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Groessl EJ, Kaplan RM, Rejeski WJ et al. Physical Activity and Performance Impact Long-term Quality of Life in Older Adults at Risk for Major Mobility Disability. Am J Prev Med 2019; 56 (1): 141-146. (DOI: 10.1016/j.amepre.2018.09.006).

3-Books

BG Katzung. Special Aspects of Geriatric Pharmacology, In:Bertram G. Katzung,Susan B. Masters, Anthony J. Trevor (Eds). Basic and Clinical Pharmacology. 10th edition, Lange, Mc Graw Hill, USA 2007, pp 983-90.

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World Health Organization. Global Health and Aging [e-book] NIH Publication; 2011. [Internet]. Available from: http://www.who.int/ageing/publications/ global_health.pdf. Accessed: 09.09.2019.

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From The Editor In Chief

The United Nations General Assembly has designated the period between 2021 and 2030 as the "Decade of Healthy Ageing".

Some main topics of their decleration are: Examining the perspectives of the concepts of old age and aging in societies, taking measures against age discrimination, improving the ability of the elderly to participate and contribute to the society and communities in which they live and expanding opportunities, spreading the concept of an age-friendly environment, providing integrated care and basic health services that respond to the needs of elderly people, and providing access to long-term care for elderly people who need it.

In this regard a wide variety and in-depth knowledge is needed about the multifaceted problems affecting the aging world. The protection, treatment and care of the elderly are complex issues and involve the expertise of many different professionals.

It is obvious that the determination of the health needs of elderly people should be based on the results of spesific scientific researches to be conducted in this field. And the results of these researches should take place in the focus of solution strategies to be planned with a realistic approach.

Researches conducted on the elderly carry various difficulties both for researchers and for the elderly participating in these studies. Regarding this issue a problem that has attracted attention in recent years is that the elderly are not adequately represented in clinical trials.

In this context, it is expected that the researches submitted and planned to be submitted to our journal will make valuable contributions not only to the world of science, but also to the protection of the health of the elder persons as well.

Yeşim GÖKÇE KUTSAL

EDITORIAL ARTICLE

UNDERREPRESENTATION OF OLDER PERSONS IN CLINICAL TRIALS

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INTRODUCTION

The older age group physiologically does not have the same characteristics as adults, and generally medications used in the elderly have not been properly evaluated. Clinical trials conducted in the adult population often involve patients between the ages of 18 and 64, so there is insufficient evidence and information about the reactions of geriatric patients to these medications (1).

This is because older people are relatively underrepresented or even absent in most drug studies. The main reason that leads to uncertainty about the risks and benefits of new treatments for the elderly is "age discrimination" in clinical trials. Frail elderly, those with multiple comorbidities and older women are not included in the studies aimed at questioning the validity and safety of most treatments (2).

With aging, physiological changes occur that can affect the pharmacokinetics and pharmacodynamics of the drugs used (For example, the duration of action of the drug may vary). Tolerability and possible negative effects can also be a serious problem. Specific treatment guidelines for the elderly are rare and physicians sometimes have to predict the correct drug dosages for their elder patients. Randomized controlled trials (RCT's) are required to provide evidence of treatment safety and drug benefits in the elderly (3).

A consortium (PREDICT) was formed to study the participation of elderly people in clinical trials and this consortium has checked whether the underrepresentation is real or not. Studies on 6 subjects have been reviewed in the last 10 years: 1-Heart failure, 2-Hypertension, 3- Coronary artery disease, 4-Depression, 5-Alzheimer's disease, 6-Colorectal cancer. The results confirmed that there is a wide deficiency / difference between the patient population in the clinics in real life and the patients included in the studies under all conditions (4).

The clinical research proposals submitted to the Research Ethics Committee covering the educational / teaching hospitals affiliated to Trinity College Dublin were examined. It was noted that patients were

excluded from the studies "based on an arbitrary upper age limit" (5).

In 226 studies that were found suitable for examination 31(13.7%) applied exclusion by setting an age limit only. Those who do not include age-based exclusion are only 22 (9.8%) (by geriatricians) and out of 22 applications, 12 studies are from the field of neurology / psychiatry.

The average upper age cut-off value was recorded as 69.2. Most of the other studies also included exclusion criteria "based on cognitive function", which further limits the participation of older people in particular. However, according to these results, the participation of older people in research at Trinity College Dublin was found to be higher than in international studies (5).

Recommendations of regulatory authorities in developed countries to researchers and industry are; 1-Avoiding arbitrary upper age limits, 2-Elderly people should not be excluded from clinical trials without a valid reason (1).

EXAMPLES BASED ON ORGAN SYSTEMS AND DISEASES

Cardiovascular Disorders: Cardiovascular diseases are a significant contributor to both mortality and morbidity on a global scale (6). There are notable distinctions between men and women in terms of the pathogenesis, clinical presentations, and consequences of cardiovascular illnesses. To gain evidence-based information on the understanding and management of cardiovascular diseases in elderly individuals and women, it is crucial to incorporate these specific subgroups into RCTs (7). The underrepresentation of elderly adults in RCTs can be attributed to both the diverse distribution of aging and the obstacles faced in patient registration, assessment, and follow-up processes. Indeed, the senior demographic constitutes the predominant consumer base for pharmaceutical products. Consequently, this group is also subject to the highest incidence of adverse medication responses. The dearth of RCTs including the older population can result in a constraint on the understanding of optimal pharmaceutical usage in terms of safety. Notwithstanding the dissemination of worldwide recommendations aimed at augmenting the involvement of senior individuals and women, the level of their inclusion and consideration in research projects remains inadequate. Due to its status as the primary research funding entity in the United States, the National Institutes of Health (NIH) wields significant influence over the conduct of scientific endeavors inside the nation. The matter of incorporating individuals who are 65 years old and above into research was a subject of deliberation during the "Inclusion Across the Lifespan" Workshop conference held by the National Institutes of Health (NIH) in 2017 (8).

A year subsequent to the implementation of the Inclusion Across the Lifespan policy, persistent difficulties were noted in effectively representing the elderly population in cardiovascular research. During this temporal interval, a significant number of research investigations, specifically one-third, continued to use age restrictions, while a larger proportion, specifically two-thirds, employed exclusionary criteria that disproportionately impacted the senior population (9). In order to enhance the inclusivity of the elderly population and women, particularly in RCTs, it is imperative to critically evaluate and modify ethical regulations and publication policies pertaining to cardiovascular diseases, as well as their associated mortality and morbidity. These revisions are necessary to effectively promote and facilitate the greater involvement of older individuals in such research endeavors.

Alzheimer's Disease: The most common cause of dementia is Alzheimer Disease. Not only the memory loss and but other cognitive abilities also interfere with daily life of the older person. The majority of Alzheimer's patients (72%) are over the age of 80. However, in researches the

representation of patients over the age of 80 is 8%. It is stated that, patients enrolled in clinical trials related to Alzheimer's disease are far from representing the true distribution of patients in the general population (10).

Low Back Pain: Low back pain is one of the health problems that negatively affect the quality of life in old age. Review of the WHO research registration database about exclusion of older adults from ongoing clinical trials related to low back pain was performed. Prospective protocols planning interventions for low back pain were examined. A total of 167 protocols were planned to include participants over the age of 65 as part of the research. Only five entries (2.99%) were designed specifically to target participants over the age of 65. In 93.6% of the protocols, there was no valid excuse for setting an arbitrary upper age limit (11).

THE REASONS OF UNDERREPRESENTATION

A Medline search for all articles that contain the word "elderly" in the title or abstract was performed. Of the 150 articles 89 were excluded because they were not actual RCTs. In the RCTs feature, 50 articles were related to the elderly. Main subjects were hypertension, neuropsychiatry, and cardiology. Reasons why the elderly are not included were summarised as: 1-Simultaneous diseases, multiple pathologies and comorbidities, 2-The fact that symptoms related to other diseases (intercurrent) that occur during the progression of a disease can cause bias, 3-Difficulties in interpreting negative events, 4-Concerns about multidrug use (especially drug interactions and poor compliance) (12).

A literature review was conducted to identify barriers to enrolling elderly people in clinical cancer trials and obstacles were categorized as:

I- Obstacles related to the physician: Tolerance of treatment, metabolism of the drug, lack of evidence for effectiveness, perceptions about age bias.

II- Obstacles related to the patient: Lack of autonomy, quality of life, concerns about the toxic effect, accessibility to clinical trials and logistical and financial difficulties.

III- Obstacles related to research (including eligibility criteria): Performance status, organ dysfunction, presence of comorbidities (13).

Factors that make it difficult for the elderly to participate in research can be summarized as:

A-Complex protocols involving long and laborious result measurements, B-Aggressive treatment protocols with possible toxicity, C-The inclusion criteria of the study can be very limited, D-Lack of expectations of the patient and his/her family for the benefit of the patient from the research (non-therapeutic studies), E-Lack of financial, logistical and social support, F-The patient's poor health condition, G-The presence of anxiety, H-Very advanced age (in some studies).

Reasons are detailed by Shenoy & Harugeri as: 1- Current difficulties in obtaining informed consent. 2- Difficulties in the outcome evaluation of multiple comorbid conditions. 3- Polypharmacy leading to drug-drug interactions. 4- Difficulties in adapting to procedures of clinical trials. 5- The need for age-appropriate formulations and packaging. 6- Fear of failure due to the confusing behavior of medication in the elderly. 7- Seniors may need supportive care. 8- Corporate and logistical problems. 9-Researcher's preferences and perceived difficulties in screening. 10- Having protocol restrictions with exclusion criteria based on age. 11- The fact that sponsors may incur higher costs for medical management and compensation (1).

PARTICIPATION OF THE ELDERLY

Methods of involving the elderly in research: Referral from other physicians, one-on-one invitation of the research team to the patient, making presentations and invitations related to working in patient/elderly associations, social

service organizations, nursing homes and meetings are recommended. Establishing communication with nursing homes, universities and health centers distributing advertisements / making announcements to the places where the target individuals can be found and to the centers where meetings or exhibitions are held can be useful.

Factors that facilitate the participation of the elderly in research: Having the approval of family members, the positive attitude of the medical team about the research are important factors. The patient's educational level being high also effects the situation. And if the person who communicates with the patient about research (especially in clinical drug trials) is a physician the participation of the elderly is much more easy.

INFORMED CONSENT

If research involves interaction with participants, or gathering identifiable information, informed consent must be obtained. Validity of informed consent depends on the fulfillment of its fundamental elements. These elements are ***competence, disclosure, comprehension of information, voluntariness,*** *and* ***consent.*** The process of obtaining consent from elderly individuals is more intricate and involves specific considerations regarding these elements (14).

Incompetency issues: Regarding the elderly, situations such as cognitive impairment, psychiatric problems, hearing and / or vision problems that affect perception, may decrease the ability to make decisions or incompetency occurs. Refraining from all forms of discrimination, especially age discrimination, every individual should be treated as competent unless the opposite is determined after careful assessment. Competence signifies the cognitive abilities of the individual and it may vary in time according to the health status of the individual. Therefore, the competence assessment conducted is specific to the moment of evaluation. According to the course of health of the individual reassessment may be required later. The evaluation of an individual's decision-making capacity is typically carried out by medical professionals; in difficult, uncertain cases, appeal to a specialist from psychiatry or other fields of medicine is common practice (14).

Scales such as Mini-Mental State Examination (MMSE), Clinical Dementia Rating and MacArthur Competence Assessment Tool for Treatment (MacCAT-T) are also used, which are complementary to the evaluations made by physicians and support the objectivity of the evaluation, without being a stand-alone determinant (15-18).

Concerning non-competent individuals, consent is obtained from a "legal representative" generally a family member based upon the assumption to be the one who knows the subject best and is most likely to make a decision that would be in keeping with the subject's values. Assent, the expression of willingness to agree to go along with research protocol or refusal, should be obtained from the elderly who cannot provide informed consent and should be taken into consideration as in the case of adolescents. Even with impaired people with dementia, assent may support the ability to reveal the subjects' values and preferences (19, 20).

Disclosure: Regarding disclosure to elder participants, the complexity, content, and presentation format of the information that will be conveyed, should be evaluated. Mainly content is comprised of: a statement that the proposal is on participating research, voluntary nature of participation, the objectives, the approximate number of participants, the amount of time that will be spent in research, description of the procedures participants will be engaged, foreseeable risks and discomforts, potential benefits, statement on the protection of confidentiality and privacy, if relevant compensations ad insurances, statement affirming that declining to participate will not result in any losses or penalties and they may leave the study any time without facing any adverse consequences.

Communication information of a contact person from the study should be shared. The format of the provided information should be as simple and clear as possible. Large fonts should be used, and decision aids such as audio or visual elements may be utilized. Elder participants may require more time to comprehend information, allocation of additional time and well-trained, empathic staff are needed. To avoid misunderstanding, subjects should be provided with the opportunity to ask questions (19).

Frail older people who are invited to participate in research accommodating in nursing homes or being hospitalized, or with dementia, may not be able to say "no" to the researchers' recommendations. At this point, extra caution, and protection on the voluntariness of the consent obtained is needed. Research staff should have awareness of the potential risk of therapeutic misconception and comply with preventive measures.

