivers of the inpatients and were subjected to comprehensive geriatric assessment, including functional assessment: activities of daily living (ADL), instrumental ADL (IADL), incidental and planned questionnaire week version, short physical performance battery, and HGS measurements using a Jamar dynamometer and sphygmomanometer.

Results: A significant correlation was found between HGS measured by sphygmomanometer and Jamar dynamometer. A conversion equation of the sphygmomanometer readings into Jamar readings was obtained. The recommended cut-off value to predict ADL dependency was ≤9 for HGS by Jamar with sensitivity 81.4% and specificity 57.9%, while it was ≤60 mmHg sphygmomanometer with a sensitivity of 58.14% and specificity of 78.9%.

Conclusion: The use of a sphygmomanometer for HGS measurements is an acceptable alternative to the Jamar dynamometer. It can predict ADL and IADL dependency in older females.

Keywords: Dynamometer, functional assessment, hand grip strength, sphygmomanometer, conversion equation

Introduction

With the global aging of the population, older adults with functional decline are expected to increase as a result of aging and comorbid chronic diseases (1). This decline presents a major challenge to public healthcare, as it is associated with poor quality of life, increased healthcare utilization and costs, nursing homes admissions, and mortality (2).

Several determinants can influence functional performance in older individuals. A recent prediction model reported a strong association between functional status and gender, gait speed, age, cognition, frailty, comorbidity, grip strength, physical activity, body mass index (BMI), instrumental activities of daily living (IADL), balance, educational level, residential status, sarcopenia, and activities of daily living (ADL) (3).

In both clinical and research settings, the evaluation of physical function has traditionally relied on self-report tools that assess an individual's ability to perform specific functional tasks, such as ADL or IADL scales. Other tools that depend on direct clinical observations of physical performance and muscle strength

Address for Correspondence: Eman Mahmoud Abdelhamid Mohamed Megahed, Ain Shams University Faculty of Medicine, Department of Geriatrics and Gerontology, Cairo, Egypt
Phone: +201015771187 **E-mail:** Eman.mahmoud@med.asu.edu.eg **ORCID:** orcid.org/0009-0000-9298-7428
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have gained popularity because they provide objective results compared with self- or proxy-reported tools. Moreover, they exhibit greater sensitivity to detect changes (4).

The gait speed test, the short physical performance battery (SPPB), the hand grip strength (HGS), and the Timed Up-and-Go test are widely used objective tools for functional assessment in older adults (4).

HGS is a simple but valid measure of overall muscle strength; it can be used to diagnose sarcopenia and determine the degree of physical disability. Many studies have reported reference values for HGS in different populations (5). Those values differed among different populations due to difference in ethnicities, body size, lifestyles, and cultural backgrounds. Thus, it is of paramount importance to use of population-specific cut-offs for HGS in order to accurately identify older adults at risk of muscle weakness (6).

Nevertheless, the limited availability of dynamometers in low-income countries remains a barrier to applying HGS measurements in different settings, primarily due to high cost, device fragility, and the need for specialized training. As an alternative, a manual sphygmomanometer, which is readily accessible, has been suggested (7).

In the current study, we aimed to validate the use of a sphygmomanometer for measuring HGS and to determine its association with functional dependency in Egyptian community dwelling older females.

Materials and Methods

Study Design and Participants

This cross-sectional study included 100 older females (60 years and older) who were recruited from outpatient clinics and from caregivers of inpatients at Ain Shams University Hospital between November 2022 and April 2023. The study was approved by the Ethics Committee of the Faculty of Medicine at Ain Shams University (approval number: FMASU MD 161 2022, date: 28.07.2022). Informed consent was obtained.

This investigation exclusively recruited elderly female participants to eliminate the influence of gender as a confounding variable on HGS.

Patients with dementia, fracture of one or more limbs or with amputation, distal musculoskeletal disorders, cerebrovascular stroke, or acute medical complaints within the previous month that affected their functional performance were excluded.

Each patient underwent comprehensive geriatric assessment, with an emphasis on functional assessment.

Functional assessment was done using the following tools:

Katz ADL: This assessment assesses the ability of patients to complete basic daily tasks, including transfer, bathing, toileting, continence, dressing, and feeding. The total score ranges from 0 to 6. Scores range from 0 to 5 indicates dependence and 6 indicates independence (8).

Lawton IADL: This measure assesses the patient's ability to perform activities, including shopping, driving, or transportation, telephone use, meal preparation, housework, medication intake, and financial dealing. Total score ranges from 0 to 8. Score range from 0 to 7 indicates dependence and 8 and indicates independence (9).

Incidental and planned exercise questionnaire week version (IPEQ-W) (10): It was designed to assess physical activity and validated for use in geriatrics population. It consists of 6 questions to assess the daily frequency and duration of planned exercise and walking. The questionnaire includes another 4 questions to assess incidental physical activities, including the weekly frequency, the daily duration of walking to go to places, the average time spent daily doing tasks outside the home, and the average time undertaking indoor tasks requiring standing on legs, such as housework or self-care. The average weekly time spent on each IPEQ-W question was calculated by multiplication of the weekly frequency by the daily duration (11).

The total time spent is summed crosswise and presented as hours/week. The score is derived by multiplying the frequency and duration score to formulate a total duration for the week score.

Moderate intensity was defined as 3-6 metabolic equivalent tasks (MET), and vigorous intensity was defined as ≥6 MET. One MET is equivalent to the energy expenditure during rest and is approximately equivalent to 3.5 mL O_2 kg^{-1} min^{-1} in adults. Physical activity data from the IPEQ-W were transformed into energy expenditure estimates as MET using published principles. To calculate weekly physical activity (MET-h $week^{-1}$), the number of hours given to each activity class was multiplied by the specific MET score for that activity.

The HGS measurements: It was measured using two methods. First, a Jamar dynamometer that was used to measure HGS through three trials by the dominant hand, with a 1-min interval between each trial. The results are presented in kilograms of strength, and the highest performance of the three measures was recorded (12). Second, HGS was measured using a sphygmomanometer, the cuff was inflated to 20 mmHg, and the patient exerted maximal grip force on the cuff. Three measurements were taken for the dominant hand, and the highest performance of the three measures was recorded (13).

The short physical performance battery (SPPB): The SPPB is a widely used tool designed to evaluate lower-extremity function and physical performance in older adults. It consists of three components: standing balance, gait speed, and chair stands. Each component is scored from 0 to 4, and the total score ranges from 0 to 12. Higher scores indicate better physical

function. SPPB is valuable for assessing functional decline, predicting disability, and guiding interventions to improve mobility and overall health among older individuals. It is a simple and quick test that provides important insights into an individual's physical capabilities (14).

Statistics

The sample size was calculated using the Pass program, assuming a rate of function decline of 60% and sensitivity and specificity of 80%, a sample of 100 participants would be sufficient to detect such a rate at the 0.80 power of the test and 0.05 alpha error. Data were collected, revised, coded, and entered into the Statistical Package for Social Sciences (IBM SPSS) version 23. The quantitative data were presented as means and standard deviations. Qualitative variables are presented as numbers and percentages. The comparison between groups regarding qualitative data was done by using chi-square test. The comparison between two independent groups with quantitative data and parametric distribution was performed using the independent t-test, whereas with non-parametric distribution was done by using Mann-Whitney U test.

Spearman's correlation coefficients were used to assess the correlation between two quantitative parameters in the same group.

The receiver operating characteristic curve was used to assess the best cut-off point according to its sensitivity, specificity, positive predictive value, negative predictive value, and area under the curve (AUC).

Multivariate linear regression analysis was used to assess the factors associated with Jamar and equation to calculate it. The confidence interval was set to 95% and the margin of error accepted was set to 5%.

Results

The mean age of the participants was 66.65±6.08 years, 52% of them were widows; the mean BMI was 31.48±6.82, with 56% of the participants were obese and 67% were illiterate. Regarding medical comorbidities, 35% were diabetic, 52% were hypertensive, and 78% had osteoarthritis (Table 1).

As regards functional assessment the mean ADL and IADL scores were 5.39±1.07 and 6.88±1.92, respectively. Dependency in ADL and IADL occurred in 43% and 37% of participants, respectively. The mean physical activity of the participants during the previous week using the IPEQ-W was 17.94±24.47 METs. Regarding SPPB, the mean total balance score was 2.19±1.85; mean score of gait speed was 1.86±1.20; mean score of repeated chair test was 1.18±1.33 and the mean total score of the test was 5.23±3.89. The mean HGS values by Jamar dynamometer and sphygmomanometer were 8.00±5.00 kg/strength and 112.52±66.42 mmHg, respectively (Table 2).

Functional dependency in ADL dependency was significantly associated with age, mini mental status examination (MMSE) score, geriatric depression scale (GDS) score, IADL, HGS (Jamar), HGS (sphygmomanometer), IPEQ-W, and SPPB (Table 3).

IADL dependency was significantly associated with age, MMSE score, IADL, HGS (Jamar), HGS (sphygmomanometer), IPEQ-W, and SPPB, but not with GDS score (Table 3).

Figure 1 and Table 4 show the AUC, sensitivity, and specificity values of HGS using a sphygmomanometer and SPPB score for prediction of ADL and IADL dependency.

The recommended cut-off value to predict ADL dependency was ≤9 kg for HGS (Jamar) with sensitivity 81.4% and specificity 57.9%, while it was ≤60 mmHg (sphygmomanometer) with a sensitivity of 58.14% and specificity of 78.95%.

Table 1. The baseline characteristics of the participants

		n=100
Age (years)	**Mean ± SD**	66.65±6.08
Marital status	**Single**	3 (3.0%)
	Married	40 (40.0%)
	Widow	52 (52.0%)
	Divorced	5 (5.0%)
BMI (kg/m²)	**Mean ± SD**	31.48±6.82
BMI classification	**Normal**	17 (17.0%)
	Overweight	27 (27.0%)
	Obese	56 (56.0%)
Education level	**Illiterate**	67 (67.0%)
	Primary school	7 (7.0%)
	Preparatory school	4 (4.0%)
	Secondary school	10 (10.0%)
	Highly educated	12 (12.0%)
Medical comorbidities		
Diabetes mellitus		35 (35.0%)
Hypertension		52 (52.0%)
Ischemic heart disease		14 (14.0%)
Heart failure		7 (7.0%)
Atrial fibrillation		0 (0.0%)
Osteoporosis		16 (16.0%)
Osteoarthritis		78 (78.0%)
Fall		2 (2.0%)
Chronic liver disease		10 (10.0%)
Chronic kidney disease		7 (7.0%)
MMSE score mean ± SD		26.27±2.73
GDS score mean ± SD		5.83±1.78

SD: Standard deviation, BMI: Body mass index, MMSE: Mini mental status examination, GDS: Geriatric depression scale

The recommended cut-off value to predict IADL dependency was ≤8 kg for HGS (Jamar) with sensitivity 72.97% and specificity 53.97%, while it was ≤60 mmHg (sphygmomanometer) with a sensitivity of 51.35% and specificity of 71.43%.

As observed, the HGS measured by the Jamar dynamometer was more sensitive but less specific than that measured by the sphygmomanometer in predicting ADL and IADL dependency. There was a positive correlation between HGS measured using the Jamar dynamometer and the sphygmomanometer (r=0.622, p<0.001), and HGS measurement using Jamar was inversely correlated with age (r=-0.361, p<0.001) (Table 5).

Table 2. The functional status of the participants as assessed by ADL, IADL, IPEQ-W, SPPB, HGS

Tool	Items	n=100
ADL, n (%)	Bathing	94 (94.0%)
	Dressing	96 (96.0%)
	Toileting	97 (97.0%)
	Transfer	95 (95.0%)
	Continence	60 (60.0%)
	Feeding	97 (97.0%)
	Score mean ± SD	5.39±1.07
	Dependency	43 (43.0%)
IADL, n (%)	Telephone	89 (89.0%)
	Shopping	93 (93.0%)
	Food preparation	87 (87.0%)
	Housekeeping	78 (78.0%)
	Laundry	78 (78.0%)
	Transportation	95 (95.0%)
	Medications	80 (80.0%)
	Finances	88 (88.0%)
	Score mean ± SD	6.88±1.92
	Dependency	37 (37.0%)
IPEQ-W, mean ± SD	Total activity	17.94±24.47
	Incidental activity	14.40±18.91
	Walking activity	6.07±10.44
	Planned activity	3.47±6.16
	Planned walking activities	3.02±5.26
	Planned sport activities	0.31±2.16
Short physical performance battery, mean ± SD	Total balance score	2.19±1.85
	Repeated chair stand	1.18±1.33
	Gait score	1.86±1.20
	Total score	5.23±3.89
Hand grip strength, mean ± SD	Jamar dynamometer (kg/strength)	8.00±5.00
	Sphygmomanometer (mmHg)	112.52±66.42

ADL: Activities of daily living, IADL: Instrumental ADL, IPEQ-W: Incidental and planned exercise questionnaire week version, SPPB: Short physical performance battery, HGS: Hand grip strength, SD: Standard deviation

Linear regression analysis for factors associated with HGS, as measured by a Jamar dynamometer, was performed to establish the conversion equation to predict HGS in kg/strength using HGS measured in mmHg using a sphygmomanometer and age as follows:

HGS as measured by Jamar (kg/strength) =10.390 + [(0.078 x HGS as measured by sphygmomanometer in mmHg) + (-0.134 x age in years)].

Discussion

The current study aimed to validate the use of a sphygmomanometer for measuring HGS and to determine its association with functional dependency in older females. The prevalences of ADL and IADL dependency for community dwelling females in the current study were 43% and 37%, respectively. A previous study by Millán-Calenti et al. (15) reported ADL dependency at 34.6% and IADL dependency at 52.1%. Discrepancies between the two studies could stem from variations in participants mean age and comorbidities. The mean age of the participants in the current study was 66.65±6.08 years, notably younger than the 75.09±7.54 years observed in the study by Millán-Calenti et al. (15). Additionally, our study excluded cases of stroke and dementia, which were not excluded in Millán-Calenti et al.'s (15) study.

Lee (16) recommended extending the use of HGS beyond research settings to include routine testing in hospitals and community healthcare. HGS was found to be a powerful predictor not only of muscle mass and physical activity levels but also of various health outcomes, including nutritional status, chronic disease incidence, quality of life, ability to perform ADL, length of hospital stay, and mortality risk. The present study aimed to validate the use of a simple, widely available sphygmomanometer as a method for measuring HGS as an alternative to the Jamar dynamometer.

The current study showed a positive correlation between HGS measured using the Jamar dynamometer and sphygmomanometer, while HGS (Jamar) was inversely correlated with age. These findings come in line with a previous study which reported a higher correlation between HGS measurements by the Jamar dynamometer and sphygmomanometer, with a correlation coefficient of 0.835 (17). This supports the potential significance of sphygmomanometers in HGS measurements. The positive correlation between HGS measured by the Jamar dynamometer and sphygmomanometer was reported in multiple previous studies in different populations with different comorbid conditions (18-20).

Based on the current analysis, a new formula has been formulated to estimate HGS measurement using a sphygmomanometer in older Egyptian females. The equation was able to predict the Jamar grip strength value in older adults using a sphygmomanometer as follows: HGS as measured by Jamar (kg/strength) =10.390 + [(0.078 x HGS as measured by sphygmomanometer in mmHg) + (-0.134 x age in years)]. This equation can be used to unify the reporting of HGS measurement by both tools.

Yahin et al. (21) reported that based on regression analysis, the prediction formula resulted in HGS values using a sphygmomanometer. The HGS can be measured using the following prediction formula (21).

Table 3. Clinical characteristics of those with ADL and IADL dependency

		ADL		p	IADL		p
		Independent	Dependent		Independent	Dependent	
		n=57	n=43		n=63	n=37	
Age (years)	Mean ± SD	65.3±4.88	68.44±7.05	0.010	64.83±4.47	69.76±7.18	<0.001
BMI (kg/m²)	Mean ± SD	30.51±6.12	32.77±7.53	0.101	31.18±7.65	31.99±5.15	0.573
BMI classification	Normal	11 (19.3%)	6 (14.0%)	0.692	14 (22.2%)	3 (8.1%)	0.117
	Overweight	16 (28.1%)	11 (25.6%)		18 (28.6%)	9 (24.3%)	
	Obese	30 (52.6%)	26 (60.5%)		31 (49.2%)	25 (67.6%)	
MMSE score	Mean ± SD	26.96±2.58	25.35±2.68	0.002	26.98±2.4	25.05±2.87	0.001
GDS score	Mean ± SD	5.44±1.73	6.35±1.73	0.010	5.67±1.79	6.11±1.76	0.198
HGS (Jamar) (kg/strength), mean ± SD		10±5	6±4	<0.001	9±5	6±5	0.008
HGS (sphygmomanometer) (mmHg), mean ± SD		130.54±67.02	70.51±34.64	<0.001	126.66±67.59	70.32±31.58	<0.001
ADL, mean ± SD					5.7±0.46	4.86±1.53	<0.001
ADL dependency, n (%)					19 (30.2%)	24 (64.9%)	0.001
IADL (mean ± SD)		7.49±1.07	6.07±2.45	<0.001			
IADL dependency, n (%)		13 (22.8%)	24 (55.8%)	<0.001			
IPEQ-W total activity, mean ± SD		20.9±24.1	14.02±24.69	0.003	24.41±25.74	6.92±17.52	<0.001
SPPB total score, mean ± SD		6.53±3.74	3.51±3.43	<0.001	6.7±3.66	2.73±2.9	<0.001

ADL: Activities of daily living, IADL: Instrumental ADL, BMI: Body mass index, MMSE: Mini mental status examination, GDS: Geriatric depression scale, HGS: Hand grip strength, SD: Standard deviation, IPEQ-W: Incidental and planned exercise questionnaire week version, SPPB: Short physical performance battery

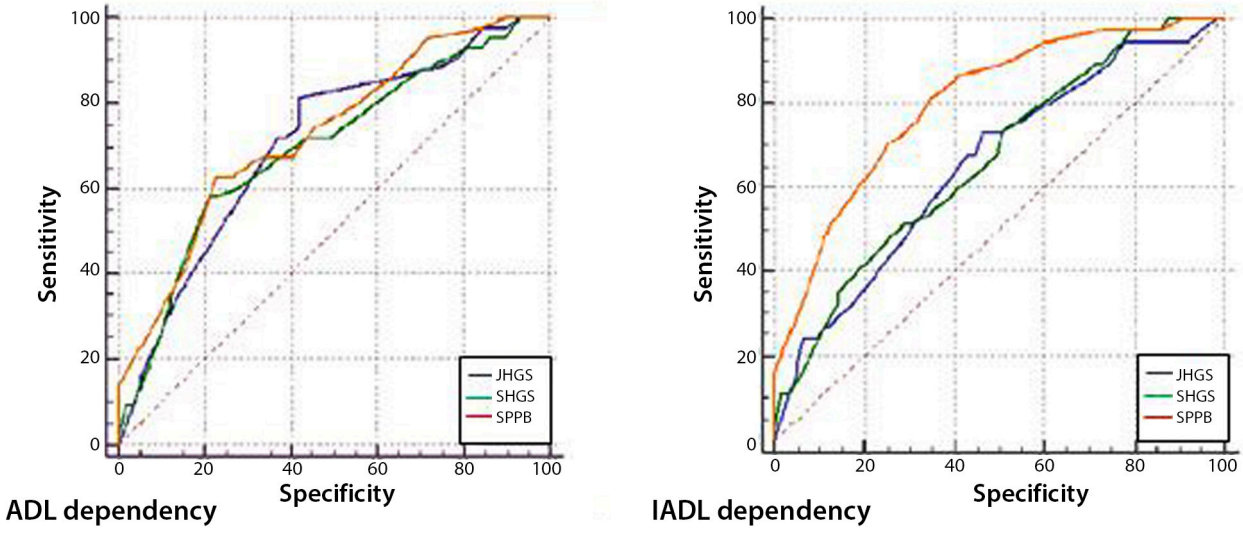

Figure 1. ROC curve analysis for AUC of HGS (Jamar, sphygmomanometer) and SPPB for predicting ADL and IADL dependency

ROC: Receiver operating characteristic, AUC: Area under the curve, HGS: Hand grip strength, SPPB: Short physical performance battery, ADL: Activities of daily living, IADL: Instrumental ADL, JHGS: Hand grip strength using Jamar, SHGS: Hand grip strength using sphygmomanometer

Table 4. The accuracy of HGS (Jamar, sphygmomanometer) and SPPB for predicting ADL and IADL dependency

	Variable	Cut-off	AUC	SE	95% CI	Sensitivity	Specificity	p
ADL dependency	JHGS	≤9	0.707	0.0516	0.608 to 0.794	81.40%	57.89%	<0.001
	SHGS	≤60	0.697	0.0534	0.597 to 0.785	58.14%	78.95%	<0.001
	SPPB	≤2	0.728	0.0502	0.630 to 0.812	62.79%	77.19%	<0.001
IADL dependency	JHGS	≤8	0.656	0.0556	0.554 to 0.748	72.97%	53.97%	0.005
	SHGS	≤60	0.665	0.0549	0.564 to 0.756	51.35%	71.43%	0.003
	SPPB	≤5	0.803	0.0443	0.712 to 0.876	81.08%	65.08%	<0.001

ADL: Activities of daily living, IADL: Instrumental ADL, AUC: Area under the curve, HGS: Hand grip strength, JHGS: Hand grip strength by Jamar dynamometer, SHGS: Hand grip strength by sphygmomanometer, SPPB: Short physical performance battery, CI: Confidence interval, SE: Standard error

Table 5. The correlation between JHGS, SHGS, ADL, and IADL

		JHGS	SHGS
Age	Spearman's rho	-0.36	-0.29
	p	<0.001	0.003
JHGS	Spearman's rho	.	0.62
	p		<0.001
SHGS	Spearman's rho	0.62*	.
	p	<0.001	
ADL	Spearman's rho	0.36*	0.36
	p	<0.001	<0.001
IADL	Spearman's rho	0.28*	0.30
	p	0.005	0.002

*: Positive correlation
JHGS: Hand grip strength by Jamar dynamometer, SHGS: Hand grip strength by sphygmomanometer, ADL: Activities of daily living, IADL: Instrumental ADL

Right HGS prediction formula: 0.0854 x right sphygmomanometer + [11.5642 x sex (female =0, male =1)] + 3.4243 x hand width – 0.2951 x age

Left HGS prediction formula: 0.0883 x left sphygmomanometer + [12.6581 x sex (female =0, male =1)] + 2.6562 x hand width – 0.2281 x age

Pujianita et al. (22) identified a conversion equation for the Jamar grip strength value using sphygmomanometer (0.1157 × sphygmomanometer grip strength value) – (5.696 × sex) + (0.0824 × age) (female =1, male =0).

The variations in the formulas across studies can be attributed to differences in body size and ethnicity. Furthermore, the two fore-mentioned studies included participants of both genders and elaborated equations adjusted for gender.

Regarding HGS measurements and functional dependency, the mean HGS values obtained using both the Jamar dynamometer and sphygmomanometer were significantly lower among the dependent group. These results align with a prior study that documented that the mean HGS score among functionally dependent females was 15.5±0.5 kg/strength compared to 18.5±0.2 kg/strength among those without functional decline (23). Although we obtained similar results, the mean HGS of our participants were lower for both the functionally dependent and independent groups compared with a previous report by Alexandre et al. (23). This difference could be attributed to personal characteristics regarding body size, medical comorbidities, and cognitive function. In the current population obesity constituted 56%, contrasting with 26.7% in the report by Alexandre et al. (23). To minimize the influence of confounding variables, we excluded patients with stroke, and 4% of the participants of their study had stroke (23). Similarly, the present study excluded patients with dementia to reduce the number of cofounders, resulting in a higher baseline MMSE score (26.27±2.73) compared with a previous study (16.1±0.1). The association between HGS and cognitive function was observed in a prospective analysis within this study revealed a significant association between HGS and cognitive function. Every 5 kg increase in HGS was associated with a 0.97 (95% confidence interval: 0.93, 0.99) lower odds of developing future cognitive impairment or experiencing cognitive decline (24). Furthermore, a systematic review and meta-analysis of cross-sectional studies demonstrated a higher prevalence of cognitive impairment in individuals with sarcopenia than in those without, even after controlling for potential confounders such as gender, age, depression, education level, functional status, and medical comorbidities (25).

In this study, HGS measurements obtained using both dynamometer and sphygmomanometer were correlated with SPPB, ADL, and IADL scores. This suggests a possible association between muscle strength, physical performance, and functional status in elderly women. However, the causal relationship between muscle strength and functional dependency requires further prospective studies.

Sallinen et al. (26) conducted a study to determine the ideal HGS cut-offs for predicting mobility limitations in older adults. They analyzed data from men and women aged 55 and older. The overall cut-off points were 37 kg for men and 21 kg for women. For men, BMI-specific cut-offs were slightly more accurate, with values of 33 kg for normal-weight men, 39 kg

for overweight men, and 40 kg for obese men. BMI-specific cut-offs for women were not significantly better than the overall cut-off (26).

A meta-analysis found that low muscle strength, low physical performance, and low muscle mass were associated with increased dependency on ADL and IADL in older adults. The association between low HGS and ADL dependency had an odds ratio of 1.51, whereas that for IADL dependency, it was 1.59. The association between low SPPB scores and ADL dependency had an odds ratio of 3.49, whereas for IADL dependency, the odds ratio was 3.09. These findings suggest that maintaining muscle strength and physical performance is important for preserving independence among older adults (27).

This study found that ADL and IADL dependencies were significantly linked to MMSE, GDS, SHGS, JHGS, IPEQ-W, and SPPB scores. Age was significantly associated with IADL dependency. A previous study reported a negative association between depression and ADL and IADL dependency (28).

Beltz et al. (29) conducted a multivariate analysis and suggested that age, gender, and ADL disability were identified as significant determinants of IADL disability. Both ADL and IADL disability were found to be inversely correlated with physical health-related quality of life. Increasing age was only significantly associated with IADL disability, not with ADL disability or physical health-related quality of life (29).

This study found that people with lower levels of physical activity (lower IPEQ-W scores) were more likely to be dependent on ADLs and IADLs. This finding suggested a negative association between the level of physical activity and functional dependency. This association is bidirectional, meaning that each variable can influence the others.

It is well known that physical activity can prevent many chronic conditions, thereby reducing the likelihood of disability. The World Health Organization has recommended regular physical exercise as an effective and affordable preventive measure for reduced functional performance in older adults (30).

According to Miller et al. (31), engaging in regular physical activity can help slow down the decline in function and independence. For those with severe compared with less severe ADL disability, even the lowest degree of physical activity level decreased the likelihood of progressive disability (odds ratio: 0.45, $p<0.001$) (31). Even in frail older adults, exercise training programs improved walking speed, balance, and the ability of older adults to perform their ADLs (32).