The distribution of burdens and benefits of research should be considered carefully by the researchers and ethics committees that will review the protocols. Excluding older people from research without appropriate reasons violates the ethical principle of "justice". Considering distributive justice, more efforts are needed by researchers, institutions, and research sponsors to involve older people in research (19).

Additionally, in accordance with non-maleficence and beneficence principles an elderly person can be taken into research that will provide real and direct benefits to her / him. It may not be appropriate to be taken into research that does not have a therapeutic effect (20).

THE RESEARCH PROCESS

General precautions for drug research on the elderly: Study protocols should be designed taking into account comorbidities and polypharmacy. There should be no "upper age limit" for participation in the study unless there is appropriate justification (within the framework of the ethical rules). More education and observation / communication are required to increase compliance in elderly individuals (e.g. telephone calls, home visits). The ideas of patient organizations and elderly individuals should also be taken.

Study design for the elderly: There is no "standardized methodology" for including older patients with comorbidities and disabilities in clinical trials. A carefully prepared and adequately resourced protocol design is important, but many clinical trial designs fall short.

Study participation: The development of clinical trials in the elderly poses a number of challenges related to study participation, data retention and data analysis. Often, the elderly patient is not alone at the decision stage, and family members or caregivers also need to be convinced by the researcher with a "friendly approach" (21).

Adaptation to research: Protocols should be made appropriate for the reception of the elderly as well. It should not include complex and difficult applications. Research should not impose an economic burden on the patient and if necessary, transportation of patients should be provided. Participating in the research should not make it difficult for the patient physically, spiritually and socially. In pharmaceutical studies, the drugs should be in an easily accessible form, blister packaged and labeled. It is also recommended to provide telephone connection with patients and rewards can be given during control visits (22).

Post-research period: The approach to elderly patients in the post-research period is very important. This approach to be applied after the research should be designed "at the very beginning" of the study and approved by the "ethics committee". At the end of the study, elderly patients should be informed about the research results. They should be monitored for unwanted side effects for a while longer and should be referred for medically necessary treatments.

PROTECTION OF THE ELDERLY

There are some spesific recommendations for protecting the elderly in clinical trials. These are: 1-Ensure the safety of the drug in the systems of organs of concern (such as kidneys, liver and cardiovascular) in the elderly. 2-Exclude the elderly population with clinical study-specific anxiety. 3-Only patients with round-the-clock caregivers at home should be included in the study. 4-Make sure that emergency medical assistance is available near the patient's residence. 5-Elder friendly clinical trial support materials and patient diaries should be kept ready. 6-Ensure that the caregiver is also present and testifies during the approval process. 7-Intensive counseling should be given by the researcher to both the patient and the caregiver. 8-Patients should be called regularly and frequent phone follow-up should be performed (1).

According to Skolnick &Alexander, registration systems should be established at the National Institutes of Health, a standard model should be developed for enrollment plans involving older adults in clinical trials. Research on new drug or device applications should include plans to ensure that older adults are adequately registered. There is no advisory board or a special department to supervise or advocate for the representation of older adults in research. A department can be created to review dosing, registration and data collection protocols in elderly populations. This department can also monitor progress in the inclusion of elderly people in important trials. There are also statements aimed at drug manufacturers for the protection of individuals at the far end of the age spectrum; 1-Providing an appropriate patent extension for conducting research for the elderly and conducting geriatric labeling studies, 2-Mandatory maintenance of post-marketing safety records in the treated elderly, 3-It should be noted that medicines can be approved after the accumulation of safety data (23).

AGAINST ELDER DISCRIMINATION

Participants of the round table discussion on reviewing the participation of the elderly in clinical trials were; 1-American Geriatrics Society, 2-European Union Geriatric Medicine Society-EUGMS, 3-US Food and Drug Administration-FDA, 4-European Medicines Agency-EMA. Cherubini A et al stated that, in the battle against age discrimination in clinical trials; there are delays, prejudices and reservations are still ongoing. Regulatory agencies should work together to propose 1-New definitions, 2-Study designs, 3-Technologies aiming at improving the evaluation of drugs in elderly people with multiple comorbidities and polypharmacy (24).

It is well documented that, elderly individuals have been disproportionately affected by the COVID-19 pandemic. There were disruptions in the provision of clinical services and there have been profound effects on the research. Research on COVID-19 and similar issues should be carried out with an inclusive approach especially the fragile elderly, elderly people with cognitive impairment or multimorbidity, and those who live in nursing homes. From the point of view of the elderly, research not related to COVID-19 is of "critical" importance and should not be hastily neglected (25).

ARTIFICIAL INTELLIGENCE

Artificial intelligence is a technology that offers new tools aimed at making clinical trials safer, faster and cheaper. In order to evaluate how drugs react at the molecular level, it is aimed to create a system that produces more drug candidates in less time and with fewer experiments by combining artificial intelligence, quantum physics, cloud computing algorithms.

As it is known; insufficient research design is a difficulty that can be encountered in clinical trials. More qualified literature review can be conducted, appropriate endpoints can be addressed, the appropriate sample size / statistical analysis method

can be determined, the possibilities of changes that may occur during the study can be reduced and inconsistencies in the protocol can be prevented by artificial intelligence technologies (26).

In research on the elderly, the use of artificial intelligence may be practical both at the design and protocol stage and also at the stage of determining appropriate endpoints. It is reported that artificial intelligence systems are developed using data that reflect the implicit and explicit biases of society, and therefore there are significant concerns about how predictive models in artificial intelligence systems increase inequality, privilege and power in society.

However, the opinion that age discrimination does not exist to a large extent prevails in the artificial intelligence bias literature, but given the aging population globally and the increase in artificial intelligence applications, it is reported that there is a need to critically examine and monitor the existence of age-related bias in artificial intelligence systems, and its ethical and legal dimensions should definitely be taken into account (27).

CONCLUSION

The most important consumers of health resources and medicines are the elderly. The use of drugs that have not been included in the elderly studies may be risky and dangerous. In drug research where the elderly are not included in the scope of the study, the reasons for "not including the elderly" should be clearly explained to readers when "the results are written as an article" (22).

Research patients who have tried medical treatments and interventions do not represent patients who are seen in daily routine practical applications in clinics. This creates problems for physicians. It is necessary to consider whether the positive or negative results obtained from the studies apply to elderly patients especially the frail ones.

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INVITED REVIEW ARTICLE

A PILLAR OF CARDIOVASCULAR DISEASES: INFLAMMAGING

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Abstract

With the prolongation of life expectancy, the increase in the number of elderly individuals in societies and the high rates of disability, frailty and morbidity associated with this situation have led to the acceptance of old age as a prior social problem. And since the 2000s, many studies have been carried out in this field.

Inflammation is a very important physiological function and a complex biological process that is initiated by the immune system in response to infection, injury or tissue damage. In connection with this process, inflammaging refers to the chronic, low-grade inflammation that occurs with aging.

As one ages, the immune system undergoes changes including a descent in the production of new immune cells and a decrease in the ability of existing immune cells to function properly that can contribute to a state of chronic inflammation. Clinical trials suggest that modulating inflammation prevents many of the chronic diseases, frailty, and disability that increases at older age.

In the light of existing information, one can predict that a possible reason for long life today is the capability of reaching an optimal balance between pro-inflammatory (C-Reactive Protein, Interleukin 6, Tumor necrosis factor-alpha) and anti-inflammatory (Interleukin-1 receptor antagonist protein, Cortisol, Interleukin-10) molecules.

Keywords: Aging; Cellular Senescence; Inflammation; Immunosenescence.

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INFLAMMATION

Inflammation is a very important physiological function and a complex biological process that is initiated by the immune system in response to infection,injury or tissue damage. It is a natural and important part of the body's defense mechanism to protect the body from invasion, infection and death resulting with the healing of the damaged tissues, but it can also contribute to various diseases if becomes chronic or aggressive (1).

Tonsils and adenoids, thymus, lymph nodes and vessels, spleen and bone marrow are the major organs that take part in the immune system by secreting macrophage and the T and B cells. Also skin, the endothelium of the digestive and respiratory trucks also act as an important surface barrier for the pathogens.

Acute inflammation is the major part of a cardiovascular surgeons routine daily practice. The perioperative period is a potentially deletirious time because the combination of anesthesia, the stress of surgery, and the immüne stimulation effect of the cardiopulmonary bypass (CPB) circuit result in a systemic inflammatory response (2).

Possible responsible etiologic factors are;

A-Cellular activation with contact of blood products with the surface of the bypass circuit,

B-Mechanical shear stress that occur due to the blood passing through the suction systems and filters,

C-Tissue ischemia and reperfusion,

D-The effect of hypotension and hemodilution,

E-Administration of blood products and

F-Mild to deep hypothermia utilization during the cardiopulmonary bypass.

The effect of surgical trauma and CPB results in complement activation by both classical (protamine related) and alternative (contact with foreign surfaces) pathways.These two pathways result in the elevation of C3a and C5a which lead to activation and degranulation of neutrophils, release of histamine from mast cells, basophills, and platelet aggregation (3).

Cytokines are produced by macrophages, lymphocytes, monocytes, and endothelial cells. These factors are either proinflammatory in the form of IL-6, IL-8 and tumor necrosis factor alpha or antiinflammatory in the form of IL-10, and IL-1 receptor antagonists.

An increase in TNF alpha has been demonstrated with increased capillary leak. Elevations in IL-6 and IL-8 result with increased inotropic requirements, severe capillary leak syndrome, and an increase in mortality.In uncomplicated cases the systemic inflammatory response is self limited and is only of a few days duration but organ dysfunction may occur in those who show an extensive systemic inflammatory response.

As mentioned above in a normal inflammatory reaction when the stress or infection occurs the immüne response begins and IL-6 and CRP release and increase in time. After recovery begins they decrease and immüne reaction ends after complete healing.

INFLAMMAGING

Inflammaging refers to the chronic, low-grade inflammation that occurs with aging. As we age, our immune system undergoes changes including a descent in the production of new immune cells and a decrease in the ability of existing immune cells to function properly that can contribute to a state of chronic inflammation (4).

There is a continuous increase in pro-inflammatory cytokines, a decrease in anti-inflammatory cytokines, and changes in the function of immune cells such as macrophages and T cells. Although the initiating factor deceased or cured dysregulated chronic inflammation continue to progress, and is believed to play a role in many

age-related diseases, including cardiovascular and pulmonary disease, cancer, neurodegenerative, autoimmune,and metabolic disorders and demantia (5, 6).

There has been a significant amount of research conducted on inflammaging in recent years to better understand its mechanisms and potential therapeutic interventions.

The level of proinflamatory markers are at baseline up to approximately 60 to 65 years both in men and woman and then begin to increase continuously due to inflammaging. Inflammatory markers IL 6 and whereas a little bit slower CRP both tend to increase very rapidly. Those who have elevated inflammation not only tend to have more disease, but also become predisposed to have an increase in the number of diseases over the subsequent years (1).

It was shown in 2015 that there is a correlation between the level of IL-6 and the number of illnesses that a patient have.For example at age 70 if you have high baseline IL-6 and faster increase of IL-6 over time, you may have 2 to 3 illnesses where as at age 90 you have more than 4 illnesses if this condition persists (7).

If treatment of the inflammation is effective it ends with healing, but if inflammation continue as in inflammaging sytemic effects occur that not only cause to multiple chronic diseases, but also the geriatric syndromes, like frailty or age-related muscle diseases and loss, as well as decreased physical endurance or decreased ability to respond to a stress, for example to recover after surgery or creating an immune response after vaccination (8, 9).

The results of the study by Ferrucci and Fabbri in 2018 suggested that inflammageing is not-only a risk factor for cardiovascular diseases (CVDs), but is also a risk factor for chronic kidney disease, diabetes mellitus, cancer, depression, dementia, and sarcopenia (10).

Factors that lead to inflammaging:

- Genetic predisposition,
- Visceral and central obesity,
- Increased gut permeability and changes in gut microbiota,
- Mithocondrial dysfunction that lead to oxidative stress,
- Intrinsic immune cells defect,
- Cellular senescence.

Mechanisms

Nowadays inflammaging is considered as a phenomenon that increases the rate of ageing and many chronic diseases that are basically related to age. So these age-related diseases can be considered as the manifestations of accelerated ageing due to inflammaging.

In connection with the genetic background of individuals, environmental factors and lifestyles may accelerate or decelerate the aging process (5).

In brain chronic inflammation activates migroglia and inhibits neurogenesis;at arteries it stimulates atherosclerosis, and inhibit endothelial reactivity; inhibits hematopoesis at bone marrow,stimulates osteoclasts and downregulates osteocalcin;inhibits muscle growth, and in the gastrointestinal system it reduces food absorbtion,and also causes insulin resistance (5, 7, 11).

The two most important mechanisms that are recognized as possible cause of chronic inflammation with aging are the cellular senescence and the increase in intestinal permeability and microbiota change which leads to a loss of protection in this very important barrier.

One of the processes that appears to be contributed to chronic low grade inflammation with aging is cellular senescence which was discovered and named in the early 1960s by observing that normally multiplying cells stop dividing.

Senescent cells are cells that have entered a state of irreversible growth arrest, meaning they no longer divide or function properly. They are especially located in skin and adipose tissue and are usually larger than non-senescent cells. Senescence is a natural process that serves as a protective mechanism to prevent damaged or potentially cancerous cells from continuing to divide and potentially causing progressive harm to the organism, The secretome of senescent cells is a very complex procedure. The products are mainly associated with inflammation, proliferation, and changes in the extracellular matrix. Also they play a pathological role in age-related diseases (4).

However, while senescence can be beneficial in some contexts, accumulated senescent cells over time can contribute to various age-related diseases and the overall aging process. Some senescent cells become very large, have increased protein production, and may exhibit a secretory state where they produce inflammatory mediators, chemokines that attract immune cells, and other factors that damage tissues around them. This chronic inflammation and tissue dysfunction are thought to play a role in age-related diseases (1, 5).

The abundance of senescent cell begins to particularly increase in the ages between 60 and 80. The older individuals have more senescent cells in their fat tissue than the younger individuals. So central and visceral obesity is a major risk factor for inflammaging.

Small numbers of senescent cells, if they're transplanted into younger individuals, can cause an aging like state. It was shown that if you transplant just a million senescent cells into a mouse resulting only one out of 10,000 cells in that mouse is a transplanted senescent cell, this is sufficient to make that mice die earlier of all age-related diseases and they exhibit the signs and markers of inflammation.

So very small numbers of senescent cells are sufficient to cause problems. There's a threshold in the number of senescent cells that will cause problems. Once you exceed that threshold, senescent cells cause senescense in other cells near and at a distance to them.By this way senescent spreads from cell to cell (4,12).

The immune system normally clear senescent cells. Once the rate of formation of new senescent cells exceeds the ability of the immune system to clear them, there will be an exponential increase in their numbers, and start getting age-related disorders and diseases (9).

OBESITY

As another important factor, pro-inflammatory and chemotactic compounds are produced by macrophages, lymphocytes, and senescent cells that are located at the central and visceral fat tissue in obese individuals contributing to inflammaging.

MICROBIATA

Our immune cells, which live in the layer underneath the gut, are constantly sampling inner microbiata in order to make decisions about which are pathogens which needs to be responded to and which are nonharmful organisms that they shouldn't respond to (13).

As the immune system ages, it loses some of this capacity, and ability to monitor and to destroy the harmful microbes. So microbial composition shifts, and this ultimately leads to microbial dysbiosis, or a harmful or unhealthy change in the gut microbiome. This age-related microbial dysbiosis promotes intestinal permeability which allow for the translocation of bacterial products from the gut into the vascular system, and once these products are in the circulation, we have systemic inflammation. Young immune system can clear these products fairly quickly. However, as getting older the systemic inflammation affects the immune cells that are required to keep that gut microbiome under control. Also the ability of macrophages to delete this

harmful bacteria decreases, inflammation continue to increase, and so the visious cycle continues (13, 14).

DIET

Researches show that in developing countries people have a high fat, low fibre diet. They have chronic stress, inactivity, and smoking. All these result in an increase in intestinal permeability and many chronic diseases in a vicious cycle. So the average age of men is 76 and women is 82.Whereas in developed countries people eat low fat, high fibre diet, and have healthy microbiome.The stress is low, they have time to exercise,have safe jobs and safe enviroment. These lead to less intestinal permeability and the mean age is 81 in men and 84 in women (5, 14).

ALVEOLER SYSTEM

The lungs are constantly exposed to environmental pollutants, allergens, and irritants, which can damage the alveoler endothelium and airways during years. As we age, these changes can accelerate, leading to a decline in lung function due to:

- The airways become narrower and less elastic. This makes it harder to breathe in and out.
- The alveoli, where gas exchange takes place, become smaller and less numerous. This reduces the surface area available for gas exchange.
- The muscles that support breathing become weaker which makes it harder to breathe deeply.
- The production of mucus decreases. This can make it more difficult to clear mucus from the airways.
- The immune system in the lungs becomes less effective. This makes it harder to fight off infections.

The same mechanism of impaired integrity of epithelial cells in the lungs, like in the gut leads to increase permeability in the lungs, disorders of mucus secretion and clearence lead to bacterial entrance and inflammation which ends in diseases such as bronchitis, asthma, chronic obstructive pulmonary disease, emphysema, pneumonia and lung cancer (15).

SMOKING

Smoking also lead to oxidative stress and cytokine production which results in inflammaging and induces and aggravates the inflammatory response in the airway that ends in age related respiratory diseases , cardiovascular disease, and cancer One study found that smoking cessation led to a significant reduction in inflammatory markers in older adults.

CARDIOVASCULAR SYSTEM

There are several molecular mechanisms that play role in cardiac and vascular inflammaging (16, 17).

Accumulation of low-density lipoprotein (LDL) cholesterol in the damaged endothelium of the arterial wall tend to be oxidized and triggers an inflammatory response and atherosclerosis begins. The initiation and progression of atherogenesis is contributed by innate and adaptive immunity starting from early endothelial dysfunction to the development of acute thrombotic complications (18). In later stages thrombotic complications can be seen that are triggered by plaque rupture or erosion. Currently, the detailed mechanisms that affect the formation and progression of atherosclerosis cannot yet be fully explained. In this context, it is believed that the different mechanisms involved in the accumulation of inflammatory markers accelerate clinical progression and lead to a vicious cycle. According to the results of researches, regardless of other cardiovascular disease risk factors, high blood pro-inflammatory markers, including high-sensitivity

C-reactive protein (hsCRP) and Interleukin 6 (IL-6) in particular, predict the risk of cardiovascular disease in both middle-aged and older adults (19).

Together with the low-grade systemic inflammation, cardiac aging leads to cardiac inflammation and downregulation of main energy regulating mechanisms, and mitochondrial dysfunction leading to endothelial/myocardial dysfunction. These changes can affect the heart's ability to pump blood and can increase the risk of heart disease,and heart failure (20, 21).

Here are some of the changes that occur in the aging heart due to inflammaging:

- The heart muscle becomes less elastic. This makes it harder for the heart to relax and fill with blood.
- The heart valves become stiffer. This can make it harder for the valves to open and close properly.
- The arteries become narrower and less elastic. This makes it harder for blood to flow through the arteries.
- The endothelium of the blood vessels becomes damaged and more susceptible to inflammation. This can lead to the formation of plaque, which can progressively narrow the vessels and restrict blood flow.
- The conduction system of the heart becomes less efficient. This can lead to arrhythmias, or irregular heart beats.

These changes can lead to a number of heart problems, including:

- Heart failure
- Coronary artery disease
- Arrhythmias
- Stroke
- High blood pressure
- Peripheral arterial disease
- Venous insufficiency

Epicardial adipose tissue (EAT), which covers 80% of the heart surface and accounts for 20% of the total heart weight, is defined as the visceral fat storage of the heart (22).

The inflammatory process that increases during aging is characterized by an increase in the release of inflammatory mediators and neuro-hormones by EAT contributing to development and progression of cardiovascular diseases by directly penetrating through the myocardium and coronary vessels. As the result of expressing their toxicity in the neighboring tissues not only coronary artery disease, but aortic stenosis, atrial fibrillation and even heart failure can be seen.

There are studies supporting the correlation between worse cardiovascular outcome and EAT accumulation. A reliable quantification of EAT is considered to be very important using different imaging techniques such as echocardiography, computerized tomography scan and cardiovascular magnetic resonance imaging in order to explore the potential impact of EAT on the progress of cardiovascular diseases. Coronary artery disease patients having more than 7 mm EAT thickness were considered to have higher risk of myocardial infarction and cardiovascular death by Tanındı et al (23).

Evaluation of EAT thickness can also be useful for predicting intensive care unit complications such as the onset of atrial fibrillation, prolonged inotrope use, and even fever after coronary bypass surgery.

BRAIN

The aging brain undergoes a number of changes that can affect cognitive function, memory, and mood. Some of these changes are:

- Decrease in the brain size and weight: The brain gradually shrinks as we age, starting in our 40s. This is due to the loss of neurons and synapses.

- Accumulation of amyloid plaques which are protein deposits that can build up in the brain and damage neurons. They are associated with Alzheimer's disease and other forms of dementia.
- Chronic inflammation can damage neurons and contribute to cognitive decline, trouble multitasking which is the ability to do two or more things at once. It can become more difficult to do as we age.
- As getting older, the blood vessels that supply the brain with oxygen and nutrients can become narrowed or blocked. This can lead to decrease in blood flow to the brain,and ends in decline in the cognitive function and mood and personality changes including depression, anxiety, and irritability (21).
- Neurotransmitters are chemicals that allow neurons to communicate with each other. As we age, the production of some neurotransmitters, such as acetylcholine, can decrease. This can lead to problems with memory loss and slowed thinking make it difficult to concentrate, learn new things, or make decisions. Memory loss is the most common symptom of aging brain. It can range from mild forgetfulness to difficulty remembering recent events or familiar faces.

EATING HABBIT

It has been shown that nutrient content, amount of food, time of meal and rhythm have a significant effect on intestinal microbiota and metabolism and maintain a basal physiological inflammation level, whereas overnutrition and inflammation may increase with changes in all these (24).

A study was conducted to identify factors influencing intention and behavior of fast-food consumption. A group of people ate fast food like meal where as a second group has eaten healthy meal. And it was shown that IL 6 began to increase in 50 minutes in both groups. But after 8 hours there was a significant increase in the fast food group.

SLEEP

Prolonged sleep deficiencies such as short sleep duration or sleep disturbances, lead to chronic, systemic low-grade inflammation (inflammaging) and is associated with diseases that have an inflammatory component, i.e. diabetes,atherosclerosis, and neurodegeneration (25).

Another research conducted on the correlation of short sleep duration and cardiometabolic risk showed that increased risk of atherosclerosis and hypertension,impaired heart rate variability and increased risk of coronary artery disease ,heart failure and arythmia,increased risk of diabetes mellitus,increased risk of metabolic syndrome and obesity,increased susceptibility to viral infections,irritability,cognitive impairment,memory lapses or loss may occur due to short sleep duration (26).

Overall, lifestyle factors can have a significant impact on inflammaging, with healthy behaviors such as a balanced diet, regular exercise, and adequate sleep helping to reduce chronic inflammation and improve healthy outcomes in older adults.

PREVENTION

There are some basic tips to keep inflammaging low:

- Get a good night's sleep: 7-8 hours sleep duration must be essential and it has been reported that older adults with poor sleep quality had higher levels of inflammatory markers compared to those with good sleep quality. Also deep sleep is important for reducing inflammation and oxidative stress.
- Drink plenty of water

- Eat lots of good veggies and nutrient-rich food; avoid high sugar and low-nutrient dense food: A diet high in processed foods, saturated fats, and sugar has been shown to increase inflammation, while a diet rich in fruits, vegetables, whole grains, and healthy fats, such as omega-3 fatty acids, can reduce inflammation. For example, a study published in the Journal of Nutrition found that a Mediterranean-style diet, which is rich in anti-inflammatory foods, reduced levels of inflammatory markers in older adults.
- Perform regular moderate exercise: Walking 20 minutes daily has been shown to reduce inflammation and slow the aging process. Studies found that older adults who engaged in regular exercise had lower levels of inflammatory markers compared to sedentary adults. Regular exercise can lower levels of pro-inflammatory cytokines and increase anti-inflammatory cytokines, leading to reduced inflammation. Additionally, exercise can also improve cardiovascular health, which is closely linked to inflammaging.
- Finally, stress can also contribute to inflammaging, with chronic stress leading to increased levels of pro-inflammatory cytokines. Relaxation techniques such as meditation and yoga have been shown to reduce stress and inflammation.

POTENTIAL TREATMENT STRATEGIES

There is currently a lot of research on how to target senescent cells in order to prevent and treat age-related diseases. Some potential therapies include:

Medicines designed to selectively kill senescent cells, and aimed at reducing tissue inflammation are named as "senolytic drugs". It has been shown that senolytics delay and prevent the development of many chronic diseases in mice, thus improving their health and quality of life.

Some examples of senolytic drugs that have been studied in preclinical and clinical trials are:

1. Dasatinib and quercetin: This combination of drugs has been shown to selectively eliminate senescent cells in mice and improve cardiovascular function.
2. Navitoclax: It has been shown that navitoclax selectively eliminate senescent cells in atherosclerotic mice and improve vascular function.
3. ABT-263: This drug also has been shown to selectively eliminate senescent cells in mice and improve tissue function.
4. Fisetin: This natural compound has been shown to selectively eliminate senescent cells in mice and improve physical function.
5. Rapamycine
6. Piperlongamine

In animal models the senolytic drugs do not kill the normal cells. It was shown that 30 to 70% of senescent cells are killed by these kind of drugs, and that's roughly correlates with the percentage of senescent cells that are trying to kill other cells and produce inflammatory markers. Also senescent cells take two to six weeks to form again. So these drugs can be given once every couple of weeks or once a month if there's continuing stimulus for new senescent cells to form (27, 28).

The development of effective drugs in this area will prevent chronic inflammation that causes aging, delay human aging, increase the quality of life and thus prolong longevity.