Study Limitations

The current study supported the use of sphygmomanometers as an affordable alternative to the Jamer dynamometer for HGS measurement in older females. This study provided a novel formula to report HGS measured by a sphygmomanometer in an alternative Jamar unit. The main limitations of this study include the relatively small sample size. Moreover, further longitudinal studies are needed to detect the impact of HGS measured by sphygmomanometer on incidental functional dependency.

Conclusion

The study provided cut-offs of different objective tools to assess functional dependency and supported the use of sphygmomanometers for HGS measurement among older females.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of the Faculty of Medicine at Ain Shams University (approval number: FMASU MD 161 2022, date: 28.07.2022). The objective of the study was to evaluate patients. The confidentiality of data was assured.

Informed Consent: Informed consent was obtained.

Authorship Contributions

Surgical and Medical Practices: E.M.A.M.M., S.A.H., D.R., K.E.E., Concept: E.M.A.M.M., S.A.H., D.R., K.E.E., Design: E.M.A.M.M., S.A.H., D.R., K.E.E., Data Collection or Processing: E.M.A.M.M., K.E.E., Analysis or Interpretation: E.M.A.M.M., S.A.H., D.R., K.E.E., Literature Search: E.M.A.M.M., S.A.H., D.R., K.E.E., Writing: E.M.A.M.M., S.A.H., D.R., K.E.E.

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ORIGINAL RESEARCH

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Comparison of Geriatric Nutrition Risk Index and Mini Nutrition Assessment-short Form in Nutritional Assessment of Older Outpatients

İbrahim İleri, Çağatay Çavuşoğlu, Burcu Candemir, Berna Göker

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

Abstract

Objective: The risk of malnutrition is higher in older patients. Malnutrition in older patients causes increased mortality rates and increased risk of infection and hospitalization. Therefore, in older patients, high-risk individuals for malnutrition should be identified and appropriate interventions for malnutrition should be made early. In this study, we aimed to compare mini nutritional assessment-short form (MNA-SF) and geriatric nutrition risk index (GNRI) screening tests in detecting malnutrition in older outpatients.

Materials and Methods: The study was conducted in a geriatric outpatient clinic. This study was conducted between January 2020 and June 2020. The study was cross-sectional. One hundred and seventy-three patients were aged 60 years and over.

Results: The median age of the whole group was 75 (71-81) interquartile range (IQR) years, and 108 (62%) of them were female. The median MNA-SF score for the whole group was 12 (11-14) IQR, and for GNRI this was 104.2 (101.2-107.2) IQR. In the receiver operating curve analysis, 103.5 points were determined as the cut-off point of GNRI. GNRI had lower specificity [specificity: 95% confidence interval (CI), 66.67 (58.8-73.9)], but optimal sensitivity [sensitivity: 95% CI, 100 (76.8-100)] compared with MNA-SF.

Conclusion: A new cut-off value of 103.5 with higher sensitivity but lower specificity than the original cut-off value is recommended when using the GNRI in the assessment of the nutritional status of older outpatients.

Keywords: Mini nutritional assessment-short form, geriatric nutritional risk index, older, outpatients, nutritional status

Introduction

The risk of malnutrition is higher in older patients. There are many reasons for this. Difficulty eating, dysphagia, decreased mobility, decreased appetite, psychological stress, difficulty in accessing healthcare, and poor oral health are some of these reasons (1-4). Malnutrition in older patients causes increased mortality rates and increased risk of infection and hospitalizations (5). Therefore, in older patients, high-risk individuals for malnutrition should be identified and appropriate interventions for malnutrition should be made early (6). Various tests are available to evaluate the nutritional status of older people (7). Mini nutrition assessment-short form (MNA-SF) is a test that can be used in nutritional screening of older patients. The geriatric nutrition risk index (GNRI) is also used to detect nutritional status in older patients. MNA-SF was developed in 2001 (8). It is a test that can be easily performed. The MNA-SF was revised in 2009. A malnutrition cut-off point was determined. Based on this cut-off point, older patients can be diagnosed with malnutrition, risk of malnutrition, or normal nutrition (9). GNRI, a prognostic index for nutritional status-related complications, is recommended for the evaluation of the nutritional status of older patients (10). GNRI is an easily applied test used to determine nutritional status and is associated with increased mortality among older patients in both acute and long-term care settings (10-13).

MNA-SF is generally used for malnutrition screening in older outpatients. However, the patient must also actively participate in this test and answer the questions. In addition,

Address for Correspondence: İbrahim İleri, Gazi University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, Ankara, Turkey
Phone: +90 312 212 68 40 **E-mail:** ibrahimileri60@hotmail.com **ORCID:** orcid.org/0000-0002-7237-5261

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body mass index (BMI) or calf circumference measurements are required to perform this test. Because dementia, vision, and hearing problems are common in older patients, they sometimes have difficulty participating in this test. Furthermore, because BMI is high in older obese patients, malnutrition assessed by MNA-SF may be missed. Therefore, GNRI may be more appropriate than MNA-SF in older outpatients (14). Assessment of nutritional status using GNRI in older outpatients has not been previously reported in Turkey. In this study, we compared MNA-SF and GNRI in detecting malnutrition in older outpatients.

Materials and Methods

Participants

We conducted the study in a geriatric outpatient clinic. The study was conducted between January 2020 and June 2020. During this period, patients who applied to the outpatient clinic were included in the study. Patients with acute illness, delirium, malignancy, rheumatological disease, and active infection were excluded. The study was cross-sectional. One hundred and seventy-three patients were aged 60 years and over.

The ethical approval was taken from Gazi University Non-Interventional Research Ethics Committee (decision number: 150, date: 10.02.2020). Informed consent was provided by the patient after providing verbal and written information about the study.

Data Collection

Within the scope of comprehensive geriatric assessment, Katz activities of daily living (ADL) and Lawton-Brody instrumental ADL tests were applied for functionality evaluation (15,16). The mini-mental state examination was used to assess cognitive status (17). The Yesavage geriatric depression scale was used for mood evaluation (18). Patients' age, gender, past medical history, and drugs were recorded.

Nutritional Assessment

We obtained data from the medical records, and the GNRI score was obtained as follows: GNRI=[1.489 × albumin (g/L)] + [41.7 × [weight/ideal body weight according to the Lorentz formula (WLo)]. WLo was calculated using the Lorentz equation: male = height -100 – [(height -150)/4]; female = height -100 – [(height -150)/2.5]. If the "weight/WLo" ratio is equal to or greater than 1, the ratio is considered as 1. Nutritional status according to GNRI was determined as follows: GNRI score <82: severe risk of malnutrition, GNRI score: 82-92: moderate risk of malnutrition, GNRI score: 92-98: low risk of malnutrition, GNRI >98 score: no risk for malnutrition (19). MNA-SF was routinely completed in all patients. Scoring in this test is as follows: score ≤7: malnutrition, score: 8-11: risk for malnutrition, score: 12-14: normal nutrition (20).

Statistics

Frequency (%) for categorical variables, mean ± standard deviation for normally distributed variables, and median [interquartile range (IQR)] for non-normally distributed variables were used. For correlation analysis, Pearson or Spearman correlation coefficient tests were used. The receiver operating curve (ROC) test was used to determine the GNRI cut-off point. SPSS software (version 21.0) was used for statistical analyses. $p<0.05$ indicates that it is statistically significant.

Results

Total 213 patients were assessed. Forty patients were excluded because they had active infection, and statistical analyses were performed for 173 patients. The median age of the whole group was 75 years (71-81) IQR, and 108 (62%) of them were female. The median MNA-SF score of the whole group was 12 (11-14) IQR, and for GNRI this was 104.2 (101.2-107.2) IQR. The median C-reactive protein value was 4 mg/L (2-7) IQR. The characteristics of the participants are given in Table 1. When MNA-SF was used, 14 (8%) patients were malnourished. According to the

Table 1. Characteristics of the study participants

Variables	Study participants (n=173)
Sex (%)	
Female	108 (62%)
Male	65 (38%)
Age (IQR)	75 (71-81)
Laboratory values	
Albumin (g/L) (IQR)	43 (41-44)
CRP (mg/L) (IQR)	4 (2-7)
Anthropometric measurements	
Height (cm) (IQR)	160 (153-168)
Weight (kg) ± SD	70.9±13.5
BMI (kg/m²) (IQR)	27.1 (24.3-30.6)
Comprehensive geriatric assessment	
Katz ADL score (IQR)	6 (5-6)
Lawton and Brody scale (IQR)	8 (5-8)
MMSE (IQR)	28 (24-29)
GDS (IQR)	2 (0-5)
Nutritional screening	
MNA-SF score (IQR)	12 (11-14)
GNRI score (IQR)	104.2 (101.2-107.2)
Comorbidities	
Diabetes mellitus	74 (43%)
Hypertension	135 (78%)
Coronary artery disease	65 (38%)
COPD	37 (21%)
Dementia	18 (10%)

n: Number, IQR: Interquartile range, CRP: C-reactive protein, SD: Standard deviation, BMI: Body mass index, ADL: Activities of daily living, MMSE: Mini-mental state examination, GDS: Geriatric depression scale, GNRI: Geriatric nutritional risk index, MNA-SF: Mini nutritional assessment-short form, COPD: Chronic obstructive pulmonary disease

GNRI, 3 (2%) patients were at high risk of malnutrition. Nutritional information of the patients is given in Table 2.

Correlation analysis revealed that GNRI had a moderate correlation with MNA-SF scores (r=0.282, p<0.001). BMI did not correlate with GNRI or MNA-SF (r=0.069 and r=0.129, p=0.367 and p=0.091). Moderate agreement was found between GNRI and MNA-SF after categorization according to the newly defined cut-off value (kappa value =0.250). The results are presented in Table 3. According to the ROC curve test, the cut-off point of GNRI was 103.5 (Figure 1). Compared with MNA-SF, GNRI had lower specificity, lower positive predictive value (PPV), higher sensitivity and higher negative predictive value (NPV) (Table 4).

Discussion

In this study, we found that the population malnutrition cut-off point for GNRI was 103.5. Correlation and kappa analyses revealed that GNRI had moderate correlation and agreement with MNA-SF. GNRI had lower specificity, but higher sensitivity, and lower PPV than MNA-SF. For diagnostic purposes, it is important for the tool to be specific, whereas for screening, the tools should be sensitive (21). In this study, GNRI has high sensitivity, making it suitable for screening; but lower specificity, making it unsuitable for diagnostic purposes. As the sensitivity of the nutritional status screening tool increases, the probability of missing malnourished patient decreases. However, this increases the false positive rate in diagnosing malnutrition and can lead to overnutrition interventions (22). GNRI had lower PPV but higher NPV in our study. This suggests that patients may be mistakenly classified as malnourished, but it is unlikely that those who are identified as well nourished are misclassified. There are studies in the literature comparing GNRI with other screening tools in hospitalized and older outpatient patients. In 2019, Abd Aziz et al. (23) studied hospitalized older patients. There were 134 patients, and GNRI and MNA were compared with the subjective global assessment. In this study, the sensitivity of GNRI was 0.622, specificity was 0.977, PPV was 0.982, and NPV was 0.558. The sensitivity of MNA-SF was determined as 0.611, specificity as 0.909, PPV as 0.932, and NPV as 0.533. The cut-off point of GNRI for detecting malnutrition was 94.95. In 2015, Baek and Heo (24) studied hospitalized older patients. There were 141 patients in the study, and the following screening tools were used to determine nutritional status: malnutrition universal screening tool, nutritional risk screening 2002, MNA, MNA-SF, and GNRI. In this study, GNRI had high sensitivity (95.2%) but lower specificity (67.1%). Saghafi-Asl et al. (14) studied GNRI in non-hospitalized older patients. In that study, 164 patients were included and GNRI was compared with MNA-SF and mini nutritional assessment-

Table 2. Nutritional assessment of patients according to MNA-SF and GNRI

Nutritional status assessed by MNA-SF		
Normal nutrition (%)	**At risk of malnutrition (%)**	**Malnourished (%)**
104 (60%)	55 (32%)	14 (8%)
Nutritional status assessed by the GNRI		
Normal nutrition (%)	**Moderate or low risk of malnutrition (%)**	**High risk of malnutrition (%)**
158 (91%)	12 (7%)	3 (2%)

MNA-SF: Mini nutritional assessment-short form, GNRI: Geriatric nutritional risk index

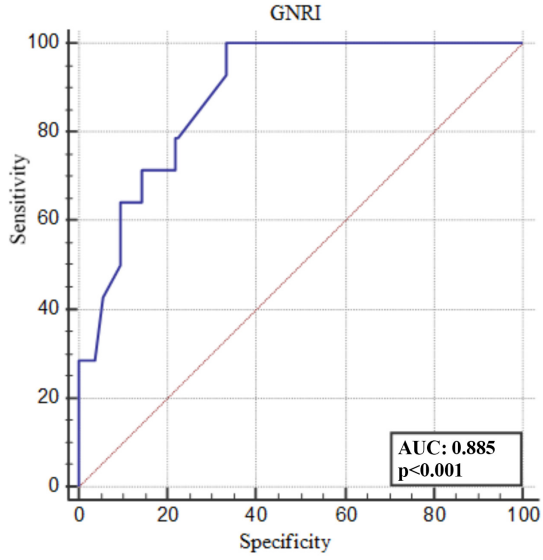

Figure 1. Receiver operating curve analysis examining the cut-off value of GNRI. (AUC: 0.885 cut-off: 103.5 p<0.001 sensitivity: 100% specifity: 66.67% Youden Index J: 0.6667)

GNRI: Geriatric nutritional risk index, AUC: Area under the curve

Table 3. Correlation and kappa test results for GNRI and MNA-SF

Correlation analysis results		
	r	**p**
GNRI, MNA-SF	0.282	<0.001
GNRI, BMI	0.069	0.367
MNA-SF, BMI	0.129	0.091
Kappa test analysis result		
	Kappa value	**p**
GNRI, MNA-SF	0.250	<0.001

GNRI: Geriatric nutritional risk index, MNA-SF: Mini nutritional assessment-short form, BMI: Body mass index

Table 4. Sensitivity, specificity, PPV, and NPV results

Sensitivity (95% CI)	100 (76.8-100)
Specificity (95% CI)	66.67 (58.8-73.9)
PPV (95% CI)	20.9 (17.5-24.8)
NPV (95% CI)	100

PPV: Positive predictive value, NPV: Negative predictive value, CI: Confidence interval

long form. Lower sensitivity but optimal specificity of GNRI were found compared with both MNA results. Lower NPV but higher PPV were found with GNRI compared with both MNA results. The agreement between the GNRI and MNA scores was moderate. The malnutrition cut-off value for the GNRI was 110.33 in that study. Malnutrition is known to cause many adverse outcomes, especially in older people; therefore, it is important to identify malnourished older patients. MNA-SF is widely used for malnutrition screening in geriatric outpatient clinics in Turkey. To calculate MNA-SF, it is necessary to be in contact with the patient and wait for patients to answer the questions; however, older patients may have hearing and speech problems. Moreover, communication with patients with advanced dementia may not be possible. In addition, MNA-SF includes parameters such as BMI and calf diameter, which may have high values in obese patients. Therefore, the risk of malnutrition in obese patients can be ignored. Therefore, GNRI can be considered as an alternative tool to MNA-SF in older outpatients. According to our results, if GNRI is used in the evaluation of nutritional status in older outpatients, the cut-off value is 103.5.

Study Limitations

This study has some limitations. First, GNRI was only compared with MNA-SF. Studies including other screening methods can be conducted. Second, it is cross-sectional; therefore, nutritional outcomes are unknown. Third, the study was a single-center study. Multicenter studies can be conducted to generalize the results.

Conclusion

In conclusion, the agreement between MNA-SF and GNRI was moderate. Compared with MNA-SF, GNRI had lower specificity but higher sensitivity. Therefore, it may be suitable for malnutrition screening in non-hospitalized older patients. A new cut-off value of 103.5 with higher sensitivity but lower specificity than the original cut-off value is recommended when using the GNRI in the assessment of the nutritional status of older outpatients.

Ethics

Ethics Committee Approval: The ethical approval was taken from Gazi University Non-Interventional Research Ethics Committee (approval number: 150, date: 10.02.2020).

Informed Consent: Informed consent was provided by the patient after providing verbal and written information about the study.

Authorship Contributions

Surgical and Medical Practices: İ.İ., Ç.Ç., Concept: İ.İ., B.G., Design: Ç.Ç., B.C., Data Collection or Processing: İ.İ., B.C., Analysis or Interpretation: Ç.Ç., B.G., Literature Search: İ.İ., B.C., Writing: İ.İ., B.G.

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ORIGINAL RESEARCH

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The Role of Hedonic Hunger As a Moderator and Mediator in Older Adults Obesity

Burak Mete[1], Lezan Keskin[2], Hakan Demirhindi[1], Ceren Kanat Şahin[1], Esra Doğan Mete[3], Ertuğrul Bayram[4]

[1]Çukurova University Faculty of Medicine, Department of Public Health, Adana, Turkey
[2]Malatya Turgut Özal University Training and Research Hospital, Clinic of Endocrinology, Malatya, Turkey
[3]Çukurova University Faculty of Medicine, Department of Child and Adolescent Psychiatry, Adana, Turkey
[4]Çukurova University Faculty of Medicine, Department of Medical Oncology, Adana, Turkey

Abstract

Objective: In the modern age, the pursuit of food is now a means of pleasure and of satisfying hunger. This study examined the role of hedonic hunger and eating behaviors on obesity in older adults.

Materials and Methods: This cross-sectional study was conducted on 400 older adults. The nutrition information system (BeBiS), bioelectrical impedance analysis, power of food scale-Turkish version (PFS-Tr), and Dutch eating behaviour questionnaire (DEBQ) were used to evaluate the subjects.

Results: The mean age of 400 people included in the study was 67.82±2.77 years. It was found that the moderator effect of the interaction of daily energy intake and hedonic hunger behaviour (PFS-Tr) on the waist-to-hip ratio was significant. In particular, the regulatory effect of low hedonic hunger scores (PFS-Tr) was significant (p=0.019) and the waist-to-hip ratio decreased as the scores obtained from the scale decreased. The mediator effect of the restrained eating (ResE) sub-dimension (DEBQ) between the average daily energy intake and body fat mass was significant (estimate =0.221, p=0.021), and an increase in ResE behavior scores resulted in an increase in body fat mass. It was found that 89.4% of the effect of ResE behaviour on body fat mass was direct and large. There was a weak positive correlation between the average daily energy intake and food available subscale of PFS-Tr (r=0.157) and food present subscale (r=0.017). Total daily energy intake had a direct effect on body fat mass (estimate =0.008, p=0.005).

Conclusion: The results of our study support a positive relationship between hedonic hunger and abdominal obesity in older adults. Decreased ResE behaviour increases the whole-body fat mass. Evaluation of hunger and implementation of programmes that support ResE behaviour may be useful in controlling obesity and its negative consequences in older adults.

Keywords: Hedonism, obesity, hunger aging, geriatrics

Introduction

To a great extent, the history of humanity witnessed man's pursuit of food to maintain energy balance and to survive by preventing hunger. However, in societies of today that have easy access to food, food consumption may occur for reasons other than energy deficiency (1). Hedonic hunger can be defined as a person's interest in food for pleasure and the desire to consume it, although there is no physical hunger (2). The global dimension of obesity is gradually increasing, and food consumption shows an increasing trend toward pleasure and not only because of calorie need (3). There is evidence that obese individuals prefer and consume more tasteful foods than normal-weight individuals (3).

The combination of the obesity epidemic and aging raises concerns. Because there is no consensus on age-related physiological changes, there are uncertainties in the

Address for Correspondence: Burak Mete, Çukurova University Faculty of Medicine, Department of Public Health, Adana, Turkey
Phone: +90 544 711 31 64 **E-mail:** burakmete2008@gmail.com **ORCID:** orcid.org/0000-0002-0780-6176
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intervention. It has been shown that calorie restriction and/or dietary modification may have favorable effects on obese older adults (4). Adequate and balanced dietary content is of great importance in combating obesity by reducing the risk of diseases that increase with aging (4). Frequent and excessive consumption of tasteful foods because of hedonic hunger may lead to many diseases such as eating disorders, obesity, hypertension, diabetes mellitus, cardiovascular diseases, non-alcoholic fatty liver disease, obstructive sleep apnea, and some types of cancer (5). Our study investigated the relationship between dietary content, hedonic hunger behavior, and obesity in older adults.

Materials and Methods

Type, Location, and Time of the Study

This cross-sectional study was conducted on individuals over 65 years of age and older who applied to the endocrinology outpatient clinic of Malatya Training and Research Hospital in 2023. Permission for this study was obtained from the Malatya Clinical Research Ethics Committee (approval number: E-23536505-619-221990829, date: 11.08.2023).

Sample Size

The sample size analysis with a power of 95%, a confidence interval of 1%, and an effect size of 0.1 yielded 391 as the minimum number of participants to be reached, rounded to 400. Consent forms were obtained for individuals who accepted to participate in the study among those fulfilling the inclusion criteria.

Study Exclusion Criteria

People under 65 years of age, those who have any organic eating disorder, recent surgery, psychiatric illness, dementia, chronic kidney disease, heart failure, and those who follow a certain diet were excluded from the study.

Dietary Content Analysis

A sociodemographic questionnaire form was applied to the individuals who applied to the outpatient clinic, and they were then asked to record the nutrition information form for two weekdays and one weekend day in a period of one week. A 3-day, 24-hour reminder method was used to assess food intake at home. How to keep the records and which days to fill in the forms were explained in detail. Completed nutrition record forms were obtained directly from the patient. Nutritional values for three days were calculated using the nutrition information system (BeBiS) software (6), which is coded for analyzing the nutritional content of foods and meals based on the data provided in the dietary record forms. The average amounts of carbohydrate, fat, protein (in grams and %), and daily energy (kilocalories) were calculated.

Bioelectrical Impedance Analysis

Body composition analyses were performed using the body composition analyzer BC-420MA device with metabolic measurements when the participants submitted their nutrition forms. The working principle of the device is bio-impedance measurement, consisting of comparing the input and output values of 50 kHz electric current sent to the body through foot electrodes and received by hand electrodes.

Power of Food Scale-Turkish Version (PFS-Tr)

The power of food scale was developed by Lowe et al. (7) to assess the psychological impact of living in food-abundant environments, in other words, the evaluation of hedonic hunger status. It measures appetite for, rather than consumption of, palatable foods at three levels of food proximity [food available (FA), food present (FP), and food tasted (FT)]. The Turkish validity and reliability of the scale, i.e., PFS-Tr scale were determined by Ulker et al. (8). The scale consists of 13 items categorized into three subscales. The first one is the FA subscale, which assesses general thoughts about palatable food that is available but not physically present (items 1,2,9,10). The second subscale, the FP subscale, consists of items assessing the attractiveness of food that the individual has direct access to; i.e., palatable food is physically present but not tasted yet (items 3,4,5 and 6). The third subscale, the FT subscale, includes items that assess the desire/pleasure obtained from food when it is first tasted but not consumed yet (items 7,8,11,12 and 13). At the end of the evaluation, four scores were obtained as three subscale scores and one total scale score. Total and subscale scores were obtained by summing the related item scores and dividing by the number of related items. An increase in the score indicates a higher predisposition to hedonic hunger (8). PFS-Tr is not only a measure of the food environment but also measures individual differences in appetite-related thoughts, feelings, and desires in environments where palatable foods are abundant and continuously available. Beyond physiological needs, this approach defines an appetite model that shows individual differences in motivation to eat, and the presence of palatable food would further increase food consumption (9).

Dutch Eating Behaviour Questionnaire (DEBQ)

DEBQ, a hedonic hunger scale, was first developed to evaluate eating behaviour by Van Strien et al. (10) in 1986. The Turkish validity and reliability of the scale were determined by Bozan et al. (11). The scale consists of three subscales evaluating emotional eating (EmoE) behaviour (e.g., do you eat sweets when you are unhappy?), externally induced eating (ExtE) behaviour (if the smell of what you eat is very good, do you eat more than you normally eat?) and restrained eating (ResE) behaviour (do you eat less than you want to eat to avoid getting fat?). The first 10 questions in the questionnaire are in the ResE subscale, questions 11-23 are in the EmoE subscale, and questions 24-33 are in the ExtE subscale. The total score of the questionnaire

is not calculated, whereas the total scores of the subscales are calculated. In the calculation, question 31 affects the total score in the ExtE subscale as a reverse question. Although there is no cut-off point for the subscales, an increase in the score is associated with negative eating behavior (11).

Statistics

IBM SPSS Statistics 22 (SPSS, Inc., Chicago, IL, USA) and Jamovi ver.2.3.28 (12) software were used for data analysis. The Kolmogorov-Smirnov test was used to test the normality of the distribution test. Parametric tests were used in the analysis of normally distributed data, whereas non-parametric tests were used in the analysis of data that did not fit the normal distribution. The data were analyzed using the t-test, Mann-Whitney U test, Spearman and Pearson correlation analysis, chi-square test, binary logistic regression, moderation effect, and mediation effect analysis. The effect size was evaluated using the rank biserial correlation coefficient (with 0.10 indicating a small, 0.30 a medium, and 0.50 or greater a large effect size). Mediation analyses were performed using structural equation modeling path analysis in Jamovi. Direct and indirect effect coefficients (estimates) were accepted as low effect if close to 0.01, medium effect if close to 0.09, and high effect if close to 0.25 (13). P<0.05 was considered statistically significant.

Results

The mean age of 400 older adults included in the study was 67.82±2.77 (min: 65-max: 80). The male-to-female ratio was 58:42, and 50% of the participants were obese. Participants with a value of body mass index (BMI) >18.5 kg/m^2 and <30 kg/m^2 were accepted as "normal BMI", while those with BMI ≥30 kg/m^2 were accepted as "obese BMI" or shortly "obese" (14). No significant difference was found between the age and comorbidity distributions of the patients according to the BMI categories. Obese patients were more common in women (Table 1).

The total daily dietary energy intake was significantly higher in obese individuals than in individuals with normal BMI, and the effect size was moderate. It was found that fat consumption was significantly higher in obese individuals, and the effect size was low (Table 2).