Immunotherapy is an another approach using the immune system to target and kill senescent cell (29).

The development of effective therapies for targeting senescent cells has the potential to revolutionize the way we treat age-related diseases.

Both in preclinical and clinical studies, while evaluating the suitable molecular biomarkers and

pathways, consideration of personal aging should be prioritized. Since there are sex differences in the process of aging and chronic diseases, both genders should be included. And for immunosurveillance, targets should be unique antigens or ligands of senescent cells.

Clinical trials suggest that modulating inflammation prevents many of the chronic diseases, frailty, and disability that increases at older age.

Due to the researches we can estimate that a possible main reason why people reach 100+ are because they are capable of reaching an optimal balance between pro-(CRP, IL-6, TNF alpha) and anti-inflammatory (IL1RA, Cortisol, IL-10) molecules (29, 30).

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ORIGINAL ARTICLE

AGE-RELATED DIFFERENCES IN PROSPECTIVE MEMORY: TURKISH VIRTUAL WEEK (VW-TR)

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Abstract

Introduction: Prospective memory, which involves remembering intended future actions, is a vital function in terms of autonomy, quality of life, and everyday functioning. The primary aim of this study is to examine how aging affects prospective memory performance; its secondary aim is to adapt a laboratory-based prospective memory task, Virtual Week, to the Turkish culture and investigate its efficacy across young and old age groups.

Materials and Method: The study was conducted with 60 young (18–25 years) and 60 old (60–87 years) participants. Participants were included based on their results on cognitive screening tests (Montreal Cognitive Assessment, Activities of Daily Living Scale, Geriatric Depression Scale, and the Beck Depression Inventory). In addition, the Stroop and Trail Making tests were administered to measure executive functions. Finally, the laboratory-based prospective memory task Virtual Week was performed.

Results: Virtual Week has been adapted to Turkish culture and shown to be reliable (Spearman–Brown: 0.82). ANOVA was conducted to analyze the effect of aging on the Virtual Week task, and the results showed that young adults were more successful than older adults in prospective memory tasks ($p < .05$).

Conclusion: The results support the theory of the aging paradox in prospective memory, which suggests that older adults exhibit lower performance in laboratory-based prospective memory tasks. The findings are discussed in the context of the relevant literature.

Keywords: Memory; Cognitive Aging; Executive Function; Young Adult; Aged.

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INTRODUCTION

Prospective memory (PM) is defined as memory that allows us to remember that a planned action must be performed based on a specific cue during an ongoing task (1). In laboratory studies, PM is examined in two ways: event-based prospective memory (EB-PM) and time-based prospective memory (TB-PM), depending on the type of cue (1). An event-related environmental cue in tasks carried out in EB-PM requires less self-initiating process and mental effort—for example, remembering to pay the rent when you see the owner. In the case of TB-PM, there is no environmental cue related to the event—the cue is elapsed time. In such a task, spontaneous processes and mental effort are more involved—for example, remembering to take medication at 9 pm (2). Remembering routine tasks (e.g., going to work) requires less retrospective memory (RM), while remembering nonroutine tasks (e.g., a dentist appointment) requires more RM (3).

The multiprocess model of prospective memory (1) and the theory of preparatory attentional and memory processes (PAM) (4) focus on monitoring, the use of limited resources, and related cues.

It has been shown that PM is a critical indicator of functional independent living by investigating PM in laboratory tasks representing daily life (5). The question of how PM performance is affected by the aging process is a matter of interest. In this context, it has been shown that PM performance increases from birth to age 35 and then begins to decline (6). PM requires multistage processes and a relatively high cognitive load. Therefore, PM performance is expected to decline with advancing age (7). Laboratory-based studies have shown that PM performance deteriorates with aging (6, 8, 9), but that older people can be as successful as young people in PM studies compatible with real-life events outside the laboratory (5, 10, 11). On the other hand, there are also studies finding no difference between old and young people in terms of EB-PM (10). The "age prospective memory paradox" (2) posits that older participants perform differently in laboratory and non-laboratory tasks. Haines et al. (12) explain the age PM paradox as a lack of environmental support and cognitive processes, whether automatic or not. Another explanation is that older participants may have developed strategies that use external assistance more in tasks representing real-life events, while young participants may not perform fully due to lack of motivation (5). It was observed that age affected TB-PM and EB-PM differently (8, 9). With aging, TB-PM may deteriorate more than EB-PM (8, 9). Older participants were found to have more success on PM only when they received social feedback (7). The young-old (60–75) and old-old (over 75) age groups showed no significant difference outside the laboratory, although the old-old group failed to perform laboratory-based PM (11).

A new technology that detects spontaneous speech production related to PM found no significant difference between younger and older adults (10). Although various tasks have been developed to evaluate PM objectively, the most structured and highly externally validated one is Virtual Week (VW) (13). Although VW is a laboratory task, it is similar to everyday life, as it involves real-life events. VW was developed in English-speaking regions in North America and Australia. It was then adapted and applied to non-native English cultures (Germany, Poland, and Italy) in Europe (5, 14, 15).

The main purpose of this study is to examine the effect of aging on PM performance. The secondary objective is to examine the functioning of VW (13) in Turkish culture.

METHOD

Participants and Materials

The study was carried out with 120 volunteers, 60 of whom were young (female = 30, male = 30) and 60 of whom were old (female = 30, male = 30). The mean age of the young group was 21.03 (1.48), and

the mean age of the older group was 71.38 (7.43). The two groups were equivalent in terms of years of education, and there was no significant difference between the groups in terms of education level (year) ($t_{(118)} = 1.53$, $p = .13$).

The Beck Depression Inventory (BDI) (16), Geriatric Depression Scale (GDS) (17), Montreal Cognitive Assessment (MoCA) (18), and Functional Activities Questionnaire (FAQ) (19) were used as inclusion criteria. The cut-off points for inclusion criteria were 17 for the BDI (16) for the young group; 15 for the GDS (17); 23 for MoCA (18); and 5 and 7 for the FAQ (19), corresponding to ages 60–70 and 70+, respectively for the older group. The mean and standard deviation scores obtained from the screening tests are summarized in Table 1. Standardization studies, in which all neuropsychological tests and scales were used, were conducted for Turkish culture, and all tests and scales had culture-specific norms.

This research employed the computerized version of the VW developed by Rendell and Henry (13). VW is a task that begins with the subject rolling a virtual dice on a representative game card on the computer screen. Some adaptations have been made because of cultural differences. Turkish culture differs from the Australian and North American contexts in which VW was developed, particularly in terms of eating habits, social habits and/or relations, and celebrities. Thus, culture-specific adjustments were made. For a screenshot of the trial-day dinner, see Figure 1. Minor changes have been made as possible. Foreign dishes in Turkish cuisine such as porridge and cereal replaced with local dishes such as lahmacun and kebab.

Table 1. Screening Tests' mean and standard deviations scores

	BDI M (S)	**GDS** M (S)	**FAQ** M (S)	**MoCA** M (S)
Age Group				
Young (n=60)	8.20 (4.80)	-	-	-
Old (n=60)	-	9.87 (4.81)	14.15 (7.38)	26.43(3.43)

BDI: Beck Depression Inventory, FAQ: Functional Activities Questionaire, GDS: Geriatric Depression Scale, MoCA: Montreal Cognitive Assessment

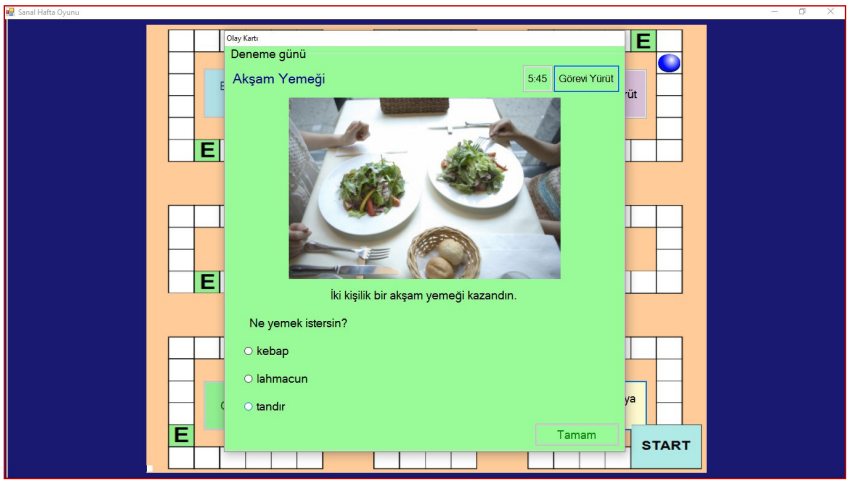

Figure 1. Turkish Virtual Week- a screenshot of the trial-day dinner

Rose et al. (3) found that the reliability coefficient of Spearman-Brown's split halves for VW was .71 in the young group and .93 in the older group. In the Italian version of the VW, the Cronbach's alpha internal consistency coefficient was found to be .64 in the young group and .92 in the older group (15). In the Polish version, Spearman-Brown's split-half reliability coefficient was .75 in the young group and .95 in the old group (14).

Procedure

Informed consent was obtained from all participants before starting the study. Then screening tests/scales were applied. After the screening test/scales, VW was carried out. VW includes regular tasks (e.g., taking medication at breakfast and dinner), regular times (e.g., taking asthma medication at 21:00), and irregular tasks that are specific to a particular day and time (e.g., calling the dentist to make an appointment at 12:00 o'clock). In addition, participants are required to perform lung function tests at two minutes and four minutes in real time. This is called a time-check task.

VW consists of one trial day and three virtual days. Each virtual day included four regular (two event-based, two time-based), four irregular (two event-based, two time-based), and two time-check tasks. A total of 30 PM tasks were used during the experiment. At the end of each virtual day, a recall test was performed to assess whether the tasks were coded by the participants. In the recall test, the planned action (e.g., buying a colored pencil) was selected from the distractors (e.g., receiving a birthday present for the participant's nephew), and the participant was asked to match it with an action cue (e.g., shopping). This study was approved by the Hacettepe University Ethics Committee (reference no. 35853172/431-71).

Statistical Analysis

All analyses were conducted with the Statistical Package for the Social Sciences (IBM®, SPSS 25). A 2 × 2 × 2 ANOVA was conducted age group (young vs. old), PM task (regular vs. irregular), and PM cue (event vs. time) to analyze the performance of VW as a function of age and task demand. The independent variable "age" was manipulated between groups and the other independent variables PM task and PM cue were manipulated within groups. Due to the real-time time-check tasks being quite separate from the virtual times a 2×3 ANOVA was also conducted on the age group (young vs. old), and PM task (regular, irregular vs. time check task) as in the other versions of VW (2, 5, 15). Analyses were conducted regarding the correct answers (responses in the right place and at the right time) to the VW-TR.

RESULTS

The Stroop test (20) and the Trail Making Test (TMT-Part B) (21) were applied to determine the executive functions of the participants. These tests were considered pertinent for prospective memory. The mean and standard deviations of the scores obtained from the Stroop test (20) and the Trail Making Test (TMT-Part B) (21) are presented in Table 2. The young group's duration of completion of the Stroop test was shorter (U = 1074.5, p < .001) and had a lower total score for error and correction (U = 1384.0, p < .05) than the older group (U = 1274.0, p < .05). In addition, the young group's TMT-Part B error and correction total scores (U = 1358.5, p < .05) were lower than those of the older group.

The Cronbach's alpha internal consistency coefficient for the Turkish version of the VW (VW-TR) was .77, and the Spearman–Brown split-half reliability coefficient was .82 in all groups. The Spearman–Brown split-half reliability coefficients were .65 for the young group and .61 for the older group.

Table 3 shows the mean and standard deviation scores of the young and older participants on the VW-TR.

Table 2. Mean and standard deviations of age, education level, and neuropsychological test scores

	Education (years)	Age	TMT-Part B duration of completion	TMT-Part B sum of error and correction	Stroop Test duration of completion	Stroop Test sum of error and correction
	M (S)	M (S)	M (S)	M (S)	M (S)	M (S)
Age Group						
Young	13.68 (.99)	21.03 (1.48)	55.36 (30.79)	.35 (.76)	17.90 (4.99)	0.48 (.93)
Old	13.28 (1.75)	71.38 (7.43)	73.82 (41.93)	.78 (.98)	22.68 (8.18)	0.92 (1.15)

TMT-Part B: Trail Making Test- Part B

Table 3. Mean and standard deviations scores of older and young participants on VW-TR

		Age Group			
		Young		Older	
Task of Type		**Event**	**Time**	**Event**	**Time**
Regular Tasks	M	.82	.79	.72	.37
	SD	.18	.22	.25	.28
Irregular Tasks	M	.85	.57	.65	.13
	SD	.15	.25	.22	.17

The 2x2x2 ANOVA revealed a significant main effect for age ($F_{(1,118)}$=150.7, p<.001, ηp^2=.56); PM task ($F_{(1,118)}$=54.7, p<.001, ηp^2=.32); PM cue ($F_{(1,118)}$=199.4, p<.001, ηp^2=.63); interaction effect of PM cue and age ($F_{(1,118)}$=44.2, p<.001, ηp^2=.27), interaction effect of PM task and PM cue ($F_{(1,118)}$=39.9, p<.001, ηp^2=.25). There was no significant interaction effect of PM task and age ($F_{(1,118)}$=2.5, p>.05), and PM task, PM cue, and age ($F_{(1,118)}$=1.61, p>.05).