Table 1. Characteristics of participants according to age, sex, and comorbidities

Characteristics	BMI groups (Mean ± SD or n)		p
	Obese* (n=200)	Normal* (n=200)	
Age	67.77±2.57	67.50±4.42	0.657
Sex (male/female)	62/138	106/94	0.002**
Chronic disease (yes/no)	196/4	194/6	0.844
Hypertension (yes/no)	138/62	118/82	0.141
Diabetes mellitus (yes/no)	154/46	126/74	0.061
Cardiovascular diseases (yes/no)	16/184	32/168	0.082
COPD or asthma (yes/no)	28/172	14/186	0.166
Cancer (yes/no)	1/199	8/192	0.369
Rheumatological disease (yes/no)	14/186	12/188	1.000

*Normal BMI: 18.5 kg/m^2 < BMI <30 kg/m^2, obese BMI: BMI ≥30 kg/m^2, **Statistically significant difference
BMI: Body mass index, SD: Standard deviation of the mean, COPD: Chronic obstructive pulmonary disease

Table 2. Comparison of the dietary content according to the presence of obesity

Nutrient content	Obesity		p	Effect size
	Obese BMI	Normal BMI		
	Median (IQR)	Median (IQR)		
Energy (kcal)	1330 (374.5)	1131 (348.3)	<0.001*	0.385
Protein (g)	45 (17.8)	48.9 (17)	0.406	0.067
Percent protein (%)	15 (6)	16 (7)	0.070	0.147
Fat (g)	58.4 (25.5)	53.5 (27)	0.006*	0.206
Percent fat (%)	43 (12.8)	42.5 (13.8)	0.789	0.039
Carbohydrate (g)	119 (55.9)	115 (36.8)	0.334	0.093
Percent carbohydrate (%)	43 (13)	42 (14)	0.315	0.002
Fibre (g)	17.8 (8.1)	16.35 (11.2)	0.133	0.255

*Statistically significant difference
IQR: Interquartile range, g: Gram, kcal: Kilocalories, BMI: Body mass index

When the correlations between hedonic hunger behaviour, eating behaviour and the main food groups in the diet were examined, no correlation was found between behaviours and the amount of carbohydrates or fat taken daily. EmoE subscale scores of DEBQ showed a positive correlation with daily protein intake but a weak negative correlation with fibre intake; i.e., conditions with emotional effects led to higher protein intake but lower fibre-rich food intake. Regarding PFS-Tr, average daily energy intake showed a weak positive correlation with the FA and FP subscale scores of PFS-Tr, whereas fat intake showed a weak positive correlation with only the FP subscale scores (Table 3).

When the correlations between hedonic hunger behavior, eating behavior, and body composition were examined, the ResE subscale score of DEBQ was found to show a weak positive correlation with both body fat mass and body fat percentage; i.e., ResE behavior led to an increase in body fat. The FA subscale score of PFS-Tr showed a weak positive correlation with muscle mass; i.e., when palatable food was available but not physically present, muscle mass increased. The waist-to-hip ratios showed a weak negative correlation with EmoE and ExtE subscale scores of the DEBQ scale; i.e., conditions with emotional effects and external factors such as attractive smell of the food etc. led to a decrease in the waist-to-hip ratio (Table 4).

When the mediator effect of the DEBQ subscales between average daily energy intake and body fat mass was analyzed, it was found that only ResE behaviour had a significant direct effect (path a) on body fat mass, comprising 89.4% of the total effect of ResE on body fat mass increase (p=0.021), i.e., an increase in ResE subscale scores of the DEBQ scale resulted in an increase in body fat mass, and this effect was found to be large (Figure 1, Table 5).

The total score of the PFS-Tr had a significant regulatory effect on the relationship between daily energy intake and waist-to-hip ratio, and the effect of the interaction of daily energy intake and PFS-Tr on the waist-to-hip ratio was significant (Figure 2, Table 6).

While the regulatory effect of high scores obtained from the scale was not significant (p=0.996), the regulatory effect of low scores was significant (p=0.019) and the waist-to-hip ratio was observed to decrease as the scores obtained from the scale decreased (Figure 3).

Table 3. Correlations between dietary content and subscale scores of DEBQ and PFS-Tr scales

Subscales (scale)	Energy (kcal)	Protein (g)	Protein (%)	Fat (g)	Fat (%)	Carbohydrate (g)	Carbohydrate (%)	Fibre (g)
ResE (DEBQ)	-0.069	-0.087	0.029	-0.010	0.044	-0.054	-0.060	0.080
EmoE (DEBQ)	-0.028	0.177*	0.155*	0.033	0.021	0.083	-0.080	-0.186*
ExtE (DEBQ)	0.12	0.115	-0.018	0.117	0.079	0.056	-0.037	-0.011
FA (PFS-Tr)	0.157*	0.007	-0.117	0.077	0.010	0.041	0.032	0.067
FP (PFS-Tr)	0.017*	0.410	0.054	0.012*	0.011	0.020	0.036	-0.113
FT (PFS-Tr)	0.115	-0.009	-0.057	0.038	-0.023	0.079	0.049	0.105
Total score (PFS-Tr)	0.117	-0.026	-0.106	0.047	-0.008	0.077	0.058	0.042

*p<0.05, **p<0.01, ***p<0.001
DEBQ: Dutch eating behaviour questionnaire, PFS-Tr: Power of food scale-Turkish version, ResE: Restrained eating subscale score of DEBQ, EmoE: Emotional eating subscale score of DEBQ, ExtE: Externally induced eating subscale score of DEBQ, FA: Food available subscale score of PFS-Tr, FP: Food present subscale score of PFS-Tr, FT: Food tasted subscale score of PFS-Tr, g: Gram, kcal: Kilocalories

Table 4. Correlations between body composition and subscale scores of the DEBQ and PFS-Tr scales

	ResE (DEBQ)	EmoE (DEBQ)	ExtE (DEBQ)	FA (PFS-Tr)	FP (PFS-Tr)	FT (PFS-Tr)	Total score (PFS-Tr)
Body mass index (BMI)	0.103	-0.104	-0.081	0.038	0.014	-0.022	0.021
Waist-to-hip ratio	0.092	-0.154*	-0.160*	0.012	0.060	-0.063	-0.006
Body fat (%)	0.174*	-0.078	-0.069	0.047	0.056	0.030	0.055
Body fat mass (kg)	0.141*	-0.097	-0.051	0.070	0.050	-0.053	0.023
Lean body (%)	0.109	-0.056	0.028	0.023	-0.010	0.012	0.010
Muscle mass (kg)	-0.094	-0.060	0.067	0.151*	0.012	-0.025	0.051
Internal organ adiposity	0.013	-0.010	0.014	0.074	0.108	-0.058	0.046

*p<0.05,**p<0.01,***p<0.001
DEBQ: Dutch eating behaviour questionnaire, PFS-Tr: Power of food scale-Turkish version, ResE: Restrained eating subscale score of DEBQ, EmoE: Emotional eating subscale score of DEBQ, ExtE: Externally induced eating subscale score of DEBQ, FA: Food available subscale score of PFS-Tr, FP: Food present subscale score of PFS-Tr, FT: Food tasted subscale score of PFS-Tr, kg: Kilogram, BMI: Body mass index

Table 5. Mediation estimates of restrained eating on body fat mass

Mediation effect	Paths in Figure 1	Mediation estimates*	SE	95% CI	Z	p	Mediation %
Indirect	a×b	-0.0263	0.0211	0.06763-0.0150	-1.25	0.212	10.6
Direct	c	0.2214	0.0956	0.03390-0.4088	2.31	0.021	89.4
Total	c+a×b	0.1951	0.0970	0.00486-0.3853	2.01	0.044	100.0

*Estimates: 0.01: Small, 0.01-0.09: Medium, 0.09-0.025: Large effect
SE: Standard error of mediates, CI: Confidence interval

Table 6. Moderation estimates of energy intake and power of food scale on waist-to-hip ratio

	Estimate	SE	95% CI		Z	p
			Lower	Upper		
Energy intake	-7.66e-5	3.83e-5	-1.52e-4	-1.46e-6	-1.998	0.046*
PFS-Tr	0.00394	0.00484	-0.00555	0.0134	0.814	0.416
Energy x PFS-Tr	3.79e-5	1.89e-5	8.90e-7	7.49e-5	2.007	0.045*

*Statistically significant difference
CI: Confidence interval, PFS-Tr: Power of food scale-Turkish version, SE: Standard error of mediates

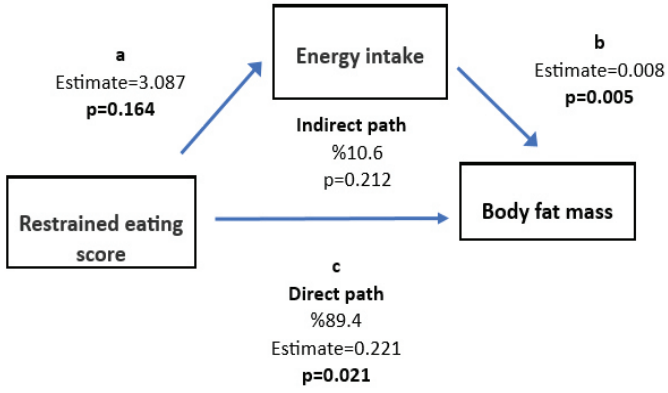

Figure 1. Path estimates of the mediation between restricted eating and body fat mass

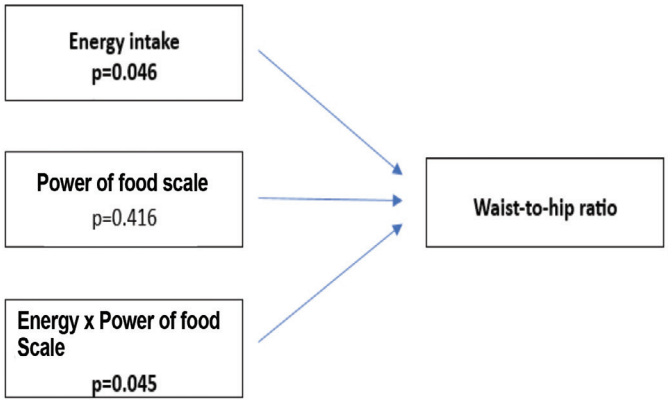

Figure 2. Moderation estimates of energy intake and power of food scale on waist-to-hip ratio

Discussion

Obesity is a condition mediated by complex neuronal and hormonal systems resulting from gene-environment interactions (15). Overeating behavior is important in the emergence of obesity, and food sensitivity among individuals may affect this condition. These may lead to the emergence of different tendencies toward obesity (16). Frequent consumption of high-energy and tasty foods in the absence of energy needs may trigger overeating behavior (17). Although hedonic differences associated with obesity have been reported, a strong relationship between BMI and hedonic hunger has not been shown (18). In our study, the relationship between hedonic hunger behavior

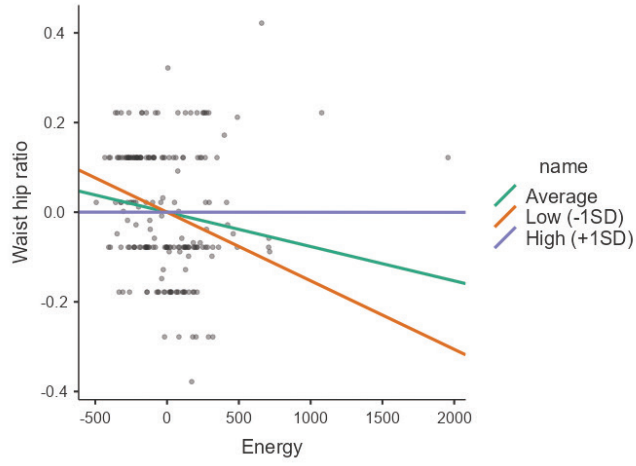

Figure 3. Simple slope plot of the regulatory effect of the power of the food scale on the waist-to-hip ratio

Name: Power of food scale scores, Low estimate: p=0.019, High estimate: p=0.996, Average: p=0.048, SD: Standard deviation of the mean. The graphic shows the effect of the predictor (energy intake) on the dependent variable (waist-to-hip ratio) at different levels of the moderator (power of food scale-Tr)

and obesity in older adults was examined. There was a weak positive correlation between "EmoE" behavior (DEBQ) and daily protein intake, a weak positive correlation between "FA" subscale (PFS-Tr) and average daily energy intake, and a weak positive correlation between "FP" subscale (PFS-Tr) and energy and fat intake. There was a weak positive correlation between "ResE" behaviour (DEBQ) and body fat percentage and fat mass and a weak positive correlation between the FA subscale (PFS-Tr) and muscle mass. There was a mediating effect of ResE behaviour (DEBQ) between average daily energy intake and body fat mass, with impaired ResE resulting in an increase in body fat mass. When the relationship between daily energy consumption and waist-to-hip ratio was examined, it was found that the regulatory effect of low scores obtained from the PFS-Tr scale was significant, and as the scores obtained from the scale decreased (as hedonic hunger behaviour decreased), the waist-to-hip ratio decreased.

In the study by Ribeiro et al. (18), a weak positive relationship was found between the hedonic hunger score and BMI. A relationship was found between the FP subscale and obesity, and each unit increase in FP scores increased the risk of obesity approximately 2-fold (odds ratio: 2.1). In a study conducted on young adults in the United States of America, the relationship between hedonic hunger and weight and dieting behaviors was examined. No relationship was found between weight and hedonic hunger, whereas a positive relationship was found between frequency of dieting, FP and FA sub-dimensions of the hedonic hunger scale and total score. High scores obtained from the hedonic hunger scale were found to be associated with more dieting cross-sectionally, but it was reported that it was not a good indicator of weight gain and dieting in the long term (19). In the study conducted by Dikyol et al. (20), it was found that the risk of being overweight/obese was higher in women who showed eating behavior even when full. The relationship between high food sensitivity and obesity is associated with unfavorable physical, social, and psychological outcomes. In the study conducted by Cappelleri et al. (9), a weak positive relationship was found between BMI and hedonic hunger sub-dimensions, and it was reported that the risk of obesity increased between 1.6 and 2.3 times as the scores obtained from the hedonic hunger scale increased. In the study conducted by Vainik et al. (21), the relationship between eating behaviors and obesity in women was examined, and the findings reflected the same basic feature: that uncontrolled eating behavior was related to weight. It was emphasised that the neuro-behavioural characteristics associated with obesity should be better understood. In the study conducted by Schultes et al. (22), it was found that obese patients had a significant increase in appetite for palatable foods and that patients who underwent gastric bypass surgery had lower scores in the sub-dimension of "FT" of PFS. The occurrence of this difference in patients after surgery shows the importance of excessive appetite in the pathophysiology of obesity.

Appelhans et al. (23) tested the interaction between palatable food, reward sensitivity, and inhibition control in overweight and obese women. They found that high palatable food reward sensitivity predicted greater consumption of palatable food at low levels of inhibition control but was not associated with food intake at high levels of inhibition control. The findings support a model between palatable food reward sensitivity and overeating, and it was emphasised that overeating was triggered when there was insufficient inhibition in the control. Burger et al. (24) reported that hedonic hunger was not a significant predictor of weight gain, but individuals reporting high hedonic hunger showed increased neuronal and perceptual responses to palatable foods, were more motivated to consume such foods, and were more likely to overeat. In the study by Witt et al. (25), the effect of hunger and exposure to palatable foods on hedonic appetite was evaluated. It was found that "ExtE" and "ResE" behaviours had no effect on hedonic hunger under hunger and food exposure conditions. Hedonic hunger represented a relatively constant structure that was not significantly affected by daily hunger changes. In our study, it was found that the mediator effect between ResE behavior and average daily energy intake and body fat mass was significant, and impairment in ResE resulted in an increase in body fat mass. In the literature, the relationships between hedonic hunger and weight were not consistent in studies conducted in different sexes, ages, and populations. A strong and positive relationship between hedonic hunger and obesity was not clearly demonstrated. The difference between our study and other studies was that it was one of the rare studies examining the relationship between hedonic hunger and obesity among older adults. The results of our study indicated a relationship between hedonic hunger and abdominal obesity. In particular, low hedonic hunger scale scores had a strong regulatory effect on abdominal obesity. ResE had a direct effect on body fat mass as a mediator and resulted in an impairment in ResE scores with an increase in fat mass.

Study Limitations

The strength of our study was that it was one of the rare studies investigating the relationship between hedonic hunger and obesity in older adults, while its limitations were that it was a single-center, hospital-based study.

Conclusion

The results of our study support a positive relationship between hedonic hunger and abdominal obesity in older adults. A decrease in restrictive eating behavior increased whole-body fat mass. There was a positive correlation between average daily energy intake and FA and a positive correlation between FP and energy and daily fat intake. Total daily energy intake had a

direct effect on the amount of body fat. In older adults, after a good clinical evaluation, assessment of hyperhedonic hunger and implementation of programs that support restrictive eating behaviour may be useful in controlling obesity and its negative consequences.

Ethics

Ethics Committee Approval: Permission for this study was obtained from the Malatya Clinical Research Ethics Committee (approval number: E-23536505-619-221990829, date: 11.08.2023).

Informed Consent: Consent forms were obtained for individuals who accepted to participate in the study among those fulfilling the inclusion criteria.

Authorship Contributions

Concept: B.M., L.K., H.D., C.K.Ş., E.D.M., E.B., Design: B.M., L.K., H.D., C.K.Ş., E.D.M., E.B., Data Collection or Processing: L.K., Analysis or Interpretation: B.M., H.D., Literature Search: B.M., L.K., H.D., C.K.Ş., Writing: B.M., L.K., H.D., C.K.Ş., E.D.M., E.B.

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ORIGINAL RESEARCH

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The Older Population's Antibody Response to SARS-CoV-2 Inactivated Vaccine (CoronaVac) is Independent to Vitamin D Levels

Zeynep Şahiner[1], Arzu Okyar Baş[1], Merve Güner[1], Serdar Ceylan[1], Merve Hafızoğlu[1], Didem Karaduman[1], Cansu Atbaş[1], Burcu Balam Doğu[1], Mustafa Cankurtaran[1], Filiz Akbıyık[2], Banu Çakır[3], Serhat Ünal[4], Meltem Gülhan Halil[1]

[1]Hacettepe University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, Ankara, Turkey
[2]Ankara City Hospital Laboratory, Siemens Healthineers, Ankara, Turkey
[3]Hacettepe University Faculty of Medicine, Department of Public Health, Ankara, Turkey
[4]Hacettepe University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Ankara, Turkey

Abstract

Objective: The purpose of this study was to determine how the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) inactivated vaccine antibody response and vitamin D levels in the older population are related.

Materials and Methods: This study included people over the age of 60 who received their second dose of the SARS-CoV-2 inactivated vaccine after 28 days. Immunoglobulin G antibodies against SARS-CoV-2 spikes were measured; levels equal to or greater than 1 U/mL were classified as seropositive, and levels below 1 U/mL were classified as seronegative. Serum 25-hydroxyvitamin D levels were evaluated in the participants; levels below 30 nmol/L were classified as low, and levels above 30 nmol/L were classified as normal.

Results: A total of 188 patients were included. A total of 152 people (80.9%) were found to be positive for the antibodies. The median [interquartile range (IQR)] age of the seropositive individuals was 71 (60-94) and the median (IQR) age of seronegative individuals was 72 (64-86) (p=0.272). While the vitamin D level was below 30 in 115 (75.6%) of the seropositive group, the vitamin D level was below 30 in 26 (70.9%) patients in the seronegative group (p=0.822).

Conclusion: In this study, we examined the association between vitamin D levels and seroconversion rate after the second dose of SARS-CoV-2 inactivated vaccine. There were no differences between the seropositive and seronegative groups in terms of vitamin D levels. In another context, it was discovered that vitamin D level has no effect on antibody response.

Keywords: COVID-19, immunology, older people, spike antibodies, vitamin D

Introduction

Even while the coronavirus disease-2019 (COVID-19) pandemic's most dangerous effects have all but disappeared, the consequences of the new variations persist, particularly in populations of older people and immunocompromised patients. Not only did the virus lose its virulence, but vaccination also put a stop to the pandemic.

Serum vitamin D insufficiency has been linked to an increased incidence of COVID-19, as well as increased severity and mortality of the disease, according to numerous observational studies (1-4). A substantial correlation was discovered in a large observational population study between the probability of contracting severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection and suffering severe illness if infected

Address for Correspondence: Zeynep Şahiner, Hacettepe University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, Ankara, Turkey
Phone: +90 506 939 84 84 **E-mail:** zynppyds@hotmail.com **ORCID:** orcid.org/0000-0003-1256-4412
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and serum vitamin D insufficiency evaluated before to the pandemic (5). On the other hand, factors other than serum vitamin D levels that affect the likelihood of COVID-19 infection include age, sex, comorbidity, and geographic location (6-8).

Vitamin D is essential for the regulation of human immune function, although it is best known for its effects on calcium homeostasis (9). The active vitamin D metabolite 1,25-dihydroxyvitamin D [1,25(OH)2D] is a pro-inflammatory in relation to monocytes and macrophages. It targets mitogen activated protein kinase phosphatase 1 (10) to regulate mammalian target of rapamycin. It has been shown to be an inhibitor of cytokine production (11) and phospholipase C in naive T cells. By inducing gamma 1 (12), it is used to support T cell activation and classical T cell receptor signaling.

25-hydroxyvitamin D [25(OH)D3], is the primary form of vitamin D that is circulating. Optimal vitamin D levels are indicated by low blood levels of the vitamin. This disease is more common in older people and is associated with increased systemic inflammation (13,14). Supplementation with vitamin D has been associated with elevated levels of circulating [25(OH)D3] in older individuals connected to the cutaneous varicella zoster virus antigen (15). A reduction in early inflammatory monocyte infiltration and T to the antigen challenge site have both been shown to considerably improve the response to challenge at concentrations of less than 75 nmol/L. Higher uptake was correlated with increased uptake of cells.

Studies are typically planned with consideration for all age groups, but there are very few that concentrate specifically on the older population with its many comorbidities, and there are still many unanswered concerns regarding immunization responses (16).

This study aimed to assess the relationship between antibody response and serum vitamin D levels in a geriatric population vaccinated with CoronaVac.

Materials and Methods

In this study, the files of patients who applied to the Hacettepe University Faculty of Medicine Hospital geriatrics polyclinic between August 2021 and September 2021 were retrospectively scanned between November 2022 and December 2022. This study was approved by the Hacettepe University Non-Interventional Clinical Research Ethics Committee (decision number: 2022/22-30, date: 27.12.2022). The trial comprised 188 older outpatients over 60 who had received their second dose of the SARS-CoV-2 inactivated vaccine (CoronaVac) after 28 days.

Criteria for inclusion in the study: (1) being over 65 years of age, (2) those who agree to participate in the study, (3) having the ability to understand and answer the questions asked.

Exclusion criteria: (1) uncooperative and unoriented patients, (2) patients for whom comprehensive geriatric evaluation cannot be performed, (3) patients who do not agree to provide serum samples for the study of antibody response and Vitamin D level parameters, (4) patients with COVID-19 confirmed by SARS-CoV-2 real-time polymerase chain reaction or thoracic computed tomography or who had clinical suspicions of COVID-19, (5) under immunosuppressive treatment, dementia, and dialysis.

The participants' demographic information, chronic disease, number of medication, polypharmacy (>5), Charlson comorbidity index (CCI), and malnutrition [mini nutritional assesment-short form (MNA-SF)] status were noted. MNA-SF to perform nutritional scanning, >11 scores were considered normal, 8-11 points indicated malnutrition risk, and 7 points indicated malnutrition (17,18). The comorbidity status of the individuals was assessed using the commonly used CCI (19).

SARS-CoV-2 Immunoglobulin G (IgG) Antibody Assay

Blood samples were obtained from patients to measure their IgG levels for SARS-CoV-2. Serum samples were centrifuged at 4000 rpm for 10 min. The samples were stored at -20˚C. IgG was detected using the Atellica IM SARS-CoV-2 IgG (sCOVG) test (11207386, California, USA). All samples and the SARS-CoV-2 spike protein receptor binding site were processed on the Atellica IM 1600 analyser. The immunological test called Atellica IM sCOVG uses chemiluminescent technology and has a measurement range of 0.50-150.00 index (U/mL). The sensitivity of the Atellica IM sCOVG assay was evaluated using the 1st World Health Organization international standard for anti-SARS-CoV-2 immunoglobulin (human), national institute for biological standards and control code 20/136. The concentration of the reference standard corresponding to the cut-off value of the 1.00 index (U/mL) was used (20). SARS-CoV-2 spike-specific IgG antibodies were identified; values >1 U/mL were considered seropositive and <1 U/mL seronegative.

Vitamin D Measurement by High-performance Liquid Chromatography (HPLC) Method

Vitamin D on Agilent 1100 HPLC device. Acetonitrile as a mobile phase for measurement a solution containing the mixture was used. Stable a vitamin D derivative internal standard was used as. Flow rate of the column 40-50 bar. The pressure was 0.7 mL per minute. Column temperature was 25˚C. 25- at a flow rate of 0.7 mL per minute retention time of 25(OH)D3 peak is 4.2 minutes, retention of internal standard His time was 7.1 minutes. Measurement 265 nm wave was performed with the help of a ultraviolet detector on the neck eld after extraction (21). Serum 25(OH)D3 levels were measured; values below 30 nmol/L were categorized as low, and values above 30 nmol/L were categorized as normal.

Statistics

The statistical analyses were performed using IBM SPSS version 23.0. To ascertain whether or not the variables were regularly distributed, both visual (histograms and probability plots) and analytical techniques were used. For normally distributed variables, descriptive statistics were displayed as mean ± standard deviation; for non-normally distributed data, as median [interquartile range (IQR)] and for nominal variables, as number of cases and (%). When there were two groups, the Mann-Whitney U test was used to compare group differences in median values. For categorical variables, data were compared using the chi-square test or Fisher's exact test and the Bonferroni correction was applied when necessary. Statistical significance was defined as $p<0.05$.

Results

The study included 188 patients, whose median (IQR) age ranged from 67 to 75. There were 101 (59%) female patients. The seropositivity ratio was 80.9% (n=152). Seropositive group, SARS-CoV-2 spike IgG serum level U/mL, median (IQR) was 4.6 (2.5-10), and seronegative group was 0.56 (0-0.6) ($p<0.0001$). Regarding age, sex (female), nutrition, polypharmacy, and concomitant illnesses apart from asthma ($p=0.272$, $p=0.779$, $p=0.196$, $p=0.822$ respectively), there were no statistically significant between the seropositive and seronegative groups. The CCI scores were higher in the seronegative group ($p=0.023$) (Table 1).

While the seropositive patients in the low vitamin D group were 115 (75.6%), the seronegative group patients were 26 (70.9%) ($p=0.822$) and the seropositive patients in the normal vitamin D group were 37 (24.4%), the seronegative group patients were 10 (29%) ($p=0.596$).

The seropositivity distribution according to vitamin D levels (µg/L) is shown in Figure 1. The median vitamin D level was found to 19 µg/L (0.5-94) in the seropositive group and median of vitamin D level in seronegative group was 19 µg/L (5-52), in both the seropositive group and the seronegative group, and no difference was observed.