Table 4 presents the mean and standard deviation scores on the regular, irregular, and time-check tasks according to the age groups.

The 2x3 ANOVA revealed a significant main effect for age ($F_{(1,118)}$=240.1, p<.001, ηp^2=.67); PM task ($F_{(2,236)}$=40.0, p<.001, ηp^2=.25); and PM task and age interaction ($F_{(2,236)}$=22.2, p<.001, ηp^2=.16). Post-hoc analyses showed that the members of the young group were more accurate in performing regular PM tasks (M=.68, S=.22) than irregular PM tasks (M=.55, S=.22) and time check tasks (M=.48, S=.36), as well as more accurate in performing irregular PM tasks (M =.55, S=.22) than time check tasks (M=.48, S=.36). In addition, post-hoc analyses revealed that the young group (M=.76, S=.14) outperformed the older group (M=.38, S=.13) overall (p<.001, ηp^2=.67): regular task for young (M=.81, S=.16) versus older (M=.54, S=.20); irregular task for young (M=.71, S=.16) versus older (M=.39, S=.14); and time check task for young (M=.75, S=.24) versus older (M=.21, S=.23). In the post-hoc analyses for age and PM task interaction, it was revealed that the older group displayed worse performance on the time check task (M=.21, S=.23) compared to the regular (M=.54, S=.20) and

Table 4. Mean and standard deviation scores on regular, irregular and time check tasks according to the age groups

PM Task	Regular Task M (S)	Irregular Task M (S)	Time Check Task M (S)
Age Group			
Young (n=60)	.81(.16)	.71(.16)	.75(.24)
Older (n=60)	.54(.20)	.39(.14)	.21.(.23)

PM Task: Prospective Memory Task

irregular tasks (M=.39, S=.14) ($p<.05$). The results for the older group were also worse on the irregular task (M=.39, S=.14) as opposed to the regular task (M=.54, S=.20) ($p<.05$). Similarly, the younger group displayed worse performance on the irregular task (M=.71, S=.16) than on the regular task (M=.81, S=.16) ($p<.05$). However, there were no significant differences between regular task (M=.81, S=.16) and time-check task (M=.75, S=.24) performance for the young group ($p>.05$). There were also no significant differences between the irregular task (M=.71, S=.16) and time-check task (M=.75, S=.24) performance for young adults. Since the older adults experienced difficulty using a mouse and requested assistance in this regard, the time to complete the VW-TR was not calculated.

DISCUSSION

As expected, young adults were more successful than older adults on PM. This difference was especially high for the irregular and time-check tasks (*see* Table 3). These results support the age-prospective memory paradox and are in line with previous research showing that older adults perform worse on laboratory tasks than younger adults (2, 5, 8, 9, 11). Due to the necessity of using RM and PM together competently, irregular tasks require a greater cognitive load. Therefore, the performance of the older adults was lower on irregular tasks where the use of RM was especially necessary. This finding is also consistent with the theories of the multiprocess framework (5) and PAM theory (6), which focus on spontaneous retrieval, demands of an ongoing task, and related cues. In a study by Rendell and Thomson (11), when young-old and old-old groups were compared, the old-old group performed worse on laboratory-based PM tasks than the young-old group. Additionally, Bozdemir and Cinan (8) found the performance of the old group was worse than that of the young group on laboratory-based PM tasks.

According to the interdependence model proposed by Imamoğlu (22) for Turkish people, collectivist, and individualist tendencies coexist in this culture. In this context, the fact that the Turkish (Middle Eastern) sample of older adults faced problems in accessing health services and led a relatively sedentary lifestyle associated with living in a collectivist culture (meaning many daily activities are undertaken by the family and relatives of the older individuals) (23) may have led to higher failure rates on laboratory-based VW-TR tasks when compared to the older individuals in the Western sample. Consistent with this evaluation, Turkish older samples' norm values determined through neuropsychological tests, such as MoCA, TMT, and cut-off points, were shown to be lower than those for the same age group in Western culture (18, 21). While neuropsychological tests did not predict naturalistic, self-report, and clinically based prospective memory performance, the obtained

results were found to be consistent with the Age Prospective Memory Paradox, due to the current study being laboratory-based, results are expected opposite to naturalistic prospective memory performance in older individuals (24) Recent research findings also suggest that intercultural differences exist in episodic memory and semantic memory performances (25). It is thought that the lower PM performance of the individuals in the Turkish older sample may be explained by the cultural differences mentioned (22, 23). Additionally, stereotype threats, such as unsuccessful memory performance and a slowdown in response speed, may adversely affect PM performance, especially in older samples (26). Stereotype threat is higher in laboratory-based tasks. Although recreational drug-related deficits in PM have been reported in recent years, we have not asked about it, by reason of they usually have not been honest about drug use in self-reports in Turkish culture (27). Age is also known to influence time-based and event-based performance differently according to the cue type (14, 15). In the other versions of the VW (Western), there was more deterioration in time-based tasks compared to event-based tasks with aging (2, 5, 14, 15). In line with Western culture, there was more deterioration in time-based and time-check VW-TR tasks with aging in Turkish culture.

In the present study, the VW-TR, which is the Turkish version of the VW, was employed. The VW was originally developed in North America and Australia and adapted in Germany, Poland, and Italy. When the reliability scores of Western culture were compared, the results in this study were relatively lower in older adults but compatible with the results for younger adults. One of the reasons for this may be due to the limited use of technology by older Turkish individuals compared to the same demographic in the West. In this study, older participants lost time by having difficulty using the mouse, and by focusing on this issue, they may have struggled to concentrate and follow the ongoing task. The variety of problems encountered, including those related to using the mouse and reading, as well as having to help participants with such difficulties, may have resulted in lower reliability scores on the VW-TR than on other versions of the VW.

The adapted VW-TR was found to be suitable for young participants, while older participants experienced some practical difficulties related to computer use. In this context, using the board game version of VW by hand or using a touchscreen computer can be recommended for future studies. It has been shown that VW, which was developed for Western culture, is also functional in Turkish culture and can be used as a comprehensive laboratory task that measures PM with various (event-based, time-based, time check, regular, irregular) and real-life tasks. It was found that the performance of PM deteriorated with aging in laboratory-based tasks. Niedzwienska et al (7), suggest that the comparison of the daily real-life tasks and laboratory-based tasks of PM will contribute to the literature. As in the study of. Haines et al. (12) the naturalistic PM task performed with older adults in MEMO (smartphone application) may be also studied in older Turkish people, and it is thought that it will be useful to compare the performance of the older adults in the naturalistic PM task with VW, which is the other leg of the '*Age Prospective Memory Paradox*' (3).

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ORIGINAL ARTICLE

EFFECTIVENESS OF ULTRASONOGRAPHY-GUIDED CAUDAL EPIDURAL STEROID INJECTION IN IMPROVING PAIN AND FUNCTIONAL STATUS OF GERIATRIC PATIENTS WITH SPINAL PAIN

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Abstract

Introduction: Treatment of lumbar spinal pain in geriatric patients is challenging. This study retrospectively investigated the effects of an ultrasonography-guided caudal epidural steroid injection on pain and functional recovery in geriatric patients (age ≥65 years).

Materials and Methods: Fifty-eight patients who received ultrasonography-guided caudal epidural steroid injection between December 2019 and March 2023 were retrospectively evaluated. Pain levels were evaluated using the Visual Analog Scale, and functional recovery was assessed using Oswestry Disability Index. The time points for evaluation were preoperative, immediately post-procedure, and at three weeks and three months post-procedure.

Results: The main underlying conditions in this cohort were lumbar spondylosis, lumbar disc herniation, and lumbar spondylolisthesis. Thirty patients had multiple-level lumbar canal narrowing, 13 had L4-5 and L5-S1 disc herniation, and five had lumbar spondylolisthesis. Ten patients had a history of lumbar spinal surgery. Fourteen patients had at least three comorbid conditions (cardiovascular disease, morbid obesity, renal disease, etc.), and six had four comorbid conditions. Pain Visual Analog Scale scores in the immediate postoperative period and at three weeks and three months were significantly lower than the preoperative score ($p < 0.001$). Oswestry Disability Index scores at three weeks and three months postoperatively were significantly better than the pre-procedure scores ($p < 0.001$).

Conclusions: Ultrasonography-guided caudal epidural steroid injection is an excellent pain management modality in the treatment of spinal pain, especially in the geriatric age group.

Keywords: Pain; Steroid; Ultrasonography; Comorbidity.

INTRODUCTION

Aging is characterized by biological, physiological, emotional, and functional changes. Individuals aged ≥65 years account for approximately 10% of the global population. This percentage is projected to exceed 16% by 2050, accounting for approximately 1.6 billion people (1). The progressive population aging has led to increased incidence and prevalence of chronic pain and related diseases in this age group (2). Degenerative sagittal imbalance is associated with back pain and poor quality of life in the geriatric population (3).

Lumbar disc herniation, lumbar spinal stenosis (LSS), degenerative spondylolisthesis, and previous lumbar operations are among the most common causes of chronic pain syndromes, affecting the quality of life (4). Approximately 70% of people aged ≥60 years are affected by lumbar low back pain (5). Lower back pain is the leading cause of activity restriction and workplace absenteeism, placing a high economic burden on the affected individuals and society (6). Over half of geriatric patients aged ≥65 years have three or more diseases (such as diabetes, heart disease, and hypertension); therefore, polypharmacy is a common problem in this age group. In addition, geriatric patients typically have reduced physiological reserves of vital organs. Consumption of additional medication or undergoing surgery or physical therapy to treat spinal pain may cause problems (7).

The treatment of spinal pain in geriatric patients usually includes modification of activities, various exercise modalities, oral analgesics, neuropathic medications, physical therapy, manual manipulations, epidural steroid injections (ESI), and in some cases, surgical interventions. ESI, a less invasive, safe, and cost-effective treatment option in geriatric patients, has become popular in recent years, as pain medications, anti-inflammatory agents, and surgery pose multiple risks for elderly patients with comorbidities. ESI has been shown to reduce pain and improve functional status in patients with low back and radicular pain due to spinal pathology. Lumbar ESI improves objective physical capacity parameters and pain scores compared to drug therapy in elderly patients with symptomatic lumbar spinal stenosis (8).

Epidural injections can be administered via interlaminar, transforaminal, and caudal approaches by injecting local anesthetic solutions, steroids, or a combination. These are usually administered to relieve pain and improve function and mobility. The caudal approach is easy to apply and is associated with a lower risk of iatrogenic dural puncture. The procedure can be performed with a blind technique or under fluoroscopy or ultrasonography guidance (9).

This study aimed to investigate pain and functional improvement in geriatric patients who underwent ultrasound-guided caudal epidural steroid injection (CESI) and to emphasize the USG-guided CESI application as one of the treatment options.

MATERIALS AND METHODS

This retrospective case-control study was approved by the institutional review board of the Ankara Bilkent City Hospital and complies with the Declaration of Helsinki (Protocol number: E1-23-3450; Dated 10/05/2023).

Patient selection

The inclusion criteria for the study were: 1) Patients aged ≥65 years who received CESI for persistent low back and/or leg pain due to lumbar spinal pathology (as assessed by lumbar MRI at the time of admission); 2) visual analog scale (VAS) pain score of ≥6; 3) patients not considered for surgical treatment due to high comorbidity or did not respond to conservative treatment. All patients were referred for CESI by neurosurgeons from Ankara Bilkent City Hospital.

The exclusion criteria were: Patients aged <65 years. A research worker (YCS) retrospectively collected patient data and screened their data against inclusion/exclusion criteria. The first author (AG), who performed the procedures, conducted the examination in detail with potential patients with exclusion/inclusion criteria and obtained written informed consent from participants.

A total of 58 patients treated between December 2019 and March 2023 qualified for the inclusion criteria and were included in this study.

Interventions

All CESI procedures were performed by the first author in an operating room environment and under sterile conditions. No needle site local anesthetic was used. After penetrating the sacrococcygeal ligament with an 18-gauge spinal needle under ultrasonography guidance (Toshiba, Tokyo, Japan), before drug induction, a single-shot image was taken with fluoroscopy (Figure 1), and the localization of the needle placed under ultrasound guidance was confirmed. After confirmation, a mixture of 1 mL betamethasone (Celestone®, MSD, USA) and 5 mL bupivacaine (Marcaine®, AstraZeneca, Turkey) 0.5% solution for injection was diluted in 5 mL of 0.9% NaCl and injected (total of 11 mL). Contrast material agents were not used during the procedures. In patients using anticoagulants, procedures were performed without discontinuing these drugs.

The pain levels of the patients were evaluated using VAS scores. Functional recovery was evaluated using Oswestry Disability Index (ODI) scores. These scores were compared retrospectively before injection, immediately after injection, three weeks after injection, and three months after injection. The presence of comorbidities (diabetes mellitus [DM], heart disease, hypertension, morbid obesity, COAH, renal disease, thyroid disease, etc.), chronic drug use, and anticoagulant drug use was noted.