Discussion

It is a well-known fact that morbidity and mortality from SARS-CoV-2 infection occur more frequently in older patients than in younger adults, taking into account a number of factors such as physiological changes and comorbidities brought about by aging. Low vitamin D levels are one of these age-related consequences. The rates of acute respiratory infections such as SARS-CoV-2 and influenza are linked to vitamin D deficiency (22). For those at higher risk of viral infections, studies recommend using higher doses of vitamin D. However, significant toxicity

Table 1. Clinical and demographic characteristics, comparison between antibody positive and negative groups after 28 days after the 2nd dose of vaccination group

	Seropositive group 152 (80.9%)	Seronegative group 36 (19.1%)	p
Age, years	71 (60-94)	72 (64-86)	0.272
Gender (female)	89 (58.6%)	22 (61.1%)	0.779
Low vitamin D group [25(OH)D3] <30 (µg/L)]	115 (75.6%)	26 (70.9%)	0.822
Normal vitamin D group [25(OH)D3] >30 (µg/L)]	37 (24.4%)	10 (29%)	0.596
Comorbidities			
HT	107 (70.4%)	28 (77.8%)	0.376
DM	65 (42.8%)	19 (52.7%)	0.277
Dementia	9 (5.9%)	1 (2.7%)	0.450
CVD	40 (26.3%)	9 (25%)	0.872
Depression	16 (10.5%)	2 (5.5%)	0.362
CRF	6 (3.9%)	2 (5.5%)	0.667
COPD	12 (7.9%)	3 (8.3%)	0.930
Asthma	12 (7.9%)	9 (25%)	**0.003***
Malnutrition (MNA <7)	13 (9%)	2 (5.5%)	0.196
Polypharmacy	88 (59.1%)	22 (61.1%)	0.822
CCI score, median	1 (0-2)	2 (1-3)	**0.023***
SARS-CoV-2 spike IgG serum level U/mL, median (IQR)	4.6 (2.5-10)	0.56 (0-0.6)	**<0.0001***

Variables were presented as n (%), mean ± standard deviation or median (IQR)
*Significance at $p<0.05$
[25(OH)D3]: 25-hydroxyvitamin D, CVD: Cardiovascular diseases, HT: Hypertension, DM: Diabetes mellitus, CRF: Chronic renal failure, COPD: Chronic obstructive pulmonary disease, MNA: Mini nutritional assessment, CCI: Charlson comorbidity index, IgG: Immunoglobulin G, IQR: Interquartile range, SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2

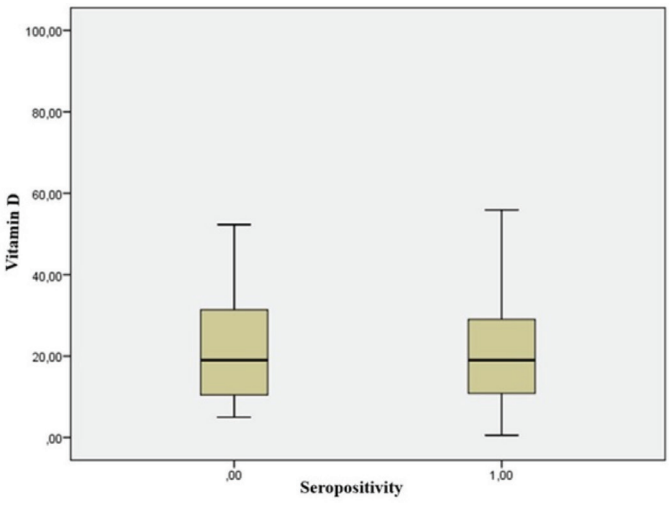

Figure 1. Seropositivity distribution according to vitamin D levels (µg/L)

and hypervitaminosis have recently been observed, and caution is required in this regard (23). On the other hand, it has been suggested that regular oral vitamin D intake of 2000 IU per day (without supplementation) is safe and protective against acute respiratory distress syndrome, especially for patients with vitamin D deficiency (24). Numerous observational studies have looked into the relationships between the immunogenicity of the SARS-CoV-2 vaccine and vitamin D levels, but these have yielded conflicting results: some have found higher post-vaccination anti-spike antibody titers in individuals who used vitamin D supplements or had higher circulating levels of vitamin D (25,26); they have reported findings opposite to those of other studies (27-29).

Vitamin D has been demonstrated to have immunomodulatory and antiproliferative effects on T cells, which reduce the expression of pro-inflammatory cytokines like interleukin-6 and tumor necrosis factor-alpha (30). Similar research indicates a connection between vitamin D levels in viral infections and vaccination responses. The ability to affect the adaptive immune response likely causes the regulatory impact. It has been suggested that vitamin D may enhance CD4+ lymphocyte production while reducing the proliferation of helper T cells. By turning B cells into plasma cells, this can boost the generation of virus-specific antibodies (31).

It is well known that active vitamin D (1-alpha, 25-dihydroxy vitamin D3) controls the immune system's adaptive response, which is produced naturally (32,33). Typically, vitamin D acts as a hormone to enhance the immunological response (34,35). Therefore, vitamin D may not make the expected contribution to the immune response because our study was conducted on an aged population, and the adaptive immune response was decreased in this group. However, several studies in the literature that included various age groups produced findings that were comparable to our findings (28).

In our study, similar to some studies in the literature, we could not detect a connection between vitamin D levels and sCOVG response. We believe that these results may have been affected by the fact that the patients received an inactive vaccine and that 28 days or more had passed, which is a long time for an inactive vaccine. Additionally, in another study that used the vaccine, no connection was found between vitamin D deficiency and immune response to the mRNA vaccine (36).

Another randomized, placebo-controlled study examined the effects of vitamin D supplementation and inactivated influenza vaccine in older participants and found that vaccine antibody titers did not change after vitamin D supplementation (37).

Two doses of inactive vaccine were used in our study; this may be considered insufficient, considering that inactivated vaccination produces limited immunity and show cumulative effects. However, a different randomized controlled trial examining the link between vitamin D levels and immune response following the second dosing showed the same results despite the use of an mRNA vaccine (27). According to one study, the highest antibody response was achieved three weeks after receiving the mRNA vaccine and continued until the eighth week. The relationship between age and antibody response was inverse, with vitamin D deficiency negatively affecting the antibody response. Additionally, only 97 participants were included in this study. However, serial antibody assessments performed after the first 4 weeks of vaccination increased the reliability of the study (38).

Studies assessing the connection between various inactivated vaccine immunogenicity and vitamin D produced similar findings. A meta-analysis that examined the relationship between vitamin D insufficiency and immunogenicity of influenza vaccination revealed that vitamin D levels did not influence the immunological response. Additionally, there was no discernible connection in a trial that assessed the immunogenicity of a different inactivated vaccination, specifically hepatitis B, in individuals who were vitamin D deficient (39).

Study Limitations

One of the limitations of our study is that the findings would have been stronger if serial antibody and vitamin D tests had been performed before and after vaccination. It is important to remember that various factors, such as comorbidities and nutrition, can affect an individual's immune response to the vaccine. Another important issue is that we tested [25(OH)D3] not the active form of vitamin D, as in many studies in the literature. In this study, we administered MNA-SF to patients due to our limited understanding of the population's dietary preferences and micronutrient utilization. At the beginning of our research and literature review, it was anticipated that vitamin D complement

activation would have particularly adaptive and hormonal effects for the older population. However, neutralizing or non-neutralizing antibodies specific to inactivated vaccines cannot be produced by vitamin D alone. Understanding metabolic and molecular mechanisms through a prospective, comprehensive population study of vitamin D levels and replacement will help determine the effects of vitamin D on cell-mediated immunity during aging.

Conclusion

To look at the antibody levels for additional vaccines in older individuals, randomized controlled trials with larger populations are required.

Ethics

Ethics Committee Approval: Between November and December of 2022, the Hacettepe University Hospital retrospectively scanned the biochemical values and demographic data of the study participants with decision number 2021/17-05 (KA-21084). This study was approved by the Hacettepe University Non-Interventional Clinical Research Ethics Committee (decision number: 2022/22-30, date: 27.12.2022).

Informed Consent: Retrospective study.

Authorship Contributions

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

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ORIGINAL RESEARCH

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Relationship Between Coronaphobia, Cognitive Functions, Sleep Quality, and Diet Quality in Older Adults During COVID-19

Leyla Ataş Balcı[1], Selda Polat[2], Dilber Karagözoğlu Coşkunsu[3], İlayda Altuncevahir[4], Bilge Meral Koç[4], Ecenur Özkul[4]

[1]Bahçeşehir University Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, İstanbul, Turkey
[2]Bahçeşehir University Faculty of Health Sciences, Department of Nursing, İstanbul, Turkey
[3]Fenerbahçe University Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, İstanbul, Turkey
[4]Bahçeşehir University Faculty of Health Sciences, Department of Nutrition and Dietetics, İstanbul, Turkey

Abstract

Objective: The relationship between the quality of diet and sleep, cognitive function, and fear related to coronavirus disease-2019 (COVID-19) among older adults in Turkey during the pandemic remains unclear. This study aimed to investigate the correlation between diet quality, cognitive function, sleep quality, and levels of coronaphobia in individuals aged 65 and above, to understand the impact of COVID-19.

Materials and Methods: Sleep quality, diet quality, coronaphobia, and cognitive status of 72 older individuals were evaluated using the Pittsburgh sleep quality index, healthy eating index 2010, Montreal cognitive assessment scale, and coronavirus-19 phobia scale, respectively.

Results: The participants had poor diet quality (54.2%), poor sleep quality (62.5%), obesity (41.7%), higher levels of coronaphobia, and cognitive impairment. There was a moderate negative relationship between sleep quality and coronaphobia and between cognitive status and coronaphobia ($p \leq 0.00$); and a weak positive relationship between diet quality and cognitive status ($p < 0.05$). However, no relationship was found between sleep quality and diet quality, and between coronaphobia and diet quality ($p > 0.05$).

Conclusion: Our study highlights the significant challenges faced by older adults during the COVID-19 pandemic, including poor nutrition quality, sleep disturbances, coronaphobia, and cognitive impairment. Our findings suggest a potential interplay between nutrition quality, sleep patterns, and cognitive function among older adults, with those experiencing coronaphobia exhibiting additional cognitive and sleep-related concerns. We advocate the implementation of targeted interventions aimed at mitigating cognitive impairment, addressing nutritional deficiencies, and improving sleep quality among older adults, irrespective of COVID-19 infection status, to enhance overall well-being during these challenging times.

Keywords: Aging, cognitive, COVID-19, diet, phobia, sleep

Introduction

Coronavirus disease-2019 (COVID-19), a global pandemic, affected over 774 million people worldwide as of February 2024. In Turkey by March 2023, it had infected more than 17 million people and caused over 100,000 deaths (1). In addition to its physical effects, COVID-19, with measures like lockdowns, mandatory mask usage, and social isolation, has also led to poor sleep quality, depression, anxiety, cognitive decline, malnutrition, and mental health problems due to the fear it creates (2-5).

Although pandemic conditions may not persist, the ongoing cases of COVID-19 and the lasting impact of isolation, restrictions, and mental health issues during the pandemic continue to affect individuals. Coronaphobia, characterized by excessive fear of being infected with COVID-19, contributes to poor sleep, malnutrition, cognitive issues, and higher body mass index (BMI) (2,6-10). In addition, media-induced stress during the COVID-19 pandemic affected the cognitive function of individuals (11,12).

Address for Correspondence: Leyla Ataş Balcı, Bahçeşehir University Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, İstanbul, Turkey
Phone: +90 505 399 52 34 **E-mail:** atslyla@hotmail.com **ORCID:** orcid.org/0000-0002-3302-3722
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In Turkey, the highest COVID-19 death rate, reaching 26.94%, was observed in individuals over the age of 80. Lockdowns targeting individuals aged 65 and above were implemented between February and March 2021 due to the heightened risk of death among older adults (13). Although these restrictions reduced mortality rates, they led to the loss of social support and decreased physical activity, which are crucial for older adults, resulting in increased risks of non-communicable diseases, depression, and diminished quality of life (14).

After the initial wave of COVID-19, older adults in nursing homes who did not contract the virus experienced declines in functional, cognitive, and nutritional status (15). Older individuals isolated at home because of COVID-19 restrictions experience sleep problems, including decreased night sleep duration, late falling asleep, and waking up in the middle of sleep (7). Strategies for coping with negative emotions, such as emotional eating behavior during the pandemic, have resulted in either consuming more food than usual or, conversely, reducing food intake (5). Reduced sleep quality and poor nutrition habits have been reported to be associated with sarcopenia, cardiovascular diseases, obesity, dementia, Alzheimer's disease, and cognitive impairment, which are frequently encountered in older adults, leading to increased morbidity and mortality (16-20). In addition, the recognition that COVID-19 has led to more severe outcomes in older adults has generated serious fear among older adults (21).

Mediterranean-type dietary patterns, regular sleep, and stress reduction play crucial roles in preventing cardiovascular diseases, cognitive disorders, and sarcopenia in older adults. Therefore, monitoring patients' nutritional status, cognitive skills, and sleep quality is essential for implementing preventive measures (22). According to 2023 data from the Turkish Statistical Institute, individuals over the age of 65 constitute 10.2% of Turkish society, with every 100 people of working age caring for 15 older adults (23). However, the relationship between diet quality, sleep quality, cognitive status, and coronaphobia among older adults living in Turkey during the pandemic remains unclear. Given these factors, our study aimed to determine the relationship between diet quality, cognitive function, sleep quality, and coronaphobia levels in individuals over the age of 65 years, comprehensively addressing the effects of COVID-19 in this population.

Materials and Methods

Study Sample

This study was conducted in İstanbul from February 2021 to March 2021. Individuals aged 65 years and older, who tested negative for COVID-19, had no previous history of COVID-19, had no psychological disorders, and voluntarily agreed to participate were included in the study. The snowball sampling method was used to reach the participants. The sample size was determined using the Raosoft Sample Size Calculator software. The ratio of the Turkish population over the age of 65 (population number 7,550,727 million) to the total population (80 million) of Turkey was calculated to be 9%, and it was determined that the sample size of the study to achieve a 95% confidence interval and 80% power should be 54. Taking the 10% drop-out rate into consideration, we aimed to reach a minimum of 60 participants at the beginning of the study; ultimately, we had 72 participants who completed the study, with one person excluded due to a lack of data. This study was approved by Bahçeşehir University Scientific Research and Publication Ethics Committee (decision number: 2021/02/52, date: 10.02.2021). Patients were provided with comprehensive explanations about the study both verbally and in writing, and consent was obtained.

Data Collection

Sociodemographic information such as age, gender, marital status, educational status, living alone status, and presence of chronic illnesses was collected using a demographic information form prepared by the researchers. The participants' sleep quality was evaluated using the Pittsburgh sleep quality index (PSQI), their diet quality was assessed using the healthy eating index-2010 (HEI-10), and their cognitive functions were evaluated using the Montreal cognitive assessment scale (MOCA). Additionally, the COVID-19 phobia scale (C19P-S) was used to assess whether participants were experiencing coronaphobia.

PSQI: The PSQI was used to determine sleep quality and the type and severity of sleep disorders within the last month. This scale consists of 24 questions, 19 of which were answered by the participants, and 5 of which were answered by their partner. The 19 questions covering sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction were answered with statements ranging from "not during the past month" to "three or more times a week". Each item was evaluated on a scale of 0-3, and the sleep quality of those with a total PSQI score of 5 or higher was considered poor (24).

HEI-10: The HEI-10 is an index that evaluates the suitability of food consumption and measures diet quality. The HEI-10 includes 12 items, each of which is scored with a 0, 5, 10, or 20. The frequencies of participants' food consumption were recorded using the food consumption frequency form and were scored according to this scale. When individuals' diet quality was categorized according to their total HEI-10 scores, those below 51 were recorded as having "poor diet quality", those between 51-80 as "diet quality needs improvement", and those over 80 as "good diet quality" (25).

MOCA: The MOCA was used in the early detection of mild cognitive disorders, with the MOCA scale evaluating various

cognitive dimensions as follows: attention and concentration, executive function, memory, language, visual-spatial skills, abstract thinking, calculation, and orientation. The total score was calculated out of 30. The threshold value was taken as 21 (a score of 20 or under referred to as cognitive dysfunction) (26).

C19P-S: The C19P-S is a 20-item scale with psychological, psychosomatic, economic, and social subdimensions that was used to evaluate levels of coronaphobia. Items were scored from "strongly disagree (1)" to "strongly agree (5)", and answers were self-reported by participants. The total scores ranged between 20 and 100. Greater scores reflect increased coronaphobia levels (6).

Statistics

Statistical Package for the Social Sciences version 22 (SPSS 22.0, IBM) was used to perform the statistical analysis of the data obtained from the study. The obtained continuous variables are expressed as mean ($\overline{X}$), standard deviation, and minimum-maximum values, and discrete variables are expressed as numbers (n) and percentages (%). Whether the data were normally distributed was evaluated using the Kolmogorov-Smirnov test. Spearman's correlation analysis was used to determine the relationship between the participants' BMI, PSQI, MOCA score, CP19-S score, and HEI-10 score. The strength of the correlation was evaluated as poor (0-0.3), moderate (0.3-0.5), or strong (0.5-0.7). Statistical significance was accepted as $p<0.05$.

Results

Seventy-two older adults [(70.95±4.67 years/median: 70); 52 females and 20 males] participated in the study. The participants' PSQI, MOCA, and CP19-S mean scores were 5.51±2.79 (median: 5), 20.68±4.17, and 55.77±16.38, respectively. The calculated HEI-10 and BMI scores of the participants were 54.40±10.00 (median: 50) and 28.84±4.15 kg/m^{T}. Most participants had poor diet quality (54.2%), poor sleep quality (62.5%), and obesity (41.7%) (Table 1).

We found a moderate negative relationship between the PSQI and CP19-S scores and between the MOCA and CP19-S scores of the participants ($p\leq0.00$). There was a weak negative correlation between BMI and HEI-10 scores and a weak positive correlation between MOCA and HEI-10 scores of the participants ($p<0.05$). However, no significant relationship was observed between BMI and PSQI, BMI and MOCA, BMI and CP19-S, PSQI and HEI-10, and HEI-10 and CP19-S scores of the participants ($p>0.05$) (Table 2).

Discussion

In this study, the diet quality, cognitive function, sleep quality, and coronaphobia levels of older individuals were examined to determine the effects of COVID-19. We demonstrated that older adults had poor diet quality, poor sleep quality and moderately high coronaphobia levels during the COVID-19 pandemic in Turkey. We observed that there might be a relationship between diet quality, sleep quality, and cognitive function in older

Table 1. Descriptive characteristics and measurements results

Characteristics (n=72)			n (%)
Gender	Female Male		52 (72.2%) 20 (27.8%)
Education	Primary school Secondary school High school University		43 (59.7%) 10 (13.9%) 10 (13.9%) 9 (12.5%)
BMI	Underweight Normal Overweight Obese		1 (1.4%) 14 (19.4%) 27 (37.5%) 30 (41.7%)
Living status	Family Alone		57 (79.2%) 15 (20.8%)
Chronic disorders	Yes No		55 (76.4%) 17 (23.6%)
Sleep quality	Poor Good		45 (62.5) 27 (37.5)
Nutrition quality	Poor Needs improvement		39 (54.2) 33 (45.8)
	x̄ (SD)	**Median**	**Min-max**
Age (years)	70.95 (4.67)	70	65-83
Height (cm)	164.05 (7.93)	-	150-182
Weight (kg)	77.47 (11.24)	-	50-108
BMI (kg/m^2)	28.84 (4.15)	-	18.3-40
PSQI	5.51 (2.79)	5	1-14
HEI-10	54.40 (10.00)	50	35-76
MOCA	20.68 (4.17)	20.5	13-29
CP19-S	55.77 (16.38)	58.5	20-85

SD: Standard deviation, BMI: Body mass index, PSQI: Pittsburgh sleep quality index, HEI-10: Healthy eating index, MOCA: Montreal cognitive assessment, CP19-S: Coronavirus-19 phobia scale, x̄: Mean, Min-max: Minimum-maximum

Table 2. The relationship between the BMI, PSQI, MOCA, HEI-10, and CP19-S scores

Variables (n=72)	r*	p**
BMI-PSQI	0.194	0.103
BMI-HEI-10	**-0.291***	**0.013**
BMI-MOCA	-0.197	0.097
BMI- CP19-S	0.150	0.210
PSQI-MOCA	-0.233*	0.049
PSQI-HEI-10	-0.156	0.192
PSQI-CP19-S	**0.431****	**0.000**
MOCA-HEI-10	**0.254***	**0.032**
MOCA-CP19-S	**-0.393****	**0.001**
HEI-10-CP19-S	0.180	0.883

*r: Spearman correlation coefficient
**p<0.05
BMI: Body mass index, PSQI: Pittsburgh sleep quality index, HEI-10: Healthy eating index, MOCA: Montreal cognitive assessment, CP19-S: Coronavirus-19 phobia scale

individuals during the COVID-19 pandemic. We also found that the cognitive function and sleep quality of individuals with high coronaphobia levels could be impaired.

Stressors can lead to impairment of cognitive functions, including attention, comprehension, retention, and judgment (27). Our study revealed that older adults who faced social isolation during the COVID-19 pandemic experienced moderate levels of coronaphobia and cognitive impairment. Previous studies have stated that social isolation exacerbates cognitive functions and might weaken memory in patients with dementia (28). Furthermore, the duration of isolation is correlated with a heightened severity of neuropsychiatric symptoms (29). Additionally, COVID-19-induced anxiety or fear is linked to regional brain atrophy in individuals with cognitive impairment (21). In their study conducted on individuals aged 18-66, Karwowski et al. (11) noted that thinking about COVID-19 and the stress caused by related news affected analytical thinking performance. Similarly, Favieri et al. (2) found that among individuals aged 18-40 in the Italian population who were not infected with COVID-19, there was a decline in performance on both the Stroop task and the go/no-go task, which are commonly employed to assess cognitive functions. Cognitive functions of individuals over the age of 65 who experienced coronaphobia were found to be low in our study, which is consistent with previous findings.

Sleep quality may deteriorate because of the effects of emotional conditions and stress, or that deterioration in sleep quality may affect emotional states during the COVID-19 pandemic (7). In addition, anxiety has been associated with COVID-19 and decreased sleep quality (4). In this study, we found that 62.5% of participants and those with high coronaphobia scores had inadequate sleep quality. As people age, cortical thinning and amyloid accumulation in regions of the brain with high neuronal activity, such as the prefrontal cortex, angular gyrus, and hippocampus, negatively affect the depth of sleep and disturb the restorative effects of sleep. These problems may lead to the loss of cognitive function and the onset of Alzheimer's disease (19). These findings support the relationship between the deterioration of sleep quality and cognitive dysfunction detected in the present study.

Adequate nutrition is a cornerstone of healthy aging. Healthy eating habits might help preserve the structure and function of the brain and increase cognitive function in older individuals. This result was attributed to the fact that such habits have been demonstrated to promote synaptogenesis, exert antioxidant and anti-inflammatory effects, regulate blood pressure and lipid levels, and enhance cerebral blood flow (16,17,22). On the contrary, malnutrition reduces physical and cognitive functions and increases the risk of cardiovascular disease in older individuals (16). Our study revealed that overall, participants' diet quality was poor or needed to be improved, and a decline in diet quality was correlated with a decrease in cognitive skills. In addition, it was found that individuals who did not have healthy eating habits had a high BMI. In accordance with the literature, our study indicated that BMI increased as the diet quality decreased (30). According to the BMI values in our study, 41.7% of the participants were obese. Studies have reported that there is a U-shaped relationship between BMI, cognitive function, and sleep quality (31,32). In this context, it is understood that too much or too little sleep can lead to obesity (32). In addition, although it has been argued that there is a relationship between obesity and cognitive impairment in middle-aged people, being overweight at an advanced age has protective effects in individuals with cognitive impairment (31). Although no relationship was found between BMI, quality of sleep, and cognitive status in our study, we believe that BMI control should be considered in older individuals, as being overweight and obese is associated with cardiovascular disease. Additionally, previous studies support that weight loss has a positive effect on cognitive function in individuals with obesity (31). In the present study, there was no relationship between BMI, diet quality, and CP19-S scores. In line with our findings, Sutin et al. (33) found that despite an increase in obesity-related COVID-19 complications, individuals with high BMIs did not report being more concerned about the virus than those with low BMIs and did not take more precautions against the virus than those with low BMIs (34). In contrast, Kaufman-Shriqui et al. (10) revealed that a decrease in diet quality and an increase in BMI may be associated with COVID-19-related anxiety. However, the average age of the participants was approximately 30 years (10). Therefore, it has been argued that diet quality and fear associated with COVID-19 may vary among different age groups. Previous studies exploring the correlation between sleep quality and nutritional habits have suggested several trends: extended periods of wakefulness may result in increased food intake; late waking and bedtime may lead to nighttime eating; and inadequate sleep may affect hormones such as leptin, ghrelin, and insulin. During the pandemic, researchers found that increased anxiety about COVID-19, disrupted sleep patterns, and a higher BMI were associated with a tendency to indulge in emotional eating (5,34). However, no significant association was found between diet and sleep quality, and existing research being largely deemed insufficient (34). Similarly, our study found no relationship between sleep quality and diet quality.

Study Limitations

The strengths of our study are the inclusion of older individuals' cognitive status and fears related to COVID-19, as well as their daily life patterns, nutrition levels, and sleep quality during the pandemic. However, despite these strengths, our study did not

provide information about the participants according to their social status, and the age distribution was not homogeneous, limiting its application to the general population.

Conclusion

Our research highlights the multifaceted impact of the COVID-19 pandemic on older adults, shedding light on distinct disabilities such as nutritional deficiencies, disrupted sleep patterns, coronaphobia, and cognitive decline. Moreover, our study revealed the relationship between nutrition, sleep, and cognitive health in this demographic group and highlighted the complex challenges faced by those struggling with the fear of COVID-19. For older adults who are already negatively affected by social isolation, fear, and restrictions, we recommend implementing interventions to alleviate their cognitive impairments, nutritional deficiencies, and declines in sleep quality they experienced during the pandemic, even if they have not contracted COVID-19.

Ethics

Ethics Committee Approval: This study was approved by Bahçeşehir University Scientific Research and Publication Ethics Committee (decision number: 2021/02/52, date: 10.02.2021).

Informed Consent: Patients were provided with comprehensive explanations about the study both verbally and in writing, and consent was obtained.

Authorship Contributions

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

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ORIGINAL RESEARCH

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Clinical and Radiographic Findings in Older and Non-older Patients Applying to the Faculty of Dentistry

Esin Bozdemir[1], Özlem Görmez[1], Sinem Sırlı Yılmaztürk[2]

[1]Süleyman Demirel University Faculty of Dentistry, Department of Dentomaxillofacial Radiology, Isparta, Turkey
[2]Likyadent Oral and Dental Health Polyclinic, Muğla, Turkey

Abstract

Objective: This study aimed to evaluate intraoral, extraoral, and radiographic findings in the jaws of older adults and compare these findings with those of a control group of non-elderly individuals.

Materials and Methods: Seven hundred randomly selected patients above 18 (350 older adults, 350 non-older) comprised the study population. A questionnaire consisting of 21 questions was used. Intraoral, extraoral, and radiographic examinations were conducted.

Results: Most older adults (85.1%) patients had at least one systemic disease. This proportion was 31.4% in non-older patients ($p<0.001$). The majority of elderly (90.3%) patients and the control group (77.1%) reported that they did not regularly go to the dentist ($p<0.001$). The most common intraoral finding in both the older adults and the control group was inflamed gums and periodontal problems. The most common extraoral finding in older adults (42.4%) was pain and sound in the temporomandibular joint and lymphadenopathy (71.7%) ($p=0.001$) in the control group. The radiographic findings showed that the number of impacted teeth and caries was significantly higher in the non-older group ($p<0.05$).

Conclusion: It is important to perform a more careful dental examination on older patients than is required for non-older individuals because these patients have more systemic diseases, a history of drug use, and inadequate oral hygiene.

Keywords: Dental caries, elderly, general health, oral mucosal lesion

Introduction

The average life span is increasing in industrialized and developed countries because of advances in medicine and the reduction in fertility. Hence, the geriatric population will increasingly attend dental offices in the future. Old age is a process of changes that leads to decreased functional capacity in tissues and organs. Both systemic and oral health deteriorate with age. For this reason, the decrease in functional abilities and the frequent occurrence of health problems among older adults have revealed the necessity for more consciously approaching older individuals and their problems. It is important for oral epidemiological investigations related to oral health in the older adults. Although there are studies in the literature related to the oral health status of older adults, no studies have compared the clinical and radiographic findings of oral health in the older and non-older populations (1).

Interactions always affect each other' oral/dental and medical health. Systemic conditions such as atherosclerotic disease, pulmonary disease, and diabetes mellitus that oral health status can either coincidentally or causally impact (2).

Many studies worldwide have documented poor oral health due to the high prevalence of coronal and root caries, tooth loss and edentulousness, periodontal diseases, and oral mucosal lesions, and an unacceptable level of oral hygiene in older dental patients (1,3-7). Poor oral health may be due to a lack of awareness regarding oral hygiene and its importance as well as an inability to access oral health services for restorative care in addition to systemic diseases and medications (7). Regular

Address for Correspondence: Esin Bozdemir, Süleyman Demirel University Faculty of Dentistry, Department of Dentomaxillofacial Radiology, Isparta, Turkey
Phone: +90 536 328 77 47 **E-mail:** dtesin@hotmail.com **ORCID:** orcid.org/0000-0002-2421-3807
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patient contact is required to detect oral diseases as early as possible (1).

Treatment planning for older dental patients must include an understanding of the chronic diseases that the patient lives with, as this plays a critical role in the acceptance and success of dental treatment plans. Radiographic examination is important for detecting pathologic findings that may affect the patient's general health or dental treatment plan. Panoramic radiography is an imaging modality that is extremely important in the diagnosis and treatment of many oral and maxillofacial diseases and is routinely used in dental clinics for treatment planning (8). The panoramic radiographs (PR) of older adults have been used to evaluate changes in the gonial angle and height of the mandibular bone with aging and indexes such as the mandibular index (9-13). Other studies have been conducted on specific subjects, such as maxillary sinus findings (14), the anatomy of the mid-palatal suture (15), and the elongated styloid process (16). In addition to oral manifestations such as caries and mucosal lesions in elderly individuals, findings such as cysts, tumors, and impacted teeth in their jaws have not received adequate attention in previous studies. There are only a few studies related to this issue (17,18).

This study aimed to evaluate oral manifestations and radiographic findings in older patients and compare them with those in a control group of non-older individuals. In this way, there will be an increase in epidemiological knowledge about oral health in the older population, which can be used for related future planning in this group.

Materials and Methods

Süleyman Demirel University Faculty of Medicine Clinical Research Ethics Committee approved this study (decision number: 69, date: 21.03.2018). Seven hundred random patients above the age of 18 who applied to the department of dentomaxillofacial radiology were included in this study. The informed consent form was read and signed by the participants to inform them about the study purpose and methodology.

A questionnaire consisting of 21 questions about the patient's sociodemographic characteristics, the reason for applying, general health status, history of drug use, oral hygiene practices, dental prosthesis use, and smoking or alcohol habits was used. Intraoral, extraoral, and radiographic examinations were performed. The number of natural teeth, caries, tooth loss, filled teeth, implants, tooth abrasions, mucosal lesions, and tongue lesions, as well as periodontal health, infection, and the presence of abscesses and fistula, were evaluated during the intraoral examination. The mucosal lesions, red-blue lesions, white lesions, vesiculobullous lesions, ulcerated lesions, pigmentation, and variants of normality were examined. In the extraoral examination, the presence of temporomandibular joint (TMJ) disease, lymphadenopathy, and swelling were evaluated. PR of the participants taken for various reasons were examined. All PR images were acquired using the same digital panoramic machine: the Promax (Planmeca, Helsinki, Finland) operated at 66 kV, 8 mA, and 16 s exposure time. On the PR, caries, periapical lesions, bone loss, sclerosis, impacted teeth, persistent root, bone components of the TMJ, stylohyoid ligament, soft tissue calcification, and the presence of cysts and tumors were recorded.

To eliminate individual differences, a questionnaire and physical examinations (intraoral, extraoral and radiological) were performed by one researcher (SSY is three years of experience). Patients were divided into two groups (350 geriatric patients aged 65 and over and 350 adult patients aged 18-65). The decayed, missing, and filled teeth (DMFT) index was used to assess oral health. Index calculations were performed with 32 teeth, including the third molars.

Statistics

SPSS software (SPSS 17.0 for Windows; SPSS Inc., Chicago, IL, USA) was used for statistical analyses, and $p<0.05$ was considered statistically significant. Descriptive statistics and the Pearson's chi-square test were used to evaluate the data.

Results

The study sample consisted of 350 (47.4% women, 52.6% men) older patients and 350 (47.1% women, 52.9% men) non-older patients. The mean age was 70.91±5.5 years (min 65, max 95) in the older patients and 33.7±12.5 years (min 18, max 63) in the non-older patients. The majority of elderly participants (55.4%) were primary school graduates. Non-elderly participants were mostly (42.9%) university graduates. The majority of elderly (85.1%) patients had at least one systemic disease, whereas only 31.4% of non-older patients ($p<0.001$) had at least one systemic disease. It was determined that cardiovascular system disease was the most common illness in both older (60.6%) and non-older (39.4%) patients ($p<0.001$) (Table 1).

Approximately 79.1% of older patients and 20.9% of the control group stated that they used drugs ($p<0.001$). The percentage of older adults using anticoagulants was 32.3%, whereas the percentage of those using anticoagulants in the control group was 2.6%. While the rate of smoking was 8% in older adults, it was 34.3% in non-older patients. Rates of oral hygiene and other habits according to groups are presented in Table 2. It was determined that the frequency of toothbrushing and the mean number of teeth increased with education level in the study population ($p<0.001$). While 19.7% of the older patients did not have any fixed or removable prosthesis, the presence of a fixed prosthesis was in the majority (33.7%). Most of the control group (76.9%) did not have any fixed or removable prosthesis

(p<0.001). While 62.6% of older patients reported having dry mouth, only 32.9% of the patients in the control group had dry mouth (p<0.001). The number of patients with complaints of bad breath was higher in the control group (44.3%) than in the older group (34.3%). The frequency of dry mouth complaints was higher in older patients with endocrine system diseases and who received chemotherapy and radiotherapy for cancer (p<0.001).

Extraoral findings were present in 13.7% of older patients and 23.1% of the control group (p=0.001). The most common extraoral finding in older patients (42.4%) was pain and sound related to TMJ. In the control group, the most common extraoral examination finding was lymphadenopathy (71.7%) (p=0.001) (Table 3). The most common intraoral finding in both the older patients and the control group was inflamed gums and periodontal problems. The prevalence of oral mucosal lesions was 82.6% in the older group. Intraoral findings according to groups are presented in Table 3.

Although the average number of teeth was 14.6±9.1 in the elderly group, 27.1±5 teeth in the non-older group. Forty-four older (14.6%) and five control (1.4%) patients were edentulous. The mean number of teeth, mean number of decayed teeth, and mean number of filled teeth were higher in the control group than in the older adults (p<0.001). The DMFT value was 20.2 in the older group, which was higher than that in the non-older group (9.9). The mean number of implants and crown-bridged teeth was higher in the older group (p<0.05). In radiographic

Table 1. The distribution of systemic diseases according to groups

	Older adults n (%)	Non-older n (%)	p
Cardiovascular disease	212 (60.6)	138 (39.4)	**0.00****
Respiratory disorders	46 (13.1)	7 (2)	**0.00****
Endocrine disorders	118 (33.7)	35 (10)	**0.00****
Hematologic disorders	6 (1.7)	17 (4.9)	**0.01***
Genitourinary disorders	27 (7.7)	3 (0.9)	**0.00****
Neuropsychiatric disorders	39 (11.1)	17 (4.9)	**0.002***
Musculoskletal disorders	24 (6.9)	9 (2.6)	**0.006***
Alergia	12 (3.4)	18 (5.1)	**0.17**
Gastrointestinal disorders	23 (6.6)	9 (2.6)	**0.009***
Dermatological disorders	4 (1.1)	3 (0.9)	**0.5**
Cancer, radiotherapy, chemotherapy	25 (7.1)	2 (0.6)	**0.00****
Eye disorders	7 (2)	3 (0.9)	**0.17**
Ear disorders	8 (2.3)	0	**0.004***

*p<0.05 , **p<0.001

Table 2. Habits of oral hgyiene and the other habits according to groups

	Older adults n (%)	Non-older n (%)	p
Tooth brushing habit **Once a day** **Twice a day** **Three times a day** **After every meal** **1-2-3 per week** **If you remember** **Doesn't brush at all**	87 (24.9) 69 (19.7) 8 (2.3) 3 (0.9) 21 (6) 67 (19.1) 51 (14.6)	107 (30.6) 115 (32.9) 16 (4.6) 3 (0.9) 17 (4.9) 65 (18.6) 22 (6.3)	**0.00****
Dental floss use	17 (5.5)	41 (11.7)	**0.00****
Reasons for applying to our clinic (the most common answer)	To make a dental prosthesis 106 (36)	Dental pain 126 (30.3)	**0.00****
Regularly dentist visit	316 (90.3)	270 (77.1)	**0.00****
When was the last time you went to the dentist? (the most common answer)	2-5 years ago 110 (31.4)	0-1 month ago 76 (24.9)	**0.01***
Bruxism	42 (12)	99 (28.4)	0.27

*p<0.05, **p<0.001

findings, the number of impacted teeth and caries in the non-older group, were statistically significantly higher than those in the older group ($p<0.05$). The radiographic findings are presented in Table 4.

Discussion

According to the results of the study, a more careful dental examination should be performed on older patients than is required on non-older individuals because these patients have more systemic diseases, a history of drug use, and inadequate oral hygiene.

One of the criteria of optimal aging is to maintain a natural, functional dentition throughout life. Poor oral health has already been determined in older patients due to conditions such as a high incidence of missing teeth, caries, periodontal diseases, tooth wear, and inadequate connection with the dentist. Although there are many studies regarding the oral health status of the elderly (2,5,7,8), no study has compared older adults with non-older patients. This study compared extraoral and intraoral findings, dental habits, demographic data, general health status, and radiographic findings of elderly and non-older patients.

Table 3. Extraoral and intraoral findings according to groups

	Older adults n (%)	Non-older n (%)	p
Extraoral findings			
Lymphadenopathy	17 (28.3)	43 (71.7)	**0.00****
Pain and sound in TMJ	28 (42.4)	38 (57.6)	**0.14**
Swelling	3 (0.4)	0	**0.12**
Intraoral findings			
Periodontal problem	304 (86.9)	346 (98.9)	**0.00****
Caries	190 (54.3)	251 (71.7)	**0.00****
Tooth wear	198 (56.6)	50 (14.3)	**0.00****
Red-blue lesions	144 (41.1)	41 (11.7)	**0.00****
White lesions	24 (6.9)	30 (8.6)	**0.24**
Vesiculo-bullous lesions	5 (1.4)	11 (3.1)	**0.10**
Ulcerated lesions	18 (5.1)	13 (3.7)	**0.23**
Pigmentation	38 (10.9)	34 (9.7)	**0.35**
Variant of normal	75 (21.4)	123 (35.1)	**0.00****
Abscess-fistula	15 (4.3)	15 (4.3)	**0.57**
Tongue lesions	192 (54.9)	131 (37.4)	**0.00****
Lesions related to prothesis	40 (11.4)	2 (0.6)	**0.00****
Infection-related lesions (such as alveolitis, pericoronitis, osteomyelitis)	6 (1.7)	38 (10.9)	**0.00****

**p<0.001
TMJ: Temporomandibular joint

Table 4. Radiographic findings according to groups

Radiographic Findings	Older adults n (%)	Non-older n (%)	p
Caries	211 (60.3)	257 (73.4)	**0.001***
Periapical lesion	139 (39.7)	113 (32.3)	**0.02***
Bone loss (horizontal or vertical)	339 (96.9)	187 (53.4)	**0.00****
Impacted tooth	21 (6)	129 (36.9)	**0.00****
Embedded residual root	44 (12.6)	19 (5.4)	**0.001***
Internal-external root resorption	2 (0.6)	8 (2.3)	**0.05**
Changes in TMJ bone structures (such as sclerosis, flattening)	139 (39.7)	110 (31.4)	**0.01***
Soft tissue calcifications	85 (24.3)	51 (14.6)	**0.001***
Stylohyoid ligament calcification	264 (75.4)	274 (78.3)	**0.21**
Cyst-tumor	9 (2.6)	8 (2.3)	**0.50**

*p<0.05, **p<0.001
TMJ: Temporomandibular joint

Treatment requirements are high due to the increasing older population and their poor oral health. Oral health is part of a patient's general health, and it has been reported that poor oral-dental status is associated with general health in older patients (19,20). It is important to understand the relationship between oral health and systemic disease to prevent the onset or worsening of chronic systemic disease. The prevalence of systemic chronic diseases was quite high among older adults, and they consume more medications than individuals in other age groups. The prevalence of chronic diseases ranges from 54.6% to 90% in older dental patients in Turkey (7,21,22). In this study, this rate was 85.1% in older adults and 31.4% in non-older patients. The literature reported that the highest incidence of disease in older adults is in the cardiovascular system; this study finds the same. Cardiovascular system diseases were more prevalent than other diseases in both older adults and non-older patients in this study. Excessive smoking (34.3%) in non-older patients may be the cause of their cardiovascular system diseases.

Polypharmacy, which causes important problems such as increased healthcare costs, adverse drug reactions, and drug-drug interactions, is an expanding concern among older adults (23). The incidence of Turkey's population aged 65 years and over receiving at least one prescription medication was quite high (65-85%); this is similar to other countries in the world (7,24-26). The prevalence of drug use was determined as 79.1% in older adults and 20.9% in non-older patients.

In this study, the use of anticoagulants was specifically questioned because it is important for dental practices due to bleeding complications (27). Since the prevalence of thromboembolic events increases with age, anticoagulant use has been more prevalent in older patients than in non-elderly patients. The prevalence of anticoagulant use in older adults (32.3%) was much higher than in non-elderly patients (2.6%). Previous studies have reported that the incidence of tooth loss is high in older adults, and this has a significant effect on oral health and quality of life (28,29). Factors associated with tooth loss in older adults included systemic diseases that caused inadequacy in providing oral hygiene and affected oral tissues with chronic systemic inflammation, periodontitis, unrestorable teeth (either from fractures or deep root caries), and various medications and treatments that caused dry mouth and education level (30). Approximately 30% of the population aged 65-74 years is edentulous, as the World Health Organization reported in 2015 (31).

Edentulism causes aesthetic problems and affects functional abilities such as speaking and chewing (32). The prevalence of edentulism in the older population has shown a decreasing tendency in recent years. Although the rate of edentulousness in the older population was 75% in 1990 in Turkey, this rate has been reported as being between 11.6% and 67.4% in studies conducted since then (7,8,33-36). The different rates between studies may be due to the use of different study populations in the studies (7,8,33-36). In this study, the edentulous rate was 14.6% in older adult patients and 1.4% in the control group.

In older adult people, the inadequacy of oral hygiene habits can result from low education levels and conditions such as systemic diseases (musculoskeletal diseases, ophthalmologic problems, etc.) that negatively affect the patient's manipulation ability (37). The reasons for poor oral health can include not visiting the dentist regularly, in addition to inadequate oral hygiene habits (38). The majority of both study groups reported not visiting the dentist regularly. The majority of the older adult reported brushing their teeth once a day, whereas the control group mostly brushed their teeth twice a day. Studies in the literature (39,40) have reported that the proportion of partially dentate or edentate elderly is more than non-older people, similar to our study. Therefore, the use of removable dental prostheses in older adults is also increasing. We are more likely to encounter poor oral health due to gingivitis, periodontitis, and root caries resulting from plaque accumulation and lack of oral hygiene practices in older adults who use removable dental prostheses. In this study, most of the older adult patients using removable prostheses were using partial dentures, whereas most of the control group did not have any fixed or removable prostheses (41).

Dry mouth or xerostomia, a subjective feeling, may be caused by medications, systemic diseases such as Sjögren's syndrome, diabetes mellitus, psychological factors, dehydration, and head and neck radiotherapy. It is a frequent complaint in the older population; however, it can occur at any age. Dry mouth was higher in the elderly who had endocrine system diseases who received chemotherapy and radiotherapy for cancer. However, a comparison of epidemiological estimates from studies on older populations concluded that approximately 1 in 5 older people suffer from dry mouth (42,43). In this study, dry mouth complained in the majority of older patients, similar to previous studies, but not in the control group. Dry mouth prevalence was found higher (62.6%) than in the studies in the literature (10% to 38%) in the older adult population. The cause of this condition may be the level of medication use and disease in elderly individuals. The other reason may be the number of removable dentures used in the majority of older adults. Arslan et al. (43) reported a significant association between problems associated with dentures and dry mouth among older adults with dentures.

Aging oral mucosa is more permeable to detrimental factors and more inclined to a mechanical hazard. Oral mucosal lesion risk increases the presence of removable dentures and dry mouth (22). The literature has stated that there is a wide variation in the

prevalence of oral mucosal lesions in older adults, ranging from 2.4% to 98%. A universally accepted classification system for oral mucosal lesions is not available, which may be the reason for this difference among the studies (44). In the present study, this prevalence was 82.6%, which was more than non-elderly. Similar to several previous studies, the present study found that tongue lesions were the most prevalent lesions among oral mucosal lesions. The literature has shown that tongue lesions constitute the majority of oral mucosal lesions, and their prevalence varies in different parts of the world (45-47).

It has been reported that the TMJ degenerates with age, similar to other joints. The prevalence of temporomandibular disorders in older adults is relatively high, but the clinical symptoms are minimal. However, it was reported that approximately 45-70% of older adults had degenerative changes in the TMJ, as perceived by radiological examination (48). In the present study, 39.7% of older adults had degenerative changes in the TMJ on radiological examination, and this rate was higher than that of non-older patients (31.4%).

Previous studies have stated that temporomandibular disorder symptoms tend to decrease with age; nevertheless, pain and sound in the TMJ were the most common findings in extraoral examination in elderly patients compared with non-older patients; this is similar to several previous studies (49,50). Because panoramic radiography imaging is quick and simple, it is a well-suited diagnostic tool for evaluating dental and jawbone changes in older adults. Recent studies have reported that dental diseases, especially ones such as apical periodontitis, are risk factors for some systemic diseases commonly found in the elderly, like coronary artery disease and diabetes mellitus. In the present study, the prevalence of periapical radiolucencies was 39.7% in older adults and 32.3% in non-older adults. Cardiovascular system disease was the most common, both in older adults and non-older individuals. However, edentulous was more common in the elderly. The prevalence of periapical radiolucencies ranging from 18% to 41% in older adults has been reported (18,51).

The prevalence of residual roots in older adults ranges from 4% to 18% (18,47). It was 12.6 % in older adults, similar to studies in the literature, and 5.4 % in non-older in the present study. The rates of impacted teeth in studies ranged from 6.4% to 15%, which is more than in the present study (18,51). In the present study found 6% in the elderly patients and 36.9% in the non-older patients. The different rates in the studies may be due to the difference in the number of elderly patients studied. However, the high rate of edentulism in older adults and the extraction of impacted teeth before the construction of removable dentures may explain the high rate of impacted teeth in non-older people.

Study Limitations

The number of the study population was a little low. Studies with a larger patient population should be conducted to represent the older population.

Conclusion

It is important to perform a more careful dental examination in older adults than in non-older individuals because these patients have more systemic diseases, drug use, and do not have adequate oral hygiene. This is particularly true because the risk of oral cancer increases with age, making it essential to not miss an examination of the oral mucosa and to perform a complete radiological evaluation. Therefore, the development of geriatric dentistry can be achieved by taking license lessons and increasing dentists' awareness during training.

Ethics

Ethics Committee Approval: Süleyman Demirel University Faculty of Medicine Clinical Research Ethics Committee approved this study (decision number: 69, date: 21.03.2018).

Informed Consent: The informed consent form was read and signed by the participants to inform them about the study purpose and methodology.

Authorship Contributions

Concept: E.B., Design: Ö.G., Data Collection or Processing: S.S.Y., Analysis or Interpretation: E.B., Literature Search: E.B., Ö.G., Writing: E.B.

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ORIGINAL RESEARCH

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Effect of Coherent Breathing Versus Inspiratory Muscle Training on Risk of Falling and Functional Capacity in Older Adults

Sherif Osama Abdelsalam Elabd[1], Rana Hesham Mohamed Elbanna[2], Hany Ezzat Obaya[2], Gehad Ali Abdelhaseeb[2]

[1]May University Faculty of Physical Therapy, Department of Physical Therapy for Internal Medicine, Cairo, Egypt
[2]Cairo University Faculty of Physical Therapy, Department of Cardiovascular/Respiratory Disorders and Geriatrics, Giza, Egypt

Abstract

Objective: This study aimed to compare the impact of inspiratory muscle training (IMT) and the coherent breathing technique on the old population's gait, balance, and functional capacity.

Materials and Methods: This randomized controlled trial included 90 older individuals who were allocated into the IMT, coherent breathing, and control groups. The participants' ages varied between 62 and 68 years, and their body mass index was 25 to 30 kg/m^2. The IMT group received an IMT program, the coherent breathing group received a program of coherent breathing exercises, and the control group did not receive any intervention. The investigation was extended to 12 weeks, with a frequency of three sessions per week. The Tinetti performance oriented mobility assessment (POMA) was employed to assess the balance and gait level of the participants, while their functional capacity was assessed utilizing the six-minute walking test (6MWT) before and after the intervention.

Results: The POMA score and the 6MWT outcomes were significantly increased in the IMT and coherent breathing exercises ($p \leq 0.05$), and no significant variation was detected in the control group. However, the IMT group showed increased improvement in balance and functional capacity compared with the coherent breathing group.

Conclusion: Our study outcomes exhibited that both IMT and coherent breathing exercises played a vital role in enhancing functional capacity and decreasing the risk of falls in older individuals. However, the IMT exhibited more efficacy in improving balance, gait, and functional capacity compared with coherent breathing.

Keywords: Breathing exercises, respiratory muscles, quality of life, fall risk, older adults

Introduction

The advanced aging of people and the issues associated with the care of older society have become an emergency for all healthcare systems. Aging has increased the need for health and social services. There is a pressing need for a fundamental change in healthcare systems, switching from a focus on managing diseases to adopting a more functional strategy based on integrated, coordinated, continuous, and patient-centric care (1). The World Health Organization has stated that policies associated with health must be examined from the perspective of an older individual's functional capacity rather than focusing on illnesses or comorbidities encountered at certain moments (2). Falls are among the primary causes of morbidity and mortality in older adults. Interruptions in motor function (e.g., balance and gait) (3), impairment of functional ability, and a variety of other variables (4) determine fall risk. Multiple studies have shown that the onset of poor gait (5) or balance (6) is a significant marker of falls in older people. Although the frequency of falls among senior Egyptians is not dangerously high, it may be lowered because the goal should be zero falls. Recent investigations have indicated that rehabilitation and

Address for Correspondence: Sherif Osama Abdelsalam Elabd, May University Faculty of Physical Therapy, Department of Physical Therapy for Internal Medicine, Cairo, Egypt
Phone: +20 106 722 74 04 **E-mail:** sherif.osama@muc.edu.eg **ORCID:** orcid.org/0000-0003-2393-9961
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Clinical Trial Registration: The clinical trial registration number is NCT05767372.

community interventions are used for training and educating older adults to increase their physical fitness and minimize their fear of falling (7). Diaphragmatic breathing training raises intra-abdominal pressure (IAP) and activates deep trunk muscles (8), leading to increased spine stiffness. Consequently, IAP modulation adds a method for the central nervous system to manage spinal stability during functional activities, as it may simplify this regulation by providing an indirect increase in stiffness (9). This acquisition of postural stability may result in positive gains in balance and functional capacity (10). Coherent breathing has been shown to modulate the production of stress hormones by supporting equilibrium in the autonomic nervous system by stimulating the parasympathetic system or secreting relaxation hormones, which help counteract the prevailing state of sympathetic dominance; consequently, coherent breathing has been shown to modulate sympathovagal balance, improving functional ability (11). Inspiratory muscle training (IMT) has been extensively utilized in many populations, including healthy individuals and those with medical disorders, particularly in older adults. Its benefits have been scientifically established not only in enhancing inspiratory muscle strength but also in reducing dyspnea, improving exercise capacity, enhancing quality of life (QoL), and impacting other medical aspects (12). Therefore, it is possible to hypothesize that different diaphragmatic training approaches, like IMT or coherent breathing, could improve gait balance and functional ability in older adults. Therefore, this investigation aimed to compare the impact of the two different breathing techniques on functional ability and balance in older individuals.

Materials and Methods

Ethical Approval

The Research Ethics Committee of Cairo University's Faculty of Physical Therapy authorized this study (approval number: P.T.REC/012/003819, date: 21.06.2022). The clinical trial registration number is NCT05767372. Before completing the informed consent form, each patient received a comprehensive description of the purposes and methodologies of the study.

Sample Size, Randomization, and Blinding

G* Power version 3.1.9.7 was used to identify the sample size. A prior type of power analysis was used with α error probability of 0.05 and power (1-β error probability) equal to 0.95. A total of 72 participants was the minimum sample size for the investigation. Considering a possible attrition of approximately 15%, the sample size was increased to 30 per group. The participants were separated into IMT, coherent breathing, and control groups at random by randomized block process (Figure 1). MS Excel 2013 software was used to produce the random sequence.