Outcome Measures

The Oswestry Disability Index (ODI) is derived from the Oswestry Low Back Pain Questionnaire used by clinicians and researchers to quantify disability caused by back pain (10). The self-completed questionnaire contains ten topics concerning the intensity of pain, lifting, ability to care for oneself, ability to walk, ability to sit, sexual function, ability to stand, social life, sleep quality, and ability to travel. The scores for all questions answered are summed, then multiplied by two to obtain the index (range 0–100). Zero equals no disability, and 100 is the maximum disability possible.

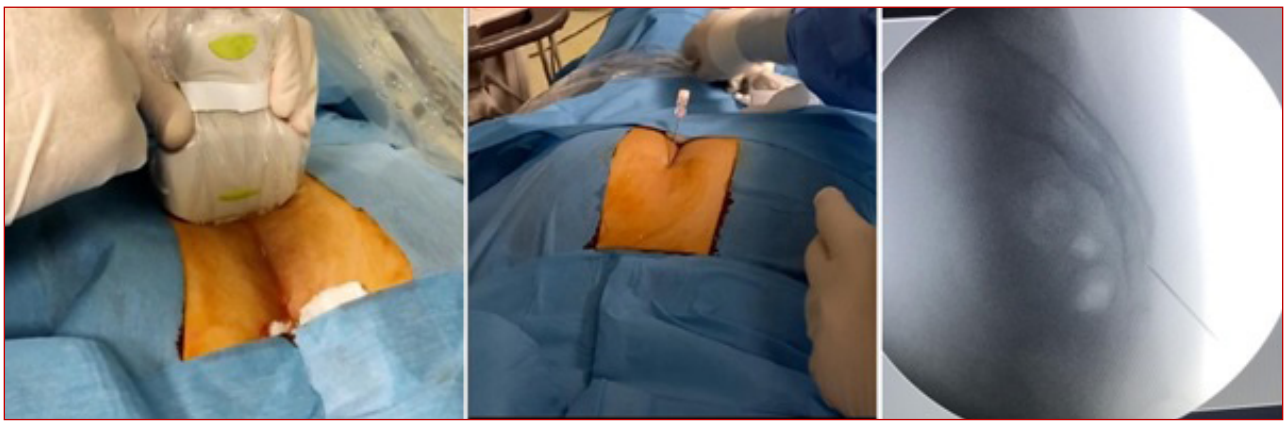

Figure 1. Lateral fluoroscopic view confirming the placement of the spinal needle in the sacral space after insertion into the sacrococcygeal ligament under ultrasound guidance.

The visual analog scale (VAS) is a subjective measure of pain (11). It consists of a 10 cm line with two end-points representing "no pain" and "worst pain imaginable," respectively. Patients are asked to rate their pain by placing a mark on the line corresponding to their pain level. The distance along the line from the "no pain" marker is then measured with a ruler giving a pain score out of 10.

All participants were asked to attend the outpatient clinic three weeks and three months after the procedure. Their subjective satisfaction was assessed using the VAS score for pain relief and the ODI for functional improvement. Patients were also asked to report any adverse events.

In the first postoperative month, a researcher (AEA) collected information regarding analgesics, the number of additional CESIs received, spinal surgery, and any side effects through telephonic interviews with all participants. These results were compared with those in the immediate postoperative and 3-week and 3-month periods. The research worker (AEA) gathered all data retrospectively. Until the completion of the study, the statisticians and intervention staff were blinded to data.

Statistical methods

SPSS (Statistical Package for Social Sciences) for Windows 23 program was used for statistical analysis. Continuous variables were presented as mean ± standard deviation, and categorical variables were presented as frequency (percentage). Measurement results before and after treatment were evaluated using repeated measures analysis of variance. The results were evaluated at the 95% confidence interval, and p values < 0.05 indicated statistical significance.

RESULTS

The study population comprised 58 patients, which included 43 females (74.1%).

The mean age of the patients was 72.7 ± 6.4 (range, 65–87) years. The mean duration of symptoms was 54.0 ± 52.8 (range, 1–240) months. The mean body mass index was 27.4 ± 3.8 (range 21.9–41.1) kg/m^2. In the radiological evaluation, 30 patients had multiple-level lumbar canal narrowing, 13 had L4-5 and L5-S1 disc herniation, and 5 had lumbar spondylolisthesis. Ten patients had a

Table 1. Demographic and clinical characteristics of the study population (n = 58)

Variable p	
Age	72.72±6.43 (65–87)
Body mass index	27.45± 3.82 (21.9–41.1)
Duration	54.00 ± 52.82 (1–240)
Sex	
Male *(%)*	15 (25.9)
Female *(%)*	43 (74.1)
Type of spinal pathology	
Lumbar spondylosis *(n)*	30
Lumbar disc *(n)*	13
Lumbar spondylolisthesis*(n)*	5
Lumbar surgery *(n)*	10
Affected side	
Right *(n)*	7
Left *(n)*	11
Bilateral *(n)*	40
Comorbidity	**4**
1 disease	16
2 diseases	18
3 diseases	14
≥ 4 diseases	6
VAS score	
Preoperative (1)	8.39 ± 1.00
Postoperative 1st day (2)	4.13 ± 1.91
Postoperative 3rd week (3)	4.65 ± 1.86
Postoperative 3rd month (4)	4.98 ± 1.77
ODI	
Preoperative (5)	58.06 ± 14.45
Postoperative 3rd week (6)	41.48 ± 15.43
Postoperative 3rd month (7)	42.72 ± 14.10

ODI: Oswestry Disability Index
VAS: Visual Analog Scale

history of lumbar spinal surgery. Five patients were operated on for narrow canals, 2 for disc herniation, and instrumentation was performed in 3 patients. In addition to low back pain in all patients, seven patients had right radicular pain, 11 patients had left radicular pain, and 40 patients had bilateral radicular pain. Table 1 summarizes the study population's primary demographic and clinical characteristics, including the distribution of comorbid diseases and the use of anticoagulant drugs.

The mean preoperative VAS score was 8.39 ± 1.00. The mean VAS scores on the postoperative first day, third week, and third month are presented in Table 2. The mean VAS scores at all three postoperative time points were significantly lower than the preoperative VAS score ($p < 0.001$) (Figure 2).

The mean preoperative ODI score was 58.06 ± 14.45. The mean ODI score in the postoperative

Table 2. Changes in VAS and ODI score immediately before, immediately after, at 3 weeks, and 3 months after the procedure.

	p
VAS preop-post op 1st day (1,2)	**<0.001***
VAS preop-postop 3rd week (1,3)	**<0.001***
VAS preop-postop 3rd month (1,4)	**<0.001***
ODI preop-postop 3rd week (5,6)	**<0.001***
ODI preop-postop 3rd month (5,7)	**<0.001***

ODI: Oswestry Disability Index
VAS: Visual Analog Scale
* p<0.001

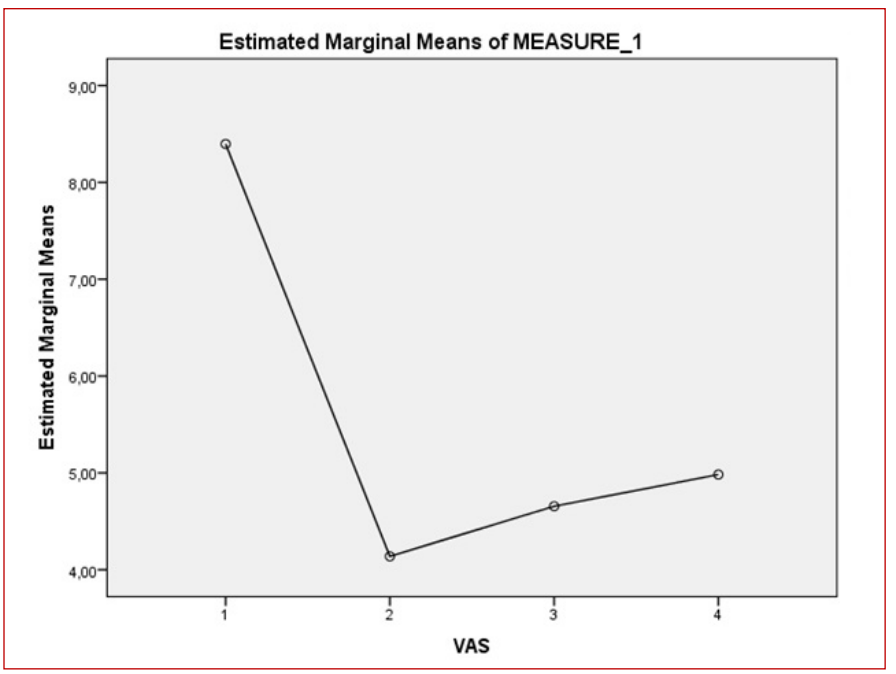

Figure 2. Change in VAS scores at various time-points after the procedure.

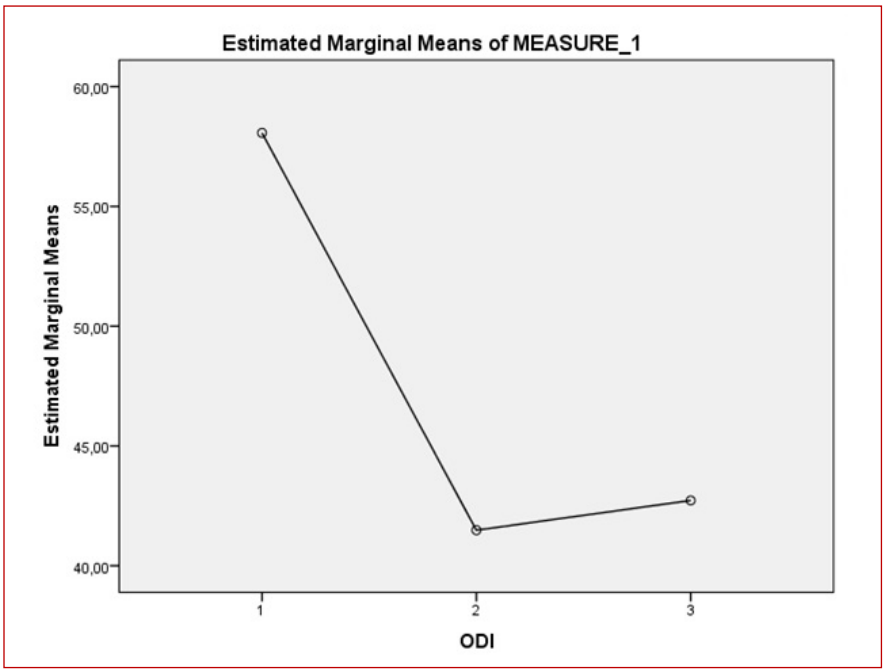

Figure 3. Comparison of improved ODI scores in the groups.

third week and third month were 41.48 ± 15.43 and 42.7 ± 14.10, respectively (Table 2).

There was a significant change in the ODI values at three weeks and three months postoperatively compared to the pre-procedure ($p < 0.001$) (Figure 3).

DISCUSSION

In this study, ultrasonography-guided CESI reduced pain and improved the functional status of geriatric patients with spinal pain during the following three months. The term spinal stenosis (SS) is an anatomical diagnosis. It tends to increase with age and can also be seen in asymptomatic individuals. Most patients aged ≥65 years who have undergone lumbar spinal surgery are operated on for SS. Generally, the use of analgesic drugs should be minimized in elderly patients with comorbidities (such as hypertension, diabetes, and cardiovascular disease) due to these drugs' cardiovascular, renal, and gastrointestinal adverse effects. Spinal pain management in geriatric patients usually includes conservative measures, but surgical intervention may sometimes be required. However, spinal surgery is associated with multiple perioperative risks in older adults (12).

ESI, a less invasive, safe, and cost-effective treatment option for geriatric patients, has become popular recently. Epidural injections usually aim to relieve pain and improve function and mobility. ESI can be performed with interlaminar, transforaminal, and caudal approaches. Fluoroscopy-guided CESI procedure entails radiation exposure and requires the use of contrast material and the application of local anesthesia at the entry site; however, the USG-guided procedure does not require a contrast agent or local anesthetic application at the entry site. This protects the patient from the potential side effects of contrast agents. In recent years, radiation exposure has been eliminated by performing this procedure under ultrasound rather than fluoroscopy (13). Ultrasonographic guidance enables localization of the sacral hiatus

and visualization of the sacrococcygeal ligament. It also detects variations, making injection easy and safe (14).

In a study of 16 patients with lumbar stenosis (age range 68–83 years) conducted by Przkora et al., lumbar ESI application improved objective physical capacity parameters and pain scores compared to drug treatment (8). In our study, most patients had lumbar stenosis and showed a significant improvement in VAS and ODI scores. Similarly, Taşdoğan et al. evaluated the short-term results of ESI in 44 elderly patients with LSS. They found that the ESI application is an effective non-surgical option for pain relief and improving physical function in elderly patients. In their study, additional injections were required in 4 patients, and surgery was required in 2 patients (15). In our study, three patients required a second dose of additional injection, but none in our cohort underwent surgery.