Participants

The investigation was designed as a prospective, parallel randomized controlled trial. This study was conducted in the outpatient clinic of Cairo University's faculty of physical therapy. Ninety older adults (62 to 68 years old) agreed to participate and were distributed equally at random into the IMT (received IMT program), coherent breathing (received coherent breathing program), and control (no intervention) groups. The participants were encouraged to consume various foods from each food group, focusing on the nutrients, including potassium, calcium, dietary fiber, and vitamin B12. In addition, they were instructed to choose foods with little to no added sugar, saturated fats, or sodium and to obtain enough protein portion (1.2-1.4 g/kg) with 800 IU of vitamin D daily. The inclusion criteria included those above sixty years old and nonsmokers. The exclusion criteria were as follows: age below 60 years, chronic pulmonary disorder (e.g., obstructive lung disease, asthma), low back pain with a moderate or severe degree (Oswestry low back pain disability questionnaire >21%), falling fear (activities balance confidence scale <67%), deficiencies of cognitive abilities (mini-mental state examination score <24), having fallen in the prior 2 years, cardiac disorders restricting physical activities, uncontrolled diabetes, taking beta-blocker medicine, vertigo in the previous six months, presently receiving balance training (like Tai Chi and pilates), using any assistive devices, and any metabolic, endocrinal, or respiratory disorder.

Intervention Procedure

Coherent Breathing Group

The key component of coherent breathing is achieving mental and physical relaxation by modulating the breathing pace to approximately five breaths per minute, inhaling for 6 s, and exhaling for 6 s so that one breath lasts for 12 s and five breaths per minute. After the evaluation, patients underwent a coherent breathing training program. They were placed in an upright, relaxed position with no inclination exceeding 45°. They were given the following instructions: take three or four deep breaths using their diaphragm, use a stopwatch to check the intervals, and put one hand on the abdomen and the other on the level of the diaphragm to assess their ability to perform breathing. Then, the participants were instructed to inspire for 4 s and then expire for 4 s, repeat this for 1 min, and repeat the previous step but elongate their inspiration and expiration for 5 s. Then, they were asked to inhale deeply and slowly for 6 s and then exhale for around 6 s. The set was continued for 10 min with two intervals for a total session duration of 30 min (13). The sessions were performed three times a week for 12 weeks.

IMT Group

This group used a threshold IMT (threshold IMT device HS730, Respironics NJ, USA) equipped with a spring-loaded one-way

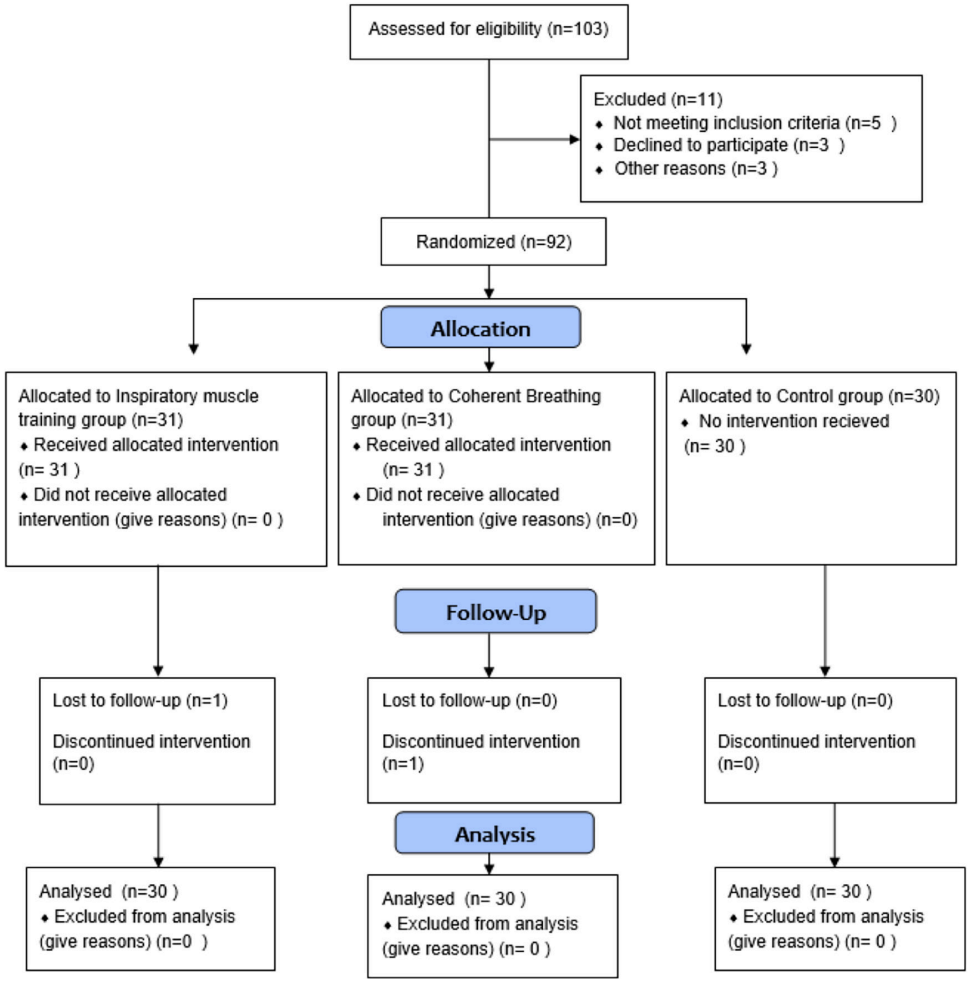

Figure 1. The flowchart

valve that offers adjustable resistance during inspiration within a spectrum ranging from 9 to 41 cmH_2O (14). The patient was lying in a high supine position (45 degrees). The participants were then instructed to put a nose clip on the nose to allow breathing through the mouth and ensure that the lips were positioned around the mouthpiece without blockage from the tongue. Then, maximum training was detected as follows: the participants detected the intensity at which they could efficiently achieve 10 breathing cycles at maximum resistance based on the individual's pace of apparent power. Subsequently, the application was initiated with a low-intensity load of 20-30% of the participants' maximum 10-repetition technique utilizing an IMT device. Then, the intensity was developed slowly and monitored carefully until achieving 50% of maximum effort over three weeks as tolerated. The subjects took complete inspiration (maximal and deep inspiration) and then expired slowly. This breathing pattern lasted for 10-20 breaths. The participants were then instructed to repeat 4-6 times with rest in between 30 s (15). The program was conducted thrice weekly over 12 weeks.

Control Group

Individuals in this group did not receive any intervention, but performed their routine activities of daily living. However, their functional capacity, balance, and gait were evaluated before and after the duration of the study (12 weeks) utilizing the assessment approaches of our investigation.

Outcomes Measures

Six-minute Walk Test (6MWT)

The functional capacity of the subjects was assessed using the 6MWT. The measurements were performed in accordance with the American Thoracic Society's directions. Participants were instructed to walk as far as they could along a 30-meter hallway at their own pace for 6 minutes. Individuals were permitted to pause and relax during the test, which was conducted before and after the intervention. The maximum 6-minute walking distance was detected in meters (16).

Tinetti Performance Oriented Mobility Assessment (POMA)

The POMA was used to evaluate the fall risk. The POMA is divided into two components: one for balance and one for gait. The

balance part was used to assess balance when sitting or standing, while the other part was used to assess dynamic balance during walking. The total potential score was 28, including 12 for POMA gait and 16 for POMA balance, and a lower overall score suggests a higher risk of falling (17). According to Lin et al. (18), compared with different tests, the POMA has greater test-retest reliability, discriminant validity, and predictive validity for evaluating the risk of falling in older individuals.

Statistics

SPSS software version 22 was used to perform all statistical analyses. A comparison between the groups' features, including age, weight, height, and body mass index (BMI), was conducted using ANOVA, while the Kruskal-Wallis test was employed for comparing sex between groups. MANOVA was performed to compare the scores of 6MWT and POMA between the groups. However, multiple comparisons were conducted to identify differences between the groups. The significance level for all statistical tests was set at $p<0.05$.

Results

Typically, 90 participants were enrolled in this investigation and allocated equally and randomly into the following three groups: IMT, coherent breathing, and control groups. No significant variations were detected regarding the features of the individuals among all groups (p-value was 0.226, 0.059, 0.150, 0.066, and 0.835 for age, weight, height, BMI, and sex, respectively) (Table 1).

The findings indicated that the intervention of IMT or coherent breathing technique had a significant impact on the 6MWT in both groups, and no effect was detected in the control group; however, no significant variation was identified between the groups before the intervention (Table 2). Furthermore, significant variations were observed between all groups after intervention (p=0.003), and multiple comparisons exhibited significant differences between the IMT and control groups (Table 2). In addition, improvement was better in the IMT group (percent of change: 8.6%) compared to the group of coherent breathing (percentage of change: 2.7%), indicating that IMT had high efficacy (Table 2).

Table 1. Comparison of characteristics between groups

	IMT group (n=30)	Coherent breathing group (n=30)	Control group (n=30)	F-value	p
	X±SD	X±SD	X±SD		
Age (years)	65.2±2.7	64.9±3.1	66.1±2.7	1.511	0.226
Weight (kg)	73.6±6.9	77.2±7.6	77.6±6.4	2.925	0.059
Height (cm)	163.9±9.2	168.2±8.9	166±6.4	1.941	0.150
BMI (kg/m^2)	27.4±1.6	27.3±1.3	28.2±1.8	2.807	0.066
	n (%)	n (%)	n (%)		
Male Female	18 (60%) 12 (40%)	16 (53.3%) 14 (46.7%)	18 (60%) 12 (40%)		0.835

IMT: Inspiratory muscle training, X: Mean, SD: Standard deviation, p: Probability value, n: Number of participants, BMI: Body mass index

Table 2. Comparison between groups regarding 6MWT (m)

	IMT group (n=30)	Coherent breathing group (n=30)	Control group (n=30)	Comparison between group	
	X±SD	X±SD	X±SD	F-value	p
Before intervention	512.8±37.9	519.1±37.3	511.4±36.7	0.360	0.699
After intervention	556.8±67.7	532±37.1	512.1±36.1	6.199	0.003*
Percentage of change	8.60%	2.70%			
Comparison within group	p≤0.05*	p≤0.05*	0.055		
			MD	p	
IMT group vs. coherent breathing group			23.83	0.178	
IMT group vs. control group			44.7	0.003*	
Coherent breathing group vs. control group			20.87	0.265	

IMT: Inspiratory muscle training, X: Mean, SD: Standard deviation, p: Probability value, *: Significance, MD: Mean difference, n: Number of participants, 6MWT: Six-minute walking test, m: Metre

The outcomes revealed that both IMT and coherent breathing exercises had a significant effect on POMA scores ($p \leq 0.05$), and no alteration was observed in the control group; however, the comparison between all groups before intervention regarding this score indicated no significant variations (Table 3). According to the POMA score findings, significant variation was detected between all groups post-intervention was detected ($p \leq 0.05$), and multiple comparisons indicated significant variations between every group and each other (Table 3). Moreover, enhancement was higher in the IMT group (percentage of change: 18.1%) than in the coherent breathing group (percentage of change: 6.2%), indicating that IMT was more effective (Table 3).

Discussion

The study outcomes revealed that both IMT and coherent breathing exercise had a vital impact on older adults' function ability, gait, and balance; however, IMT exhibited more efficacy than coherent breathing exercise.

Stressful life events result in excessive activation of the fight or flight response, known as sympathetic overload, which has significant implications for morbidity and mortality. This imbalance in the autonomic nervous system results in a persistent state of excessive activity across all bodily functions. It is characterized by elevated biochemical levels, such as cortisol and epinephrine, elevated energy expenditure, and the generation of free radicals as byproducts. Consequently, this chronic state of hyperactivity leads to the depletion of energy (19). Prior investigation exhibited that coherent breathing has been shown to modulate that imbalance in the autonomic nervous system (11), improving functional ability, which might explain our study findings.

Restricted diaphragmatic movement impairs bodily functions and exerts additional strain on cardiovascular and gastrointestinal systems. Coherent breathing refers to the practice of slow and deep breathing, maintaining a pace of five breaths per minute while consciously relaxing during the exhalation phase, which serves as a means of exercising the diaphragm (20). The use of this self-regulatory approach has the potential to facilitate an equilibrium between the mind and body, thus enhancing overall health and perceived wellness.

According to previous reports, increased respiratory muscle strength has been demonstrated to benefit individuals with heart failure. These include the postponement of diaphragmatic fatigue, enhancement of ventilatory efficacy, and reduction of blood flow demands placed on the respiratory muscles during exercise (21). Consequently, sympathetic activity is reduced, leading to enhanced systemic vasodilation and improved perfusion of peripheral muscles, thereby increasing functional capability (21). Subsequently, according to this mechanism, IMT might increase functional capacity in older individuals.

Consistent with our research findings, a previous study implemented a 12-week IMT intervention, which yielded statistically substantial enhancements in forced vital capacity, forced expiratory volume in 1 second, forced expiratory flow 25%-75%, peak expiratory flow, maximal inspiratory and expiratory pressures, as well as 6-minute walking distance among older adults with atrial fibrillation (22). In their meta-analysis, Gosselink et al. (23) found a statistically significant minimum difference of 32 m in the 6-minute walking distance when comparing individuals with chronic obstructive lung disease who underwent IMT to those in the control group. According to a previous study, a 6-week regimen of thoracic stretching and breathing exercises conducted at home had favorable outcomes regarding thoracic cage expansion and physical function. These outcomes were assessed using the pulmonary function test and the 6MWT in a sample of healthy older adults (24). In addition, previous research included 45 patients who had three times of respiratory therapy using

Table 3. Comparison between groups regarding POMA

	IMT group (n=30)	Coherent breathing group (n=30)	Control group (n=30)	Comparison between groups	
	X±SD	X±SD	X±SD	F-value	p
Before intervention	21±1.1	21.1±1.1	20.9±1.1	0.179	0.836
After intervention	24.8±0.8	22.4±0.8	21±1.04	13.79	$p \leq 0.05^*$
Percentage of change	18.10%	6.20%			
Comparison within groups	$p \leq 0.05^*$	$p \leq 0.05^*$	0.577		
			MD	p	
IMT group vs. coherent breathing group			2.33	$p \leq 0.05^*$	
IMT group vs. control group			3.83	$p \leq 0.05^*$	
Coherent breathing group vs. control group			1.5	$p \leq 0.05^*$	

IMT: Inspiratory muscle training, POMA: Tinetti performance oriented mobility assessment, X: Mean, SD: Standard deviation, p: Probability value, *: Significance, MD: Mean difference, n: Number of participants

the active cycle of breathing approach per week for two consecutive months, and the findings illustrated a statistically significant enhancement in the outcomes of the 6MWT (25). Furthermore, the findings of a previous investigation have shown the efficacy of coherent breathing training in enhancing cardiorespiratory fitness among individuals in good health (26).

Furthermore, prior research exhibited that home-based pulmonary rehabilitation may have beneficial effects on functional ability, anxiety, depressive symptoms, and QoL in older individuals with chronic obstructive pulmonary disease and chronic respiratory failure (27). Moreover, a previous study indicated that a duration of 8 weeks of IMT resulted in enhancements in inspiratory muscle function, specifically peak inspiratory flow rate, maximal inspiratory pressure (MIP), peak inspiratory power, and dynamic balance capability, as evidenced by an increase in the mini-balance evaluation systems test score. Therefore, IMT was feasible and efficient for older adults without needing supervision, as it was conducted at home with no adverse consequences like falls or discomfort (28).

In contrast to the results obtained in our study, it was observed that in a cohort of older adults who were in good health and exhibited normal spirometry, respiratory muscle strength, and physical fitness, the implementation of IMT led to an increase in MIP and peak inspiratory flow; however, no significant changes were observed in other spirometry assessments, DNA damage levels in peripheral blood mononuclear cells, plasma cytokine concentrations, dynamic inspiratory muscle function, inspiratory muscle endurance, distance covered in the 6MWT, physical activity level, or QoL (29).

The outcomes of a previous study revealed that a thorough chest physiotherapy (PT) program lasting eight weeks led to notable enhancements in dynamic postural stability, spirometry, respiratory muscle strength, and functional capacity among pediatric patients diagnosed with cystic fibrosis; however, including IMT in chest PT did not result in further enhancements, except for the MIP value (30), which was in contrast with our findings.

Study Limitations

Some notable limitations should be addressed in this research. First, the physical activity history of the participants should be considered. Second, the psychological aspects of the individuals should be evaluated. Furthermore, our study participants comprised an integrated cohort of older individuals with a limited age range. Consequently, it is important to acknowledge that our findings may not be generalizable to the entire older adult population.

Conclusion

Coherent breathing technique and IMT can significantly improve functional capacity, gait, and balance in older individuals. However, the findings of our study indicated that IMT was more efficient than coherent breathing exercises.

Ethics

Ethics Committee Approval: The Cairo University Faculty of Physical Therapy's Research Ethical Committee provided written informed consent (approval number: P.T.REC/012/003819, date: 21.06.2022).

Informed Consent: Prior to completing an informed consent form, every patient received a comprehensive explanation of the objectives and methodologies of the research.

Authorship Contributions

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

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ORIGINAL RESEARCH

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Frailty as a Significant Predictor of COVID-19 Among Vaccinated Older Adults

Merve Hafızoğlu[1], Arzu Okyar Baş[1], Ahmet Sertçelik[2], Filiz Akbıyık[3], Merve Güner Oytun[1], Zeynep Şahiner[1], Serdar Ceylan[1], Cafer Balcı[1], Burcu Balam Doğu[1], Mustafa Cankurtaran[1], Banu Çakır[2], Serhat Ünal[4], Meltem Gülhan Halil[1]

[1]*Hacettepe University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, Ankara, Turkey*
[2]*Hacettepe University Faculty of Medicine, Department of Public Health, Ankara, Turkey*
[3]*Ankara City Hospital Laboratory, Siemens Healthineers, Ankara, Turkey*
[4]*Hacettepe University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Ankara, Turkey*

Abstract

Objective: To investigate polymerase chain reaction (PCR) confirmed symptomatic coronavirus disease-2019 (COVID-19) infection incidence in vaccinated older adults.

Materials and Methods: This prospective study comprised 483 adults aged 60 years and older, all vaccinated with 2 doses of inactivated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine. All participants had their anti-SARS-CoV-2 immunoglobulin G antibody titers checked and were simultaneously evaluated by comprehensive geriatric assessment, including frailty. We defined the overall survival time as the period from the date of blood collection for antibody responses through the event date [i.e., PCR confirmed (COVID-19) diagnosis] (if any), the time of the last visit or at the termination of data collection (November 25, 2021), whichever occurred first. Individuals who were vaccinated with the 3rd dose of any type were censored at the time of vaccination and removed from further follow-up.

Results: The incidence of symptomatic COVID-19 was significantly higher in the frail group, with a cumulative incidence of 7.1% and 2.2% in the frail and non-frail groups, respectively (p=0.02). In Cox regression analysis, the clinical frailty scale (CFS) score was found to be a significant predictor for breakthrough COVID-19 infection [hazard ratio: 3.2 (95% confidence interval: 1.0-9.9), p=0.04].

Conclusion: High CFS scores among vaccinated older adults should be considered as an easy-to-assess, high-risk marker for predicting breakthrough COVID-19 infection.

Keywords: SARS-CoV-2, Sinovac, CoronaVac, older people, frailty

Introduction

Coronavirus disease-2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first reported in late 2019. The World Health Organization declared the pandemic on March 11, 2020 (1). SARS-CoV-2 causes a wide variety of clinical conditions, from pneumonia to multi-organ failure. In older adults, symptoms and course of COVID-19 may be different from those in young individuals; hospitalization and mortality rates may be higher; and the efficacy and effectiveness of the COVID-19 vaccine may be lower because of immunosenescence, which may not be explained solely by biological aging (2).

Frailty is defined as a clinical syndrome of decreased reserve to stressors and is strongly associated with increased disability, hospitalization, and mortality rates (3). Frail older adults have a poor prognosis for COVID-19, and some guidelines recommend routine evaluation of frailty status in COVID-19 patients (4). The majority of studies published so far have examined the

Address for Correspondence: Merve Hafızoğlu, Hacettepe University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, Ankara, Turkey
Phone: +90 530 159 29 18 **E-mail:** mervehafizoglu@gmail.com **ORCID:** orcid.org/0000-0002-5401-223X
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relationship between frailty and the relevant course of COVID-19 only in unvaccinated individuals.

This prospective cohort study was a continuation of an earlier cohort study showing that frailty affects seroconversion in older adults, especially those 90 days and more after the second dose of vaccination (5). This study was conducted to investigate the occurrence and risk factors of breakthrough COVID-19 infections among those fully vaccinated (i.e., 2 doses) with the inactivated SARS-CoV-2 vaccine.

Materials and Methods

The study was conducted with 483 individuals, aged 60 years and older, who were subsequently admitted to the geriatric outpatient clinic from April 1, 2021, through July 1, 2021, for any reason and agreed to participate in the study. All participants were recruited from those vaccinated 2 doses of inactivated SARS-CoV-2 vaccine in the national COVID-19 mass vaccination program. At least 28 days following full vaccination, vaccine-induced anti-spike immunoglobulin G (IgG) antibody levels were measured, and a comprehensive geriatric evaluation was performed for each participant. Findings till this point have been published (5). The same cohort was further followed up until November 25, 2021, for breakthrough infections (if any) and related risk factors. Individuals reporting any other vaccine in the month preceding data collection and those receiving chemotherapy, immunosuppressive therapy, or regular dialysis treatment were excluded from the study.

For comprehensive geriatric assessment, the Katz activities of daily living (ADL) scale (6), Lawton-Brody instrumental ADL (7), mini-mental state examination (MMSE) (8), Yesavage's geriatric depression scale (YGDS) (>5 points were defined as depression) (9), Charlson comorbidity index (CCI) (10), strength, assistance walking, rising from a chair, climbing stairs, and falls (SARC-F) questionnaire (11), mini nutritional assessment-short form (MNA-SF) (scores ≥12 points were defined as normal, scores <11 malnutrition and risk of malnutrition) (12), 4 m walking test for gait speed measurement (where values below 0.8 m/sec were evaluated in favor of low physical performance), and handgrip strength (HGS) test (where the low HGS was described as HGS <16 kg for women and <27 kg for men) were performed successively (13). Information was also collected on post-vaccination side effects (fever, myalgia, headache) and polypharmacy (≥5 drug usage) (if any).

Frailty status was evaluated using the clinical frailty scale (CFS), as validated earlier in the Turkish population by Özsürekci et al. (14). CFS was performed by giving a score between 1 and 9 (1: very fit; 2: well; 3: well with the treated comorbid disease; 4: apparently vulnerable; 5: mildly frail; 6: moderately frail; 7: severely frail; 8: very severely frail; and 9: terminally ill). Participants were later grouped as "frail" (CFS >4) and "non-frail" (CFS ≤4), based on the total scores obtained from the CFS (14). The CFS scores of all participants were determined by the same specialist physician who had previously been trained.

Blood samples were collected at least 28 days after the second dose of Sinovac's SARS-CoV-2 inactivated vaccine (CoronaVac). SARS-CoV-2 spike-specific antibody IgG levels were quantitatively measured using a Siemens Atellica IM sCOVG kit with a measuring interval between 0.50 and 150.00 index (U/mL) for all cohort members. Individuals with IgG value ≥1.0 were defined as "seropositive", while any value <1 was reported as "seronegative". The concentration of the reference standard that corresponds to the cut-off value of 1.00 index (U/mL) for the assay is 21.80 BAU/mL (15). Technical methods are detailed in a previous study (5).

The primary dependent variable (event in survival models) was defined as contracting symptomatic COVID-19, as confirmed by reverse transcription-polymerase chain reaction (PCR). In the survival analysis, 3 groups were determined according to the end of the follow-up period. The follow-up period started from the date when the blood sample was obtained for antibody testing for all participants. The study was completed for the first group at the time of symptomatic COVID-19, for the second group at the time of the 3rd dose of anti-SARS-CoV-2 vaccine, and for the third group at the time of November 25, 2021 (as patients in the third group did not receive their third dose of vaccines or did not have symptomatic COVID-19 until the end of the follow-up period).

The study's ethics approval was obtained from the Hacettepe University Clinical Research Ethics Committee [approval number: 2021/29-09 (KA-21129), date: 14.12.2021]. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Informed consent was obtained from all participants included in the study.

Statistics

Data collected were analyzed using SPSS v.22.0 (IBM). Categorical variables are presented as counts and percentages (n/%). The chi-square test or Fisher's exact test were used for intergroup comparisons. The Kruskal-Wallis test was used to compare numerical parameters with more than two categorical data. The distribution of continuous variables was evaluated using the Kolmogorov-Smirnov test. Measures of central tendency and dispersion are presented as mean (± standard deviation) or median [interquartile range (IQR)], as appropriate. Bonferroni correction was used in a post-hoc analysis, as needed. Kaplan-Meier analysis was used to estimate the probability of

outcomes of interest, considering the time to event/censoring. Univariate effects of variables on survival were investigated using the log-rank test. The full (initial) Cox regression model included all potential confounders besides frailty (the main exposure) and seropositivity at baseline; the most explanatory multivariate model was presented as the final model. Variables with p<0.2 were determined as candidates by the chi-square test. In terms of the multicollinearity problem, the final model was created by considering the correlation status and model fit. The omnibus test result was used to evaluate the model fit, and the multivariate model omnibus test p-value was 0.18. A 5% type 1 error was used to infer statistical significance in all analyses.

Results

Of the 483 recruited participants, the CFS scores were completed for 465 individuals; thus, the sample size was 483 for descriptive and 465 for frailty-associated analyses. Of the participants, 99 (21.2%) were considered "frail". The median (IQR) age was 72 (11) years; 295 (61.1%) were female. The median follow-up time was 64 (58) days, with a range of 1-234 days. The time from the second dose of vaccination to the measurement of antibody response ranged from 28 to144 days with a median (IQR) of 74 (52) days. The number of seropositive participants was 328 (70.2%) in the study group, and the median (IQR) serum spike IgG levels were 2.1 (4.5) AU/mL and 46.1 (104.5) BAU/mL.