Manchikanti et al. demonstrated the efficacy of caudal epidural injections with or without steroids in treating chronic lower back pain associated with central lumbar stenosis in 100 patients (16). In this study, betamethasone 1 mL was preferred as a steroid, and 0.5% lidocaine 9 mL was preferred as a local anesthetic; however, in our study, we used betamethasone 1 mL and 0.5% bupivacaine 5 mL as a local anesthetic.

In the study by Shabat et al., conservative treatment for LSS was unsuccessful in elderly patients with LSS (17). Anesthesia techniques in orthopedic surgery procedures may affect postoperative results in elderly patients. General anesthesia is associated with the risk of in-hospital mortality, acute respiratory failure, more extended hospital stay, and a higher readmission risk than spinal or regional anesthesia (18).

Surgical decompression is appropriate for people with lumbar spondylosis who do not respond to non-surgical interventions or have neurological problems that severely impair function (19). However, what is generally considered a minor complication in young adult patients may be associated with more severe outcomes in older patients and can significantly prolong the hospital stay. (20,21)

While planning the geriatric surgery process, the patient's physiological loss, the effect of multiple chronic diseases, drug use, preferences, opinions, and sociocultural characteristics should be respected. Following the principles of quaternary prevention, the patient should be protected from vital risks, ageist attitudes and prejudices, and unnecessary pain and suffering. Therefore, the risks and benefits of an operation should be carefully evaluated in elderly patients with more complex problems that negatively affect their health outcomes.

In a retrospective study evaluating the effect of frailty on postoperative complications in geriatric patients undergoing multi-level lumbar fusion surgery, frailty was associated with higher odds of all perioperative complications, length of stay, and all-payer costs. Fragile patients had significantly higher 90-day and 180-day readmission rates and higher 90-day wound deterioration rates. In the subgroup analysis, minimally invasive surgery was associated with significantly reduced surgical complication rates, especially in frail patients. The results showed that frailty status is an essential determinant of perioperative complications and prolonged readmissions in geriatric patients undergoing multi-level lumbar fusion. Thus, fragile patients should be operated using minimally invasive techniques to minimize the risk of surgical complications (22).

Recent studies have revealed a relationship between the severity of foraminal stenosis and the analgesic outcome of ESI (23).

In another study, although transforaminal ESI effectively relieves pain regardless of the severity of foraminal stenosis, patients with severe foraminal stenosis reported a significantly smaller decrease in pain scores over time (24). In our study, patients with severe foraminal stenosis showed a lesser change in VAS scores.

Olgun et al. demonstrated ESI's effectiveness in treating low back pain in the elderly. In their study, elderly patients with disc herniation responded better to treatment than those with spinal stenosis and failed back surgery. There was no difference in radiation dose between the interlaminar, transforaminal, and caudal approaches. In the present study, the procedure was performed with a caudal approach under USG guidance, and the patients and surgical team were exposed to very low radiation. In addition, ODI scores for evaluating functional recovery and comorbid diseases were also examined in our study. Moreover, the number of patients with spinal stenosis in our study was higher, and the procedure was considered successful in all groups (25).

Advanced age and comorbidity are risk factors for LSS-related complications. Therefore, ESI is an effective non-surgical pain relief therapy that can be used in a select group of elderly patients. Performing the procedure via the caudal route under ultrasonography guidance significantly reduces the radiation exposure to the patient and the surgical team (13).

Some limitations of this study should be considered while interpreting the results. This was a single-center study, which may have introduced selection bias. The lack of a placebo group was another limitation. A more extensive prospective study is required to draw more robust conclusions.

CONCLUSIONS

USG-guided CESI is an excellent pain management modality in treating spinal pain, especially in the geriatric age group where surgery is not required or is high-risk. It may be the first-choice method in treating spinal pain in the age group.

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Conflicts of Interest

The authors declare that no conflicts of interest are associated with this study.

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ORIGINAL ARTICLE

COGNITIVE AND MOTOR PERFORMANCES IN DUAL TASKS IN OLDER ADULTS WITH CHRONIC NECK PAIN: A RANDOMIZED CONTROLLED CLINICAL TRIAL

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Abstract

Aim: There is limited information on dual-task performance in older individuals with chronic neck pain. This study aims to investigate cognitive and motor performances during dual tasks in older adults with chronic neck pain.

Methods: Thirty-five older adults with chronic neck pain and 35 older adults without neck pain were included in the study. The timed up and go test evaluated individuals' single-task performance. To assess the dual-task performances of the groups, the individuals were given motor and cognitive (forward and backward digit span) tasks simultaneously with the timed up and go test. During cognitive dual-task, the cognitive performances of individuals were evaluated and the duration of their timed up and go test was recorded.

Results: There was no difference between the groups in terms of single-task timed up and go test ($p > 0.05$). There was also no difference between the groups in terms of cognitive-forward and cognitive-backward ($p > 0.05$). However, cognitive performance of the chronic neck pain group during dual-task was worse than that of the control group ($p < 0.05$). Additionally, the motor dual-task of older adults in the chronic neck pain group was worse than the control group ($p < 0.05$).

Conclusion: Older adults with chronic neck pain struggle more in motor dual-task situations than asymptomatic older adults. Therefore, gait assessment with a motor dual task should be performed for older adults with chronic neck pain. In addition, during cognitive dual-task conditions, the cognitive performance of older adults should be evaluated in addition to their gait performance.

Keywords: Aged; Gait; Neck Pain; Postural Balance; Task Performance and Analysis.

INTRODUCTION

Neck pain is a common issue that often accompanies aging, and it is the second most common musculoskeletal problem (1,2). Its prevalence has been reported to be between 20–34.4% (3,4). Damage to structures such as ligaments, muscles, joints, discs, and neuromuscular junctions in the neck can cause neck pain. Additionally, degeneration and functional changes in these structures due to aging can cause pain. Approximately 50–85% of individuals with neck pain do not fully recover and can develop chronic neck pain (CNP) (5). CNP can limit daily activities and reduce quality of life by affecting upper extremity function. Furthermore, afferent proprioceptive input from cervical muscles, along with vestibular and visual inputs, is transmitted to the central nervous system to maintain postural control. Abnormal cervical afferent input in individuals with CNP can lead to impaired postural orientation and balance (6).

Functional balance is usually assessed with static and dynamic tests, such as the Romberg test, single leg stance test, or timed up and go (TUG) test. However, single tasks are rarely performed in daily life. Movements are often performed as dual or triple tasks. Therefore, attention is important in addition to the systems that maintain balance and central nervous system orientation (7). To evaluate dual-task (DT) performance, cognitive or motor tasks are often added to gait tasks, creating a simulation of real-life situations. Performance in DT situations is known to decrease compared to single tasks, referred to as the DT effect (8). DT performance provides important information in attention, as well as balance and risk of falling. Therefore, when evaluating tasks, both the basic motor and the performance of the cognitive tasks given should be assessed.

Although there are various approaches to explaining and classifying attention processes, there is no complete consensus on these classifications. The classifications generally focused on alertness/arousal, selective attention, sustained attention (wakefulness), and divided attention. (9). Performance reduction during DT is mainly associated with divided attention (9).

Several studies have investigated single or DT performance in individuals with CNP, but there is no consensus on the findings (1,10-12). To our knowledge, no study in the literature has investigated cognitive and motor performance simultaneously during dual-task situations in older individuals with CNP.

This study aimed to investigate cognitive and motor performance during dual-task situations in older individuals with chronic neck pain. According to our hypothesis, neck pain, which is directly related to abnormal proprioceptive inputs, may affect motor performance, or older individuals may allocate more cognitive capacity to compensate for this loss of motor performance.

MATERIALS AND METHODS

Ethical Situation

Written and verbal consent was obtained from all participants included in the study. Permission was obtained from the non-interventional ethics committee of the university to perform the study (Ethics no: 2023/1287). In addition, institutional approval was obtained from the hospital where the study was carried out (issue no: E-34771223-774.99-214732932).

Study Design and Participants

GPower 3.1 software was used to calculate the sample size in this prospective randomized control study. With an effect size of 1.01, a power of 95%, and a significance level of 0.05, a total sample size of 46 was required for the study (1).

Thirty-five older individuals with CNP (CNP group) and 35 older individuals without neck pain (control group) who applied to the outpatient neurosurgery

clinic were included in the study. Detailed anamnesis was taken from these individuals. Individuals with CNP were selected according to the examination and magnetic resonance imaging results of patients who had neck pain due to straightening of the cervical lordosis or the onset of cervical disk herniation for at least three months and did not require surgery. The imbalance and fall status of the individuals were questioned, and the neck disability index (NDI) of the subjects was calculated. Participants were excluded if they had a traumatic neck injury/surgery, vestibular diseases, such as BPPV and Meniere's disease, neurological and uncontrollable systemic disease, visual impairment, cognitive impairment [Standardized Mini Mental Exam: SMME <24 (13)], and musculoskeletal injury/diseases that may affect gait.

Neck Disability Index

The NDI, adapted and assessed for validity and reliability in the Turkish context by Kesiktas et al. (14), consists of 10 questions. Individuals can score each question between 0 and 5. Notably, the disability increases as the total index score increases.

Visual Analogue Scale

Individuals' imbalances were assessed using the visual analogue scale (VAS). A straight line, 10 cm in length, was drawn on a piece of paper, with 0 representing "no imbalance" and 10 representing "very severe imbalance." Participants were instructed to mark the point on the line corresponding to the severity of their imbalance, and the imbalance score was determined by measuring this point with a ruler.

Time Up and Go Test

The main task used in our study was the TUG test. Participants were seated in a chair at the starting point of a 3-meter track and were given the command to "stand up, walk as quickly as possible along the track, and sit back down in the chair." The time taken by each participant to complete the task was measured using a stopwatch.

Digit Span Test

The visual-aural digit span test, a subtest of the Wechsler Memory Scale-Revised, whose Turkish validity and reliability (confidence correlation coefficients .38-.87) study was conducted by Karakas et al. (15) is part of a large neuropsychological test battery (16). The visual-aural digit span test consists of four subtests that evaluate verbal and written responses to aurally or visually presented number sequences. In our study, only the computer-generated visual-aural digit span test was applied to assign additional cognitive tasks to individuals. Although the computer-generated digit span test does not have novmative values in elderly individuals, it facilitates the application of the test. In addition, it was stated that the computerized form of the test increased the test-retest score (17). The computer-generated digit span test was used instead of the classical digit span test in our study because the problem of holding a pencil (fine motor) and hypermetropia is common in elderly individuals. On the other hand, the computer-generated visual-aural digit span test can be adjusted in figure size and applied to elderly individuals more quickly. In addition, the computer-generated digit span test is frequently used in dual-task research due to its ease of application (18). The reason for applying only the visual-aural digit span test is that hearing loss may occur in elderly individuals, and hearing loss may affect auditory digit span test results.

The digit span test, which evaluates attention and short-term memory, was applied as forward-digit span and backward-digit span tasks as stated by Powell and Hiatt (19). The number strings were visually presented using PowerPoint on a 17-inch monitor with a resolution of 144 points. The number sequences ranged from 2 to 9. Participants were informed about the application of the test. The

test began with a triple number sequence, and the number of sequences increased by one when the individual correctly repeated the numbers. A binary number sequence was applied if the individual could not repeat the triple number sequence correctly. If the participant could not repeat the number sequence, another number sequence of the same length was presented. If the participant could not repeat the second number sequence, the test was terminated, and the number sequence threshold was determined. First, the forward digit span test was completed and then the barkward digit test was applied. For the backward digit span task, the participants were asked to repeat the number sequences presented on the computer screen in reverse order using the same method. Thus, the forward and backward digit span thresholds (maximum number of digits with correct answers) of each participant were determined.

Dual-Task Performance

Secondary cognitive and motor tasks were added to the main task (TUG) to assess dual-task performance. The TUG and digit span tests were performed simultaneously as additional cognitive tasks. Participants were presented with a number sequence at their digit span threshold and were asked to say the sequence after completing the TUG. The time it took for participants to complete the TUG with the additional cognitive task ($TUG_{forward}$ and $TUG_{backward}$) was measured and recorded using a stopwatch. Additionally, the participants' digit span performance during the dual task was recorded as either "correct repetition" or "false repetition."

To evaluate the individuals' motor performance during the TUG, they were asked to carry a glass of water on a tray while completing the task (TUG_{motor}). Participants were asked to walk quickly on a three-meter line and hold the tray with both hands. The completion time of the TUG task for each participant was measured with a stopwatch and recorded.

The following formula was used to evaluate dual-task cost (DTC) for each participant (20).

$$\frac{\pm(\text{Single Task - Dual Task})}{\text{Dual Task}} \times 100 = \%DTC$$

Statistical Analysis

Statistical analysis was performed using IBM SPSS 21 software. The normality of the data distribution was checked using the Shapiro–Wilk test. Normally distributed data were presented as mean ± standard deviation (sd), while non-normally distributed data were presented as median (minimum–maximum). To compare the numerical data between the two groups, the independent simple t-test was used when the normality assumption was met, and the Mann–Whitney U test was used when it was not. Categorical variables were evaluated using the chi-square test. A p-value of less than 0.05 was considered statistically significant in all analyses.