Table 1. Demographic features according to the frailty status

	Frail n=99 (21.2%)	Robust n=366 (78.7%)	p
Age (year)	75.5 (12)	71 (10)	<0.001
Female gender [n (%)]	61 (61.6%)	224 (61.2%)	0.51
Comorbidities [n (%)]			
DM	40 (40.4%)	151 (41.3%)	0.90
HT	77 (77.8%)	261 (71.3%)	0.25
HL	24 (24.2%)	111 (30.3%)	0.26
CHF	11 (11.1%)	28 (7.7%)	0.30
CAD	33 (33.3%)	85 (23.2%)	0.05
AF	16 (16.2%)	34 (9.3%)	0.06
Hypothyroidism	13 (13.1%)	72 (19.7%)	0.14
CKD	13 (13.1%)	12 (3.3%)	<0.001
CA	11 (11.1%)	44 (12%)	0.48
Rheumatological disease	9 (9.1%)	32 (8.7%)	0.84
Depression	9 (9.1%)	25 (6.8%)	0.51
COPD-Asthma	10 (10.1%)	37 (10.1%)	0.58
Basic ADL	5 (4)	6 (0)	<0.001
Instrumental ADL	4.5 (5.25)	8 (0)	<0.001
MMSE	24 (6.25)	28 (4)	<0.001
Geriatric depression scale	5 (6)	2 (4.5)	<0.001
Charlson comorbidity index	1 (2)	1 (2)	<0.001
CFS	5 (1)	3 (1)	<0.001
SARC-F	5 (3)	1 (2)	<0.001
MNA-SF	12 (4)	14 (2)	<0.001
Polypharmacy [n (%)]	73 (73.7%)	193 (53.2%)	0.001
Handgrip strength (kg)	16.1 (7.05)	21.1 (12.1)	<0.001
Gait speed (m/sec)	0.52 (0.42)	0.90 (0.30)	<0.001
Presence of adverse reactions [n (%)]	12 (12.5%)	25 (6.9%)	0.07
SARS-CoV-2 spike IgG serum level (AU/mL)	1.69 (4.67)	2.15 (4.80)	0.31
SARS-CoV-2 spike IgG serum level (BAU/mL)	36.8 (101.8)	46.8 (104.5)	0.31
Seropositivity [n (%)]	62 (62.6%)	266 (72.7%)	0.06
COVID-19 diagnosis confirmed by PCR positivity [n (%)]	7 (7.1%)	8 (2.2%)	0.02

DM: Diabetes mellitus, HT: Hypertension, HL: Hyperlipidemia, CHF: Chronic hearth failure, CAD: Coronary artery disease, AF: Atrial fibrilation, CKD: Chronic kidney disease, CA: Cancer history, COPD: Chronic obstructive pulmonary disease, ADL: Activities of daily living, MMSE: Mini-mental status examination, CFS: Clinical frailty scale, SARC-F: Strength, assistance walking, rising from a chair, climbing stairs, and falls, MNA-SF: Mini nutritional assessment-short form, SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, IgG: Immunoglobulin G, COVID-19: Coronavirus disease-2019, PCR: Polymerase chain reaction

Participants were compared by their frailty status. Accordingly, ADL scores, MMSE, YGDS, CCI, CFS, SARC-F, MNA-SF, prevalence of polypharmacy, HGS test, and gait speed were significantly different among frail participants versus those considered as non-frail (p<0.001). Rates of adverse vaccine reactions were relatively higher in the frail group, but the difference was not statistically significant (p=0.07). PCR-confirmed COVID-19 incidence was significantly higher in the frail group (n=7, 7.1%) than in the non-frail group (n=8, 2.2%), (p=0.02) (Table 1). There was no significant association between frailty and serum anti-spike IgG levels (p=0.31) or seropositivity rates (p=0.06).

During the follow-up period, PCR-confirmed COVID-19 infection was detected in 15 participants (3.1%). Eight adults diagnosed with symptomatic COVID-19 infection later received a third dose of COVID-19 vaccine. The other 7 patients with a COVID-19 diagnosis did not have a third COVID-19 vaccine before the end of data collection. Of the 15 incident COVID-19 cases, 10 had mild disease and were treated at home; 3 patients were hospitalized in COVID clinics and 2 patients required intensive care unit (ICU). Computerized tomography findings were in 4 of the patients followed in the hospital. Four patients required non-invasive mechanical ventilation and one patient required invasive mechanical ventilation. While a patient followed in the ICU died, the others were discharged with full recovery. The fatality rate for COVID-19 was 6.7% (n=1) and the mortality rate from all other causes throughout the data collection period (up to 8 months total) was 2.3% (n=11).

Kaplan-Meier survival curves comparing the risk of symptomatic COVID-19 infection across age groups, seropositivity, and frailty did not suggest any statistically significant difference across groups. However, divergence in curves was prominent in all figures (1-3) after day 150.

Breakthrough COVID-19, in Cox regression, was found to be statistically significantly associated with the CFS score [hazard ratio: 3.2 (95% confidence interval: 1.0-9.9), p=0.04], controlling for age, gender, MNA-SF score, CCI, and seropositivity at baseline (Table 2).

Discussion

In this study, two findings are remarkable assets to the literature: 1) Frailty is associated with symptomatic breakthrough COVID-19 infections in vaccinated older people, adjusting for vaccine-induced seropositivity; 2) CFS can be used as a high-risk marker for symptomatic breakthrough COVID-19 infections, controlling for age, gender, CCI, MNA-SF score, and anti-SARS-CoV-2 antibody titers. The study confirmed that vaccine-induced seropositivity is highly protective against symptomatic breakthrough COVID-19 infections in older adults vaccinated with two doses of the inactivated CoronaVac vaccine. Unfortunately, the rather short follow-up period warrants further research on the protective effect of CoronaVac over longer periods.

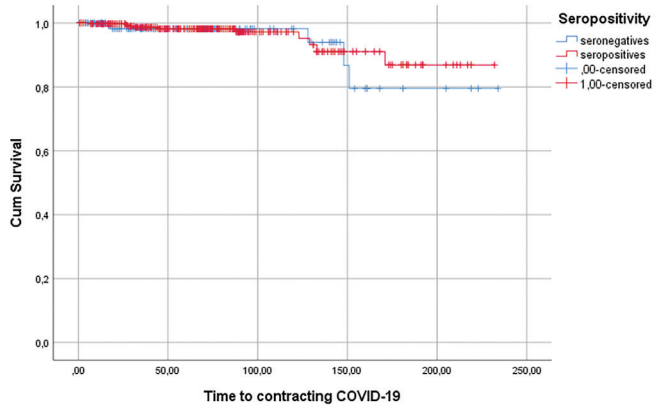

Figure 1. Kaplan-Meier analysis of the seropositive group and seronegative group (p=0.66, log-rank test)

COVID-19: Coronavirus disease-2019, Cum: Cummulative

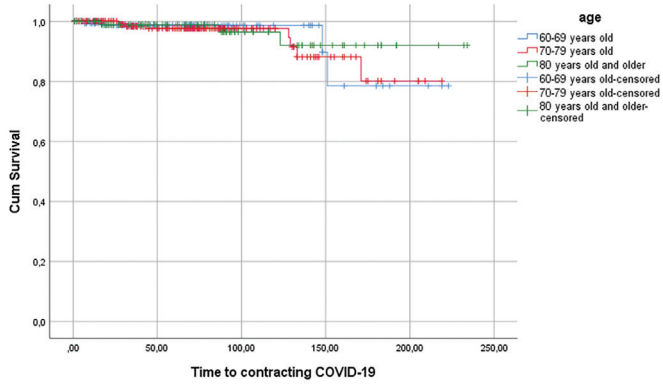

Figure 2. Kaplan-Meier analysis of the age groups (p=0.79, log-rank test)

COVID-19: Coronavirus disease-2019, Cum: Cummulative

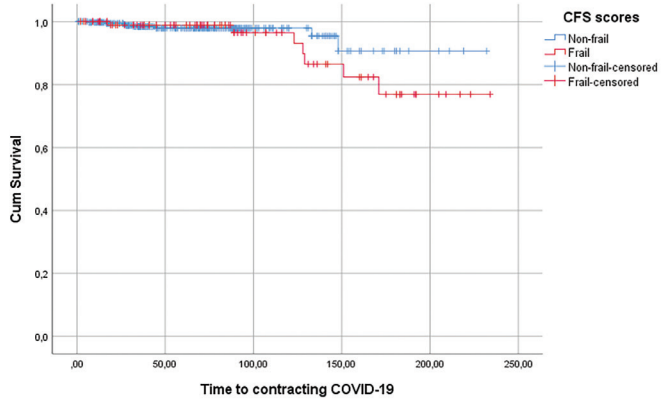

Figure 3. Kaplan-Meier analysis of the frail group and robust group (p=0.73, log-rank test)

COVID-19: Coronavirus disease-2019, Cum: Cummulative

Table 2. Risk factors for contracting COVID-19 in the regression analysis

	Univariate		Multivariate	
Risk factor	HR (95% CI)	p	HR (95% CI)	p
Age	0.98 (0.91-1.05)	0.54	0.95 (0.88-1.03)	0.26
Female gender	0.56 (0.20-1.56)	0.26	0.44 (0.15-1.28)	0.17
CFS score	1.76 (0.61-5.07)	0.29	3.2 (1.0-9.9)	0.04
MNA-SF score	1.30 (0.91-1.86)	0.14	1.45 (0.99-2.14)	0.05
CCI	1.02 (0.75-1.39)	0.88	1.02 (0.75-1.38)	0.65
Seropositivity	0.78 (0.26-2.29)	0.65	0.73 (0.24-2.22)	0.58

HR: Hazard ratio, CI: Confidence interval, COVID-19: Coronavirus disease-2019, CFS: Clinical frailty scale, MNA-SF: Mini nutritional assessment-short form, CCI: Charlson comorbidity index

Frailty is a multifactorial clinical condition, and tests performed to assess frailty have been developed on 2 basic frailty models: the biological frailty model and the cumulative deficit model (16). CFS is a reliable cumulative deficit screening tool to identify frailty and is easy to use in both outpatient and inpatient clinics, including emergency departments and ICUs (3). In this study, frailty was ascertained by CFS. The diagnosis of COVID-19 confirmed by PCR positivity was found to be significantly higher in the frail group. Meta-analyses showed that frail patients were more susceptible to COVID-19, and even that each 1-point increase in the CFS score was associated with a 12% increase in mortality (3). In our study, frail patients were older and had lower overall geriatric assessment scores. Similarly, vaccine-induced antibody levels were negatively associated with frailty but did not reach statistical significance. Previous studies have shown higher rates of hospitalization, morbidity, and mortality in men (17). Similarly, women had better COVID-19-free survival rates in our study. Accordingly, in the survival analysis of the model, the potential association between frailty and symptomatic COVID-19 infection in vaccinated older adults, age, geriatric assessment scores, and seropositivity were adjusted for as potential confounders.

In a recent study, frailty was a better predictor of poor prognosis in COVID-19 patients than comorbidities, and the authors recommended early frailty assessment to improve outcomes (18). Hewitt et al. (19) showed that frailty was a better predictor than age for survival in hospitalized patients diagnosed with COVID-19. Mortality rates in hospitalized COVID-19 patients were found to be higher in the frail group in another study that used the hospital frailty risk score for frailty assessment (20). In our study, a 1-point increase in the CFS score resulted in a 3.2-fold increased risk of COVID-19. We found frailty, but not biological age, as a predictor of PCR-confirmed COVID-19 infection among fully vaccinated older adults. Age, gender, CCI scores, and vaccine-induced antibody responses did not reveal any significant evidence for risk stratification. However, the COVID-19 diagnostic risk was positively associated with the MNA-SF scores, although close not significant at alpha 0.05. This has led us to emphasize the importance of malnutrition in older adults. Although COVID-19 itself can cause malnutrition, the presence of malnutrition also increases the risk of COVID-19 (21). Malnutrition was associated with an increased risk of transfer to the ICU in COVID-19 patients in an earlier study, emphasizing the importance of early nutritional screening in older people during the pandemic (22).

In our study, the prevalence of COVID-19 was 3.1%, and most patients presented with mild diseases. Of the infected participants, only one patient died because of COVID-19. In a short report published in our country, vaccination with the inactivated COVID-19 vaccine provided 90% protection from death (23). As of November 25, 2021, in Turkey, 12,840 deaths were reported out of 467,730 PCR-confirmed COVID-19 cases (24). This corresponds to a fatality rate of 2.7%. The fatality rate in our study population was 6.7% among the vaccinated. The inability to detect all COVID-19-related deaths at the national level may explain the inconsistency of observed versus expected fatality rates. The absence of national COVID-19 fatality data with breakdown by age, gender, comorbidity, etc., and the burden of variations in circulating variants over time hinder our ability to apprehend the magnitude of the fatality rate of 6.7% among vaccinated older adults, corresponding to the "expected" rate among their unvaccinated counterparts.

In both efficacy and effectiveness studies, the length of follow-up time is crucial to differentiate the potential effects of the vaccine, durability of vaccine-induced immunity, types of circulating variants, compliance with public preventive measures, daily case numbers, and the possibility of exposure to infected individuals. The shorter the follow-up time, the more likely it is that the true protective effect of COVID-19 vaccines can be established. In this study, the median follow-up was approximately 2-4 months after full vaccination, with the median (IQR) serum spike IgG level being 2.1 (4.5) AU/mL and 46.1 (104.5) BAU/mL. More precise results could be obtained with longer follow-ups, but the national mass vaccination campaign motivated all elderly individuals to receive a third

dose of the COVID-19 vaccine starting from July 1, 2021, which negatively affected our long-term follow-up. Therefore, our results for frailty on symptomatic breakthrough infection should be considered as "short-term" effects, and studies on longer follow-up times are warranted for conclusive answers.

The strengths of the study should also be highlighted. In the literature, most studies examining the relationship between the course of COVID-19 and frailty in older adults were conducted before the vaccination period. Because we evaluated the participants with known antibody responses in this study, we had the opportunity to show that the clinical frailty score may be superior to the antibody response in demonstrating the risk of contracting COVID-19.

Study Limitations

The findings of our study must be interpreted in light of several limitations. First, in our cohort, only symptomatic patients had a chance to be tested; thus, all events in the analysis were dependent on symptomatic COVID-19 cases. We may have missed cases who had asymptomatic disease after or were symptomatic, yet did not provide PCR samples. Second, given that the study included only those who presented to the geriatric outpatient clinic (for prescription, medical report, routine check-ups, or acute disease), the study findings may not be generalized to all vaccinated older adults. Third, in Turkey, the first 2 doses of vaccine were administered with the inactive vaccine by the national healthcare program, but personal preferences were at the forefront in the 3rd and 4th doses of vaccines; therefore, we could not continue the follow-up period after the 2nd dose of vaccination. Fourth, the actual time from the second dose of vaccination to the measurement of antibody response ranged between 28 and 144 days, which yields widely variable follow-up times for a given individual, which in turn affects COVID risk. Fifth, although patients on chemotherapy or immunosuppressive therapy were excluded, patients with immunosuppressive states or those who were not actively taking these therapies but had pre-existing diseases (such as malignancy in remission) were included, which may also affect vaccine response. Also, in the analysis, subgroup analysis of independent variables suggested a divergence after approximately day 150. This corresponds to the fall (September through November) in our timeline when national COVID-19 case numbers were inclining and delta variants became prominent in the population (24). These might have made the differences more prominent across groups. Similarly, variations in behavioral factors across subgroups and/or overtime need to be assessed in future studies for their potential role in breakthrough infections. Finally, the sample size of the population and especially the events were very small, with only 15 cases of COVID-19.

Conclusion

To the best of our knowledge, this is the first study investigating the outcome of older adults with known vaccine-induced antibody response after 2 doses of inactivated SARS-CoV-2 vaccination. We only found CFS scores as a significant predictor of breakthrough COVID-19 infection, controlling for age, gender, and seropositivity. High CFS scores among vaccinated older adults should be considered an easy-to-assess, high-risk marker for predicting breakthrough COVID-19 infection. Frail older people should be prioritized in COVID-19 vaccination campaigns, with the highest effective vaccine type at hand, and booster doses should be given earlier. Such an approach will not only maximize individual health among older adults but also COVID-19-related morbidity and mortality rates in populations.

Ethics

Ethics Committee Approval: The study's ethics approval was obtained from the Hacettepe University Clinical Research Ethics Committee [approval number: 2021/29-09 (KA-21129), date: 14.12.2021].

Informed Consent: Informed consent was obtained.

Authorship Contributions

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

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ORIGINAL RESEARCH

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The Impact of Geography and Occupation on the Perspective of the Good Death Among the Healthcare Professionals: A Cross-sectional Study

Fatma Özge Kayhan Koçak[1], Sibel Çavdar[2], Hülya Eskiizmirli Aygör[2], Süleyman Özçaylak[3], Ertan Saylan[4], Sevnaz Şahin[2], Yasemin Yıldırım[5]

[1]Bakırçay University Çiğli Training and Research Hospital, Clinic of Internal Medicine, Division of Geriatrics, İzmir, Turkey
[2]Ege University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, İzmir, Turkey
[3]University of Health Sciences Turkey, Gazi Yaşargil Training and Research Hospital, Clinic of Internal Medicine, Diyarbakır, Turkey
[4]Ege University Faculty of Medicine, Department of Internal Medicine, İzmir, Turkey
[5]Ege University Faculty of Nursing, Department of Internal Medicine Nursing, İzmir, Turkey

Abstract

Objective: The aim of this study was to investigate the perspective of good death and related factors among healthcare professionals (HCPs), as well as to compare the perspective of good death regarding to live region and occupation.

Materials and Methods: This cross-sectional study was performed one hundred ninety-five HCPs. The good death scale (GDS) was used to assess the perspective of HCPs on the concept of good death.

Results: A total of 195 HCPs were included in this study. One hundred twenty-four (63.6%) participants were women. Ninety-eight (50.3%) and 95 (48.7%) of the participants were registered nurses and were living in the east, respectively. Seventy-five (38.5%) of the participants had 11 years or more of professional experience, and 132 (67.7%) of them grew up in the region where they worked. The mean score of all participants in GDS was 57.5±6.3, and the mean scores of the sub-dimensions were 30.9±3.8 for the "psychosocial and spiritual sub-dimension", 10±1.9 for the "personal control sub-dimension" and 16.6±2.4 for the "clinical sub-dimension". In multiple linear regression, living in the east, being a nurse, being a woman, and taking education on "good death" were positively related to the GDS score of the HCPs.

Conclusion: Given the growing importance of "good death," it is increasingly important to clarify the definitions and constantly raise awareness by providing appropriate education. In this study, the small number of participants and the inhomogeneous distribution of the sample by age, gender, occupation, and region could lead to potential biases and concerns about generalizability. It is recommended to conduct research using a scale to assess nurses' and doctors' perceptions of death in a more homogeneous and larger group.

Keywords: Advance directive, geriatric nursing, geriatric palliative care, geriatric psychology, good death, psychological gerontology, social gerontology

Introduction

As known, the place of death has changed over the years, and most deaths from all causes occur in the hospital. This suggests that in the last moments before death, people are more likely to be accompanied by healthcare professionals (HCPs) than by their families. Therefore, HCPs are increasingly focusing on providing patient-centered care that respects individuals' values, preferences, and dignity, especially at the end of life and, the concept of a good death is becoming more significant in the daily practice of HCPs.

Address for Correspondence: Fatma Özge Kayhan Koçak, Bakırçay University Çiğli Training and Research Hospital, Clinic of Internal Medicine, Division of Geriatrics, İzmir, Turkey
Phone: +90 505 284 54 28 **E-mail:** drozgekayhankocak@gmail.com **ORCID:** orcid.org/0000-0002-6447-2352
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The definition of a "good death" is indeed subjective and can vary depending on various factors, such as political, individual, social, cultural, and religious perspectives (1). Common fundamental features of "good death" in modern medicine are pain relief, preserving dignity, family support, respect for patients' autonomy at the end of life and chance to "settling personal matters". Furthermore, it should reflect the needs of the community, especially those of the dying individual and their relatives (2). Advance directives (ADs) play a significant role in facilitating good death by allowing individuals to express their preferences and provide guidance to their HPCs. However, the good death can be difficult to adapt these definitions conceptually to life in practice, especially in countries without ADs.

Previous studies have shown that western society values individualism, independence, and autonomy of the individual, while eastern society generally values collectivism, interdependence, and autonomy, which is mainly centered on the family. Turkey, located at the crossroads of Europe and Asia, has a rich structure that is a synthesis of eastern and western cultures. In addition to the differences in regional perspectives on good death, there may be differences in the professional perspectives of HCPs (3). For example, although there is agreement among HCPs with painless death, dying in sleep and not being a burden to the relatives of the patients are seen as more important to nurses (4). We must create a one-size-fits-all approach that meets all of these expectations. Therefore, for a society that has not yet established ADs, studies on attitudes toward and perspectives on the concept of good death are needed first. Good death studies in Turkey are generally conducted with nurses, patients, and family members. The differences between eastern and western cultures were not investigated in these studies. The purpose of this study was to investigate factors affecting the perspectives of HCPs on the concept of good death, especially in terms of region and profession. This study can provide valuable insights into the cultural, ethical, and professional factors that shape end-of-life care practices.

Materials and Methods

Setting and Participants

G*Power 3.1 software was used for sample size estimation. The sample size was calculated as 184 participants, 92 participants at the western tertiary hospital, 92 participants at the eastern tertiary hospital, with an effect size of 0.5, a margin of error of 0.05, and a power of 0.95 to represent the universe (5).

This cross-sectional study was performed with 100 HCPs at Ege University Hospital (western group) and 95 HCPs at University of Health Sciences Turkey, Gazi Yaşargil Training and Research Hospital (eastern group) between November 2022 and December 2022. The HCPs included in the study were divided into groups according to region (west or east) and occupation [internal medicine physician (MD) or registered nurse (RN) working in internal medicine ward]. Ethical approval for the study was granted by Ege University Clinical Research Ethics Committee (approval number: E-99166796-050.06.04-978843, date: 08.11.2022).

Study Measurements

The questionnaire form was developed following the literature review of "good death" issue. The online questionnaire was entered into Google Forms through Google Drive to share with participants and collect data. Data from HCPs participating in this study were collected online. At the beginning of the online survey, a section was created in which the participants declared that they were willing to participate, as well as providing informed consent and information about the study. Demographic data, attendance to courses or modules of death education, definition of death, and good death were asked, and a good death scale was administered. The characteristics of HCPs affecting the view on good death were assessed through sociodemographic characteristics (age, sex, occupation, region), individual experience (definition of death and good death, getting education on "good death" and "end of life", having family member with cancer, previously giving care to family member with terminally ill), and professional experience (working time in internal medicine clinic, talking about "death") (6).

The good death scale (GDS) was used to assess the perspective of HCPs on the concept of good death (7,8). This scale was developed by Schwartz et al. (7) in 2003 to measure perceptions of good death among HCPs. The validity and reliability of the Turkish version of the good death scale was adapted, and the general Cronbach's alpha coefficient was found to be 0.92. The scale comprises 17 questions and three sub-dimensions. The first sub-dimension consists of 9 questions describing the psychosocial and spiritual aspects of death (4^{th}, 6^{th}, 7^{th}, 8^{th}, 9^{th}, 10^{th}, 11^{th}, 12^{th}, 13^{th} questions) and is named the psychosocial-spiritual sub-dimension. The second sub-dimension consists of 3 questions that define mental attention, communication ability, and control of physical functions (15^{th}, 16^{th}, 17^{th} questions) and is named personal control sub-dimension. The third sub-dimension consists of 5 questions describing the clinical or biomedical aspects of death (1^{st}, 2^{nd}, 3^{rd}, 5^{th}, 14^{th} questions) and is named the clinical sub-dimension. Each item in the scale was evaluated using a four-point Likert scale (not necessary: 1 point, desirable: 2 points, important: 3 points, essential: 4 points). There are no reverse-scored items. The total scale score varies between 17-68 points.

Statistics

All statistical analyses were performed using SPSS Statistics 25.0. A p-value of <0.05 was considered statistically significant.

Data normality was obtained using skewness and kurtosis (acceptable values felt between -3 and +3). The chi-squared ($\chi 2$) test and Fisher's exact test were used to compare categorical variables, while the independent sample t-test and Mann-Whitney U test were used to compare continuous variables. Baseline characteristics of the study population are presented as means ± standard deviations for normally distributed continuous variables or medians and minimum-maximum values for skewed continuous data. The multivariate analysis included parameters that were significant in univariate analysis. Multiple linear regression, the "backward" method, was used to define descriptive variables on the good death scale. P<0.05 was identified as significant in this study. Numbers and percentages are used for categorical variables.

Results

Characteristics of the Participants

One hundred ninety-seven individuals answered the online questionnaire. Two of them were excluded due to their refusal to participate in the study. The mean age of all participants was 32.8±6.6 years (63.6% female, 63.1% married, 50.3% RN). A total of 49% (n=95) were participants in the east. Seventy-five (38.5%) of the participants had 11 years or more of professional experience, and 132 (67.7%) of the participants grew up in the region where they worked. The mean score of all participants in GDS was 57.5±6.3, and the mean scores of the sub-dimensions were 30.9±3.8 for the "psychosocial and spiritual sub-dimension", 10±1.9 for the "personal control sub-dimension" and 16.6±2.4 for the "clinical sub-dimension". The mean scores of the GDS, the psychosocial-spiritual sub-dimension and the clinical sub-dimension were higher in RNs than in internal medicine MDs (p=0.008, p=0.05 and p=0.006 respectively), while the mean score for the personal control sub-dimension was higher in the east than in the west (p=0.04). As a further analysis, the scores given by west and east, by nurses and physicians to the 17 questions of the scale were analyzed separately on a question-by-question basis and are presented in Table 1. When the mean scores for GDS items were examined, "that it be peaceful" (3.87±0.4 vs 3.8±0.4 for west and east, 3.8±0.4 vs 3.9±0.3 for MDs and RNs) and "that the person's spiritual needs be met" (3.7±0.5 vs 3.8±0.4 for west and east, 3.7±0.5 vs 3.8±0.4 for MDs and RNs) were found to be the items with the highest mean scores in both region and occupation. However, "that it be painless or largely pain-free" was more important item on "good death" for MDs, while "that loved ones be present" was more important item on "good death" for RNs. Sub-dimensions and items of GDS regarding occupations and regions are presented in Supplementary Material.

The statistics related to scale scores and their results are presented in Table 2. Backward multiple regression analysis showed that region, occupation, gender, and education on "good death" were associated factors of good death scale (R^2 =0.114, F =6.128, p<0.001; Table 3). Living in the east, being a nurse, being a woman, and taking education on "good death" were positively related to the HCPs' score on the good death scale.

Discussion

The perception of good death can be influenced by education, faith, the environment in which we have grown up, and personal experiences. Using the good death scale, we investigated the impact of geography and occupation on HCPs' views of good death. The good death scale score was higher for RNs than for MDs, but there was no statistical difference between the west and the east. Backward multiple regression analysis revealed that living in the east, being a nurse, being a woman, and taking education on "good death" were positively associated with good death scores of HCPs.

Most studies have investigated MDs' attitudes toward euthanasia, physician-assisted dying, or knowledge about brain death. Unfortunately, there are only a few studies on the attitude toward death of MDs. RNs have a more positive attitude toward death than MDs in our study. Studies have shown that nurses have adopted the phenomenon of death as a natural process of human life (9). Nurses may also have a higher perception of good death, as palliative care and end-of-life care are core components of the nursing curriculum in Turkey. However, these issues play a comparatively minor role in medical education. Medical education in Turkey is more focused on disease diagnosis and treatment.

Table 1. The statistics of answers given by the healthcare professionals to the scale questions

QN, questions	West mean ± SD	East mean ± SD	p	MD mean ± SD	RN mean ± SD	p
Q3. That it be sudden and unexpected	3.2±0.8	3.4±0.8	0.139	3.13±0.8	3.4±0.8	0.027
Q5. That it occur naturally, without technical equipment	3.1±0.9	3.2±0.7	0.221	3±0.9	3.3±0.7	0.003
Q7. That loved ones be present	3.6±0.8	3.7±0.5	0.24	3.5±0.7	3.8±0.6	0.001
Q8. That the person's spiritual needs be met	3.7±0.5	3.8 ±0.4	0.03	3.7±0.5	3.8±0.4	0.226
Q17. That the ability to communicate be present until death	3.2±0.7	3.5±0.7	0.021	3.3±0.8	3.4±0.7	0.354

QN: Question number on the good death scale, X: Means, SD: Standard deviation, MD: Internal medicine physician, RN: Registered nurse

Table 2. Statistics of the healthcare professionals on good death scale and sub-dimension of psychosocial-spiritual, personal control, and clinical

	Good death scale X±SD	Psychosocial-spiritual X±SD	Personal control X±SD	Clinical X±SD
Gender, n (%)				
Female, 124 (63.6)	58.4±5.5	31.3±3.4	10.1±1.8	17±2.2
Male, 71 (36.4)	56±7.2	30±4.2	10±2.2	16±2.5
p	**0.017**	**0.026**	**0.769**	**0.04**
Marital status, n (%)				
Married, 123 (63.1)	57.7±5.7	30.9±3.7	10.1±2	16.8±2.2
Single, 72 (36.9)	57.1±7.2	30.8±4	10.1±1.9	16.3±2.5
p	0.495	0.836	0.710	0.195
Professional experience, n (%)				
10 years and less, 120 (61.5)	57.2±7	30.7±4	10.1±2	16.4±2.6
11 years and more, 75 (38.5)	58±5	31.1±3.4	10±2	16.9±2
p	0.351	0.394	0.652	0.148
Growing up in the region where he/she work, n (%)				
Yes, 132 (67.7)	57.8±5.9	31.1±3.5	10.1±1.9	16.7±2.3
No, 63 (32.3)	56.7±6.9	30.4±4.2	9.9±2	16.5±2.4
p	0.238	0.246	**0.4**	0.554
Region, n (%)				
West, 100 (51.3)	57.1±6.5	30.8±4	9.8±2	16.5±2.4
East, 95 (48.7)	57.9±6.1	30.9±3.7	10.3±2	16.7±2.4
p	0.324	0.817	0.04	0.564
Occupation, n (%)				
MD, 97 (49.7)	56.3±6.7	30.3±4	9.8±2	16.1±2.4
RN, 98 (50.3)	58.7±5.6	31.4±3.5	10.2±2	17.1±2.3
p	**0.008**	**0.05**	**0.148**	**0.006**
Education on "good death", n (%)				
Yes, 12 (6.2)	62.3±6.7	33±3	10.4±2.7	18.8±1.7
No, 183 (93.8)	57.2±6.1	30.7±3.9	10±1.9	16.5±2.3
p	**0.006**	**0.041**	0.469	**0.001**
Presence of comorbidities, n (%)				
Yes, 38 (19.5)	58.4±5.4	31.6±3.3	9.7±1.7	17.1±2
No, 157 (80.5)	57.3±6.5	30.7±3.9	10.1±2	16.5±2.4
p	0.304	0.156	0.224	0.145
Having family member with cancer, n (%)				
Yes, 134 (68.7)	57.5±5.9	30.9±3.6	10±1.9	16.6±2.3
No, 61 (31.3)	57.4±7.1	30.7±4.1	10.1±1.9	16.6±2.5
p	0.956	0.777	0.607	0.9
Previously giving care to family member with terminally ill, n (%)				
Yes, 75 (38.5)	57.4±5.8	30.8±3.8	10±2	16.5±2.4
No, 120 (61.5)	57.5±6.6	30.9±3.8	10.1±1.9	16.7±2.3
p	0.863	0.872	0.652	0.737
Talking about "death", n (%)				
Yes, 149 (76.4)	57.7±6.4	31±3.9	10.1±1.9	16.7±2.4
No, 46 (23.6)	56.7±5.8	30.5±3.5	9.9±2	16.3±2.1
p	0.331	0.444	0.715	0.289

Less than 0.05 and significant p-values are indicated in bold
SD: Standard deviations, X: Means, MD: Internal medicine physician, RN: Registered nurse

Table 3. Factors influencing good death scale scores in the healthcare professionals		
	Good death scale total	
Variables	β (95% CI)	p*
Region (west)	0.158 (0.202, 3.738)	0.029
Occupation (MD)	0.144 (-0.00, 3.607)	0.051
Gender (female)	-0.165 (-4.060, -0.214)	0.03
Education on "good death" (no)	0.232 (2.440, 0.606)	0.001
	R^2 =0.114, Adj. R2 =0.096, F =6.128, p=0.000	

*Backward multiple regression analysis
CI: Confidence interval, MD: Internal medicine physician, Adj. R^2: Adjusted R^2, β: Standardized estimates

Nurses have more contact with end-of-life patients than other HCPs (10). Thus, most research on attitudes toward death has focused on nurses. The good death scores assessed by GDS range from 52 to 60 in RNs working in different clinics. Our results revealed that nurses' attitudes toward death were similar to those reported in other studies (6,11,12). It is known that nurses play a significant role in understanding AD and end-of-life care (13,14). Attitudes toward death were positively correlated with attitudes toward AD (15). Turkey is a country where written AD is not legal. Nevertheless, previous studies have shown that Turkish nurses' attitudes toward death were positively. This gives us the advantage of planning a good death even if we do not have an AD procedure.

In our study, "that loved ones be present" was more important component of "good death" in RNs than in MDs. Likewise, Yun et al. (16) found that "that loved ones be present" has been recognized as the most important fundamental element of a good death by patients and their families but not by MDs. On the other hand, "not being a burden to the others" had the importance on definition of good death for both RNs, MDs, and patients in the studies, as well as in our study (4,16). In addition, "that it be painless" was considered the most important component of a good death for MDs. The reason is that the MDs' views on a good death were more biomedical than those of RNs. Individual health beliefs and perspectives on good death care are important components in developing strategies to improve AD. This means that HCPs should be aware of the cultures and beliefs of patients in their care (17). HCPs are ambivalent about the dignity of dying, as they try to define what it means to good death (18).

Uzunkaya Oztoprak and Terzioglu (6) showed that talking to patients about death did not influence views about a good death and attitudes toward the principles of dying with dignity, but had a positive impact on attitudes toward care for dying patients. Our study also found that talking about death did not affect attitudes toward death. Nurses are frequently required to accompany and care for dying patients (19). Most symptoms experienced by patients at the end of life are often reported to nurses or assessed by hospital nurses. Therefore, nurses typically spend more time with patients in the hospital than MDs during the latter days of patients (6). In our study, RNs had a higher score for good death than MDs. Nurses' attitudes toward death may be more positive than those of MDs, as nurses often care for dying patients. The concept of "good death" may be secondary, as the primary goal of physicians is to prolong patient life. However, a recent study indicated that MDs should play a leadership role in ensuring a good death for patients at the end of life (20). Another reason may be that MDs focus entirely on treatment, whereas nurses focus on care and healing. Acceptance of death also influences HCPs' attitudes toward death (21). Sofia et al. (22) found that RNs were more "afraid of death" but more likely to accept death than MDs.

The attitude toward death is influenced by subjective well-being, age, gender, working in intensive care units, losing relatives with cancer, death experience, personal and professional characteristics (6,9,11,23,24). However, we found that only female gender had a positive effect on GDS scores. Similar to our study, recent studies have shown that female gender has a positive effect on attitudes toward death (6,25).

The effect of education on attitudes toward death has been demonstrated to be important. Ceyhan et al. (11) reported that intensive care education status and receiving information about death at the end of life had no effect on good death scores. In contrast to "end of life" education, "good death" education had a positive effect on GDS scores. Even though the number of individuals with education on "good death" was small in our study, the impact of such education was still noticeable. Therefore, it is important to include issues of good death in nursing education programs as well as in-service training programs.

In Turkey, AD planning includes only organ and tissue donation by law. Do-not-resuscitate orders are strictly prohibited. Patients in inpatient wards have the right to refuse treatment only which will not cause fatal organ damage. This means that HCPs have to decide what is best for the patient, even at the end of life. Stigma against suicide in HCPs decreased with increasing positive attitudes toward death (26). Therefore, the perception of good death is of particular importance in developing countries that do not have written AD.

Study Limitations

One of the limitations of this study is that it was conducted with a small number of participants. Sample distribution by age, gender, occupation, and region was not homogeneously. The quality and content of the received education on "good death" were unknown. In addition, the perspective of good death can be influenced by many factors, depending on personality, culture, and the individual. Therefore, the low R-squared value in the linear regression indicates that this study should be repeated with larger and more homogeneous groups, with the addition of more factors that may influence the perspective of good death.

Conclusion

It may not be possible to achieve a single definition of good death, mostly because it depends on the complex interaction between the needs of the limitations of the healthcare system and the dying patients (18). A positive attitude toward death improves the quality of death. Given the growing importance of "good death," it is increasingly important to clarify the definitions and constantly raise awareness by providing appropriate education. It is recommended to conduct research using a scale to assess nurses' and doctors' perceptions of death in a more homogeneous and larger group.

Ethics

Ethics Committee Approval: Ethical approval for the study was granted by Ege University Clinical Research Ethics Committee (approval number: E-99166796-050.06.04-978843, date: 08.11.2022).

Informed Consent: All patients were informed about the study protocols in details and their informed written consents were provided.

Authorship Contributions

Surgical and Medical Practices: F.Ö.K.K., S.Ç., H.E.A., S.Ö., E.S., S.Ş., Y.Y., Concept: F.Ö.K.K., S.Ş., Y.Y., Design: F.Ö.K.K., S.Ş., Y.Y., Data Collection or Processing: F.Ö.K.K., S.Ç., H.E.A., S.Ö., E.S., Analysis or Interpretation: F.Ö.K.K., Y.Y., Literature Search: F.Ö.K.K., Y.Y., Writing: F.Ö.K.K., Y.Y.

Conflict of Interest: The authors declare that there is no conflict of interest.

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Supplementary Material. Sub-dimensions of "good death scale"

	West n=100	East n=95	p	MD n=97	RN n=98	p
The psychosocial-spiritual sub-dimension	30.8±3.9	30.9±3.7	0.817	30.3±4	31.4±3.5	0.05
4. That family and doctors follow the person's wishes	3.6±0.6	3.6±0.6	0.201	3.5±0.6	3.7±0.5	0.113
6. That it be peaceful	3.9±0.4	3.8±0.4	0.36	3.8±0.4	3.9±0.3	0.126
7. That loved ones be present	3.6±0.8	3.7±0.5	0.24	3.5±0.7	3.8±0.6	**0.001**
8. That the person's spiritual needs be met	3.7±0.5	3.8 ±0.4	**0.03**	3.7±0.5	3.8±0.4	0.226
9. That the person is able to accept death	3.5±0.7	3.5±0.8	0.586	3.4±0.7	3.5±0.7	0.394
10. That the person had a chance to complete important tasks	3.4±0.7	3.3±0.8	0.228	3.4±0.8	3.4±0.8	0.672
11. That the person had an opportunity to say "good-bye"	3.6±0.8	3.5±0.7	0.831	3.6±0.7	3.6±0.8	0.966
12. That the person was able to remain at home	2.7±0.9	2.8±1	0.375	2.7±1	2.8±0.9	0.190
13. That the person lived until a key event	2.9±0.9	2.8±1	0.618	2.8±1	2.9±0.9	0.290
The personal control sub-dimension	9.8±1.9	10.3±1.9	**0.04**	9.8±2	10.2±2	0.148
15. That there be mental alertness until the end	3.3±0.7	3.4±0.8	0.311	3.3±0.7	3.4±0.8	0.408
16. That there be control of bodily functions until death	3.2±0.8	3.5±0.7	0.051	3.2±0.7	3.5±0.8	0.051
17. That the ability to communicate be present until death	3.2±0.7	3.5±0.7	**0.021**	3.3±0.8	3.4±0.7	0.354
The clinical sub-dimension	16.5±2.4	16.7±2.4	0.564	16.1±2.4	17.1±2.3	**0.006**
1. That it be painless or largely pain-free	3.8±0.5	3.7±0.6	0.129	3.73±0.5	3.74±0.6	0.864
2. That the dying period be short	3.5±0.6	3.6±0.7	0.567	3.49±0.6	3.59±0.7	0.3
3. That it be sudden and unexpected	3.2±0.8	3.4±0.8	0.139	3.13±0.8	3.4±0.8	**0.027**
5. That it occur naturally, without technical equipment	3.1±0.9	3.2±0.7	0.221	3±0.9	3.3±0.7	**0.003**
14. That death occurs during sleep	2.9±0.9	2.9±1.1	0.851	2.8±1	3±1	0.133

MD: Internal medicine physician, RN: Registered nurse

CASE REPORT

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A Rare Cause of Bone Pain in an Older Adult with Pulmonary Sarcoidosis

Tuğba Tolu[1], Büşra Can[2], Nurdan Şentürk Durmuş[2], Çigdem Alkaç[2], Aslı Tufan[2]

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

Abstract

The pathophysiology of sarcoidosis includes defective T cells and macrophages, which lead to the formation of granulomas. On the other hand, increased turnover of osteoclasts has been observed in Paget's disease, where osteoclasts are a member of the macrophage family. There may be a common intrinsic factor associated with the vitamin D receptor gene receptor that triggers the defective activation of macrophages in both disorders. More than half of patients with Paget's disease are asymptomatic; thus, the coexistence of the two disorders may go unnoticed. To the best of our knowledge, the coexistence of Paget's disease and pulmonary sarcoidosis in the same patient has not been previously reported. Whether bisphosphonate can be used for the treatment of osseos sarcoidosis is a subject for future research. Herein, we report a case of Paget's disease in an older patient with pulmonary sarcoidosis.

Keywords: Bone disease, bone pain, clinical geriatrics, pain, sarcoidosis

Introduction

Paget's disease cause of that fracture and deformity osteoarthritis, neuropathy, bone tumor (1%), is presentation symptomatic or asymptomatic on especially calvarium, pelvis, ekstremite and vertebrae bones. Due to increase malignancy cases, the clinician often miss the main reason of symptom. Because malignancy screening been important step in examination for especially some symptoms and nobody want miss malignancy. We present a case report about paget disease that second most common bone disease in elderly. Consent forms have been obtained from the patient for case presentation.

Case Report

A 78-year-old-female presented to the geriatrics outpatient clinic with headache and pain in her right upper arm dating four years back. The patient described a constant, throbbing pain on both sides of the head. The pain in the right arm radiated to the right shoulder. On a scale from 0 to 10, the patient rated the pain as 4. Five years before the current presentation, the patient was diagnosed with pulmonary sarcoidosis in the pulmonary medicine clinic of the same hospital. The patient was not taking steroids because she had stage II disease characterized by bilateral hilar lymphadenopathy and pulmonary infiltrates with mildly abnormal lung function. Other medical history included hypertension and benign paroxysmal positional vertigo. Her medications included betahistine dihydrochloride, candesartan, and cilexetil. The family history included a younger brother diagnosed with laryngeal carcinoma and a younger sister with glioblastoma multiforme. Her right upper arm was sensitive to palpation.

Plain radiograph of the right humerus shows osseous expansion (Figure 1A). Plain radiograph and computed tomography (CT) of the head revealed several hypodense lesions in the skull (Figures 1B, 2A). Whole-body fluorodeoxyglucose positron emission tomography (PET)-CT detected heterogeneous lesions in the calvarial bones and T5 vertebral body (maximum standardized uptake value: 2.5). Bone scintigraphy revealed increased diffuse osteoblastic activity in the calvarial bones, right humeral head, and right aspect of the T11 vertebral body.

The patient was diagnosed with polyostotic Paget's disease based on diagnostic radiological findings and elevated serum

Address for Correspondence: Tuğba Tolu, Marmara University Faculty of Medicine, Department of Internal Medicine, İstanbul, Turkey
Phone: +90 216 625 45 45 **E-mail:** tugbatolu139@gmail.com **ORCID:** orcid.org/0000-0001-8881-4583
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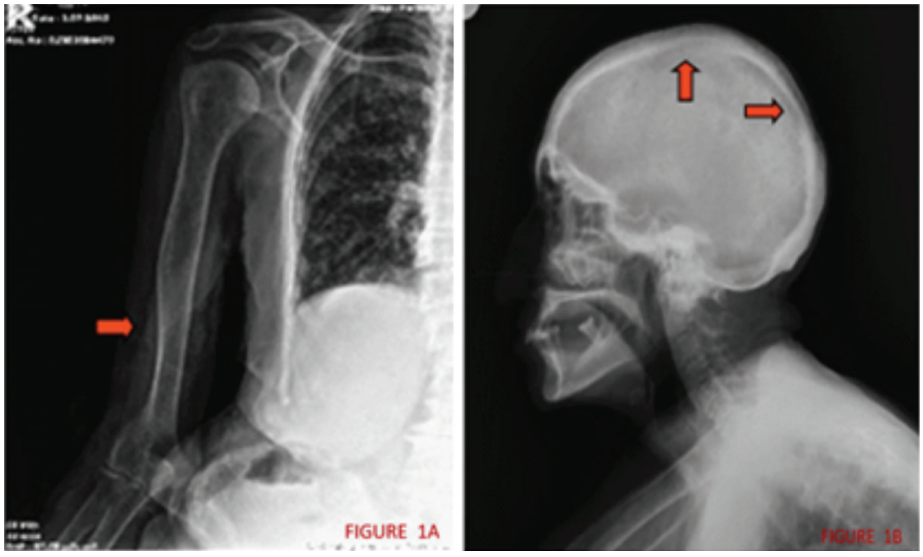

Figure 1A. Plain radiograph of the right humerus, **Figure 1B**. Plain radiograph of the head

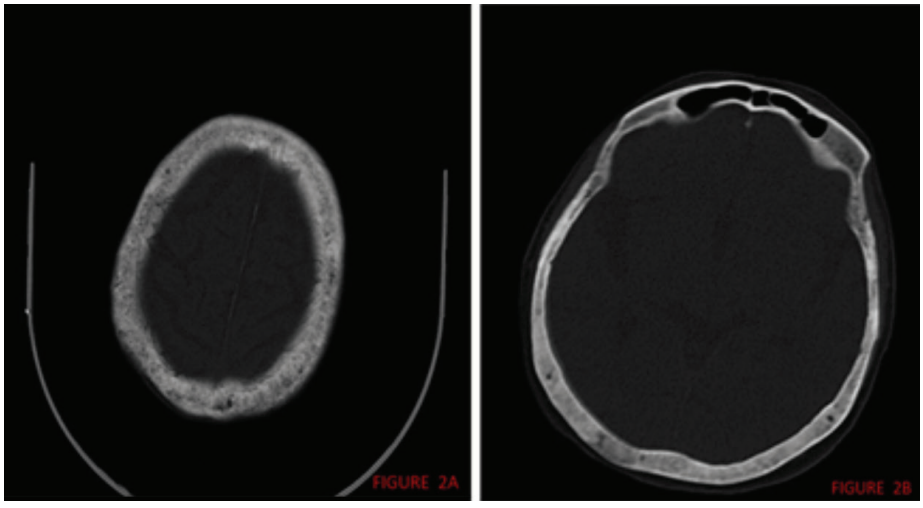

Figure 2A. Cranial CT before treatment, **Figure 2B**. Cranial CT after treatment

alkaline phosphatase (ALP). Treatment with intravenous yearly zoledronic acid therapy was initiated along with oral nutritional supplements for malnutrition. At follow-up, the patient reported no headache or bone pain. Follow-up cranial CT after treatment with zoledronic acid showed complete resolution of the cranial lesions (Figure 2B).

Discussion

Sarcoidosis is a multi-system inflammatory disorder with a complex pathophysiology. Unknown antigens trigger a cell-mediated immune response that leads to the accumulation of T cells and macrophages, followed by the formation of granulomas. Demaria et al. (1) reported bone involvement in sarcoidosis to be 14%. The relationship between macrophage activation and vitamin D metabolism has been proposed as the pathophysiological mechanism underlying sarcoidosis (2). The first-line treatment for bone involvement in sarcoidosis is steroids (3).

Paget's disease is a chronic bone disease affecting either single or multiple bones. The prevalence of this condition is relatively low in Africa and Asia compared with Europe and the United States (4). The treatment aims to suppress osteoclasts and osteoblasts with bisphosphonate therapy (5). Kurihara et al. (6) showed that osteoclasts in Paget's disease have increased vitamin D3 receptor sensitivity, which may be associated with higher vitamin D receptor (VDR) gene expression. Moreover, Ishizuka et al. (7) reported that bone resorption in Paget's disease can be prevented using vitamin D antagonists.

VDR is a regulatory transcription gene that belongs to the nuclear receptor family. VDR plays a role in cell proliferation, differentiation, immune response, and ligand-dependent pathways including the calcium-phosphorus balance, in the body. The effect of vitamin D3-VDR signaling on the immune system is increasingly recognized, as VDR expression and activity play important roles in both T cell development and

differentiation (8). VDR shows sequence similarity to steroid and thyroid hormone receptors (9). Interestingly, glucocorticoids, the first-line therapy for sarcoidosis, have been shown to reduce VDR gene expression (10).

Initially, the differential diagnoses of our patient's bone lesions included malignant bone metastases, multiple myeloma, bone involvement of sarcoidosis, and metabolic bone diseases. Normal immunofixation electrophoresis and whole body PET-CT scan exonerate metastatic malignancies and multiple myeloma. Noy et al. (11) also excluded similar differential diagnoses in the cases they presented.

Bone involvement in sarcoidosis mostly occurs in the form of lytic and sclerotic lesions (12,13). However, our patient exhibited osteoblastic changes on imaging, which decreased the suspicion of osseous sarcoidosis. No granular lesions were observed in the liver relating to the patient's sarcoidosis, and liver enzymes other than ALP were within the normal reference range. We therefore arrived at the diagnosis of Paget's disease in this older patient with sarcoidosis.

Conclusion

The etiologies of Paget's disease and sarcoidosis are not well-defined. The pathophysiology of sarcoidosis includes defective T cells and macrophages, which lead to the formation of granulomas (3). On the other hand, increased turnover of osteoclasts has been observed in Paget's disease (14), where osteoclasts are a member of the macrophage family. There may be a common intrinsic factor associated with the VDR gene receptor that triggers the defective activation of macrophages in both disorders. More than half of patients with Paget's disease are asymptomatic; thus, the coexistence of the two disorders may remain unnoticed. Whether bisphosphonates can be used in the treatment of osseous sarcoidosis is a topic for future research.

Ethics

Informed Consent: Consent forms have been obtained from the patient for case presentation.

Authorship Contributions

Design: T.T., Data Collection or Processing: T.T., B.C., Analysis or Interpretation: N.Ş.D.,Ç.A., A.T., Literature Search: B.C., Writing: T.T.

Conflict of Interest: Aslı Tufan is Associate Editor in European Journal of Geriatrics and Gerontology. She had no involvement in the peer-review of this article and had no access to information regarding its peer-review. Other authors have nothing to disclose.

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LETTER TO THE EDITOR

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Comments on "Frailty As a Significant Predictor of COVID-19 Among Vaccinated Older Adults"

Elaheh Sanjari[1], Hadi Raeisi Shahraki[2]

[1]Shahrekord University of Medical Sciences, Student Research Committee, Shahrekord, Iran
[2]Shahrekord University of Medical Sciences Faculty of Health, Department of Epidemiology and Biostatistics, Shahrekord, Iran

Dear Editor,

Recently, Hafızoğlu et al. (1) published a paper that showed that frailty is a significant predictor of coronavirus disease-2019 (COVID-19) among vaccinated older adults. Although their study makes a valuable contribution, taking into account some methodological issues to avoid misinterpretation of the study's results is necessary.

Violation of the Proportionality of Hazards (PH) Assumption

The PH in the Cox regression is a critical assumption, which means that the hazard of variables is independent of time. The PH violation leads to unreliable and biased estimates (2). The displayed Kaplan-Meier curves indicate a dramatic violation of the PH assumption due to the crossed curves for the seropositive and age clinical frailty scale (CFS) scores. Therefore, using the Cox regression leads to unreliable estimates.

A Very Low Infection Rate

The Cox regression model was implemented to assess the hazard of COVID-19 infection when the total number of infected participants was lower than 20%. Thus, the event did not occur for most patients, and the nature of the data shows a plateau survival curve, which may be the expected infection rate in the general population. In this situation, Cox regression is no longer applicable, and the cure model must be used. In addition, cure models have more advantages than Cox regression models in terms of both assumptions and applications.

The Lower P-value and Largest Hazard Ratio Doesn't Necessarily Indicate the Strongest Association

Comparing regular hazard ratios to assess the strongest predictor is not true because the types of units and scales differ dramatically among variables. Instead, the authors must use the standardized hazard ratios extracted from the standardized coefficients.

Lack of Prediction Capability Assessment

To demonstrate that high CFS scores among vaccinated older adults should be considered an easy-to-assess, high-risk marker for predicting breakthrough COVID-19 infection, the prediction accuracy of factors must be determined using receiver operating characteristic analysis or other appropriate indices.

In conclusion, the performed statistical analysis by Hafızoğlu et al. (1) may not be appropriate, and the findings must be interpreted with caution.

Keywords: Aging, aging biology, frailty, geriatrics, healthy aging

Ethics

Authorship Contributions

Surgical and Medical Practices: E.S., H.R.S., Concept: E.S., H.R.S., Design: E.S., H.R.S., Data Collection or Processing: E.S., H.R.S., Analysis or Interpretation: E.S., H.R.S., Literature Search: E.S., H.R.S., Writing: E.S., H.R.S.

Address for Correspondence: Hadi Raeisi Shahraki, Shahrekord University of Medical Sciences Faculty of Health, Department of Epidemiology and Biostatistics, Shahrekord, Iran
Phone: +98 383 333 56 53 **E-mail:** raeisi.shahraki_hadi@yahoo.com **ORCID:** orcid.org/0000-0003-3071-5587
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