RESULTS

Of older adults in the CNP group, 24 (68.6%) were female, 11 (31.4%) were male, and the mean age was 70.11 ± 4.59 (65-81). Eighteen (51.4%) of the older adults in the control group were female, 17 (48.6%) were male, and the mean age was 72.25 ± 6.10 (65-84). There was no difference between the groups in terms of age and gender (p=0.192, 0.143, respectively).

Of the individuals in the CNP group, 19 (54.3%) were primary school graduates, 12 (34.3%) were secondary school graduates, 3 (8.6%) were high school graduates, and 1 (2.9%) were university graduates. Of the individuals in the control group, 15 (42.9%) were primary school graduates, 14 (0.4%) were secondary school graduates, 5 (14.3%) were high school graduates, and 1 (2.9%) were university graduates. There was no difference between the groups in terms of educational status (p=0.771).

Table 1. Fall, imbalance (VAS) and single-task TUG scores by groups.

	CNP Group Median (min-max) n:35	**Control Group** Median (min-max) n:35	**p**
Single-Task TUG (sec)	10.19 (7.19-18.77)	9.28 (6.62-16.30)	0.366[a]
VAS	2.00 (0-10)	1.00 (0-7)	0.351[a]
Falls (n)	11 (31.4%)	5 (14.3%)	0.088[b]

TUG: Time up and go test, VAS: Visual Analogue Scale, a: Mann Whitney-U test, b: Chi Suare Test

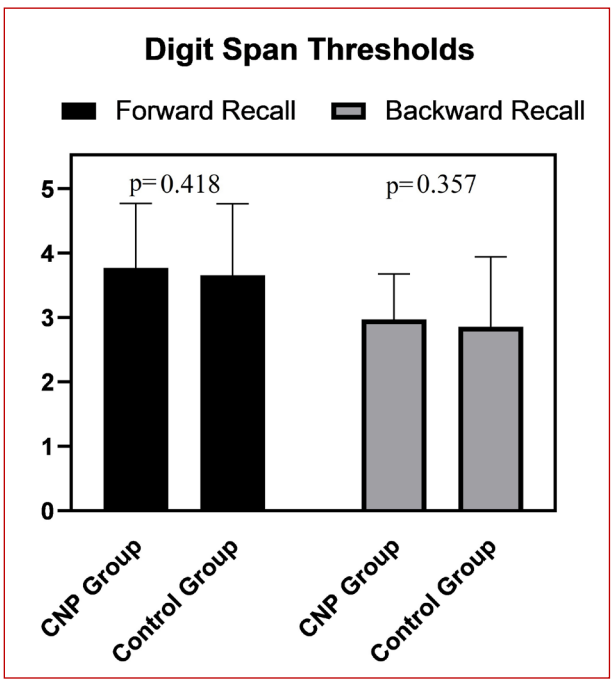

Figure 1. Forward and backward digit span thresholds by groups.

The median value for neck pain duration in the CNP group was 12 months (range: 3–240), and the median value for the NDI was 23 (range: 12–38). There was no significant correlation between neck pain duration and NDI score (p=0.846). Although the older adults in the CNP group had a higher incidence of falls than those in the control group (OR: 2.750), there was no significant difference between the two groups (p >0.05). Similarly, there was no difference between the two groups in terms of VAS and single-task TUG (p >.05). Table 1 shows the fall, imbalance, and single-task TUG scores for both groups.

There was no significant difference between the two groups in terms of forward and backward digit span thresholds (maximum number of digits with correct answers) (p >0.05, as shown in Figure 1). Similarly, there was no difference between the two groups in terms of $TUG_{forward}$ and $TUG_{backward}$ durations (p >0.05). However, the CNP group had a longer TUG_{motor} duration compared to the control group (p <0.05). Table 2 presents the $TUG_{forward}$, $TUG_{backward}$, and TUG_{motor} durations and DTCs for both groups.

Regarding the digit span success of the groups during the dual task, older adults in the CNP group had a significantly lower success rate than those in the control group in both forward digit span (OR: 3.244) and backward digit span (OR: 2.875) (p <0.05). Figure 2 presents the forward and backward digit span results for both groups during the dual task.

The mean of forward digit span thresholds of the participants in the CNP group was 3.77±1.00 and the mean of backward digit span thresholds was 2.97±0.70. Participants in the CNP group had more difficulty in the backward digit span test (p<0.001). Looking at the backward and forward digit span performances during the dual task in the

Table 2. $TUG_{forward}$, $TUG_{backward}$ and TUG_{motor} durations and dual task costs by groups.

	CNP Group Median (min-max) n:35	**Control Group** Median (min-max) n:35	**p***
$TUG_{forward}$ (sec)	9.76 (7.31-19.61)	9.20 (6.70-16.39)	0.259
DTC (%)	0.47%	1.80%	
$TUG_{backward}$ (sec)	10.23 (7.35-18.29)	9.92±2.40	0.259
DTC (%)	0.37%	2.41%	
TUG_{motor} (sec)	11.35 (9.10-23.58)	10.43±2.72	0.006
DTC (%)	14.83%	2.58%	

Mann Whitney-U test, TUG: Time up and go test, DTC: Dual-task cost

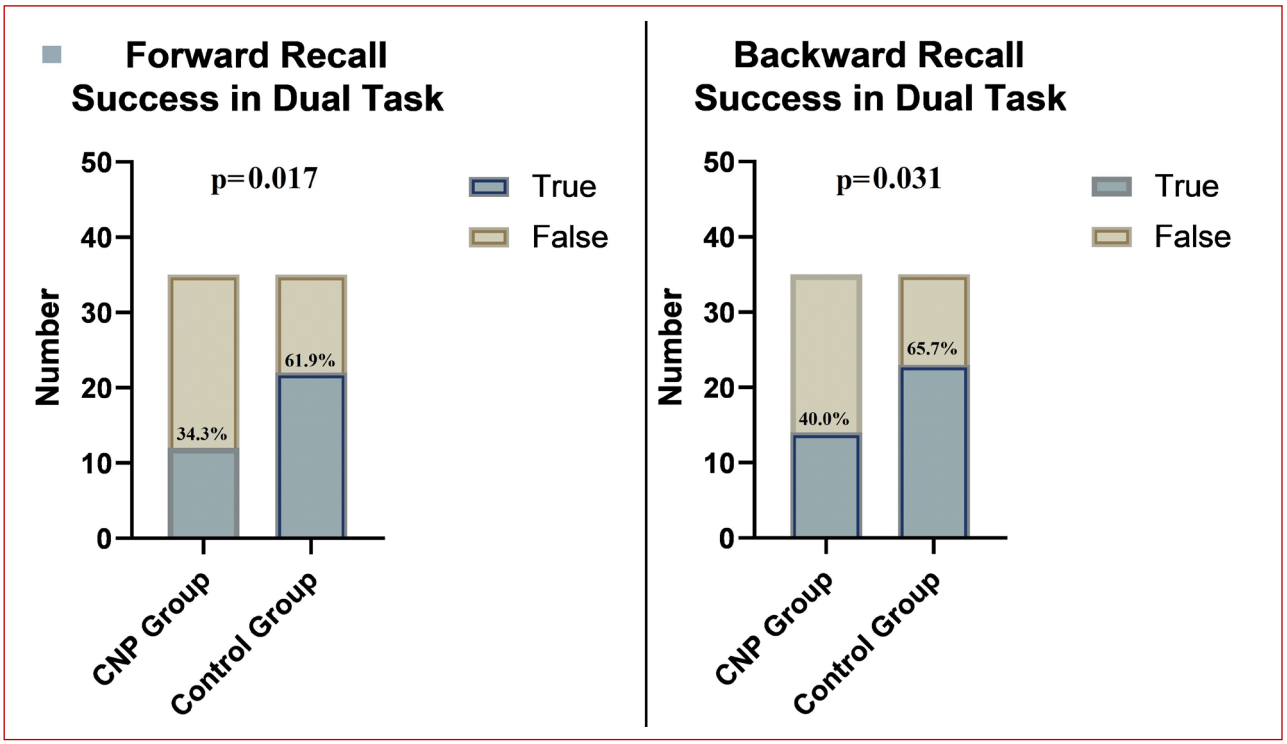

Figure 2. Forward and backward digit span results during dual-task by groups.

CNP group, the backward success of the individuals was 14 (40%) correct and the forward success was 12 (34.3%) correct. There was no difference in the backward and forward digit span performances in the CNP group (p=0.621).

DISCUSSION

Although vestibular disorders are often believed to be the primary cause of imbalance, multisensor dizziness is also prevalent, particularly in older adults. It is considered the second most common

disorder after benign positional paroxysmal vertigo (21). Multisensor dizziness refers to a decline in balance systems due to aging. Further, aging may exacerbate the impact of abnormal somatic afferent information from the upper cervical region in older adults with CNP. As a result, walking, which is the most crucial balance parameter, may be more affected in these individuals (22). Therefore, our study aimed to investigate the cognitive and motor performances of older adults with CNP during dual tasks. Specifically, we aimed to identify any changes in attention and cognitive capacity that occur during walking in older adults with CNP. Our results showed no significant differences in the duration of single-task TUG, $TUG_{forward}$, and $TUG_{backward}$ (TUG with dual task) between the CNP and control groups. However, we observed that the cognitive performance of older adults with CNP during dual tasks was worse than that of older adults in the control group, although the TUG duration remained unchanged. Similarly, the TUG_{motor} duration of older adults with CNP was worse than that of individuals in the control group.

Studies investigating dual-task performance in older adults individuals have reported that during dual tasks, the stride length and speed of older adults change, and these gait changes are associated with an increased risk of falling (10,23). Safe walking ability is crucial for mobility and independence in old age, providing social participation, increasing self-confidence, and preventing falls. Therefore, the ability to perform dual tasks can determine the risk of falling, and dual-task exercises can help reduce this risk (8).

Only a few studies have investigated walking speed during dual-task performance in older adults with CNP (24). Poole et al. (24) examined walking speed with (dual task) and without head rotation (single task) in older adults with CNP using a 10-meter walking test. The authors reported that older adults with CNP had a longer gait cycle and that older adults with CNP preferred a slower self-selected gait speed in head rotation walking. The authors suggested that the impairment in gait may be due to the dual-task effect or the change in cervical somatosensory input caused by fear of pain or pain during neck rotation.

Other studies investigating DT in individuals with CNP have been performed on adult populations (1,11,12). Saadat et al. (1) evaluated walking speed in adults with CNP under three conditions: basic TUG, TUG with an easy cognitive task, and TUG with a difficult cognitive task. The authors reported that individuals with CNP exhibited a decrease in walking speed in all conditions, and the duration of TUG was prolonged as the cognitive task became more difficult. Kirmizi et al. (11) evaluated the balance skills of 22 adult women with CNP under different sensory and dual-task conditions. The authors applied tests with eyes open and closed using four different methods: standing silently, head rotation, counting backwards, and standing on a foam pad. The authors reported that the balance skills of women with CNP were impaired, especially in head rotation with eyes open and counting backwards. Patients with CNP exhibited worse balance performance in different sensory and dual-task conditions. Sremakaew et al. (12) evaluated the walking speed of 30 adults with CNP under four different conditions: comfortable walking, single-task tandem gait, cognitive dual-task gait, and motor dual-task gait. In contrast to Saadat et al. (1) and Kirmizi et al. (11), the authors found that the DT performance of individuals with CNP was not affected and that they only performed worse on the single-task tandem gait test. Therefore, the authors concluded that the effect of neck pain on walking speed is not related to attention but may be due to biomechanical limitations. Unlike these studies, we assessed both walking speed and cognitive performance during dual-task situations in older adults with CNP. In the present study, we found no difference in the duration of single-task TUG and cognitive dual-task TUG ($TUG_{forward}$ and

$TUG_{backward}$) between older adults with CNP and asymptomatic older adults. However, the cognitive performance and TUG_{motor} duration of older adults with CNP during dual tasks were worse than those in the control group.

In the tandem walking test, one foot is placed toe-to-heel with the other foot and walked in a straight line, making it more challenging than regular walking. In our study, we used the single-task TUG test, which is similar to a comfortable gait, as noted by Sremakaew et al. (12). Therefore, abnormal somatosensory inputs caused by neck pain, which can impair postural control, may not have affected the performance of the single-task TUG. However, according to the cross-competition model, tasks of the same type require the same cognitive skills, leading to competition between tasks (25). Simultaneously performing similar tasks may cause further performance degradation in the tasks. Further, as Moreira et al. (26) suggested, abnormal somatosensory inputs from the neck may impair neck image and decrease neck awareness, further affecting motor performance during TUG in older adults with CNP. Therefore, the difficulty in carrying a glass filled with water on a tray while performing TUG in our study may be due to impaired multisensor balance interaction and decreased neck awareness in older adults with CNP.

A study demonstrated that balance evaluation system test scores deteriorated during normal aging and decreased even more in older adults with CNP (27). Our study revealed no difference in the subjective perception of imbalance between older adults with CNP and asymptomatic older adults. However, although not statistically significant, we found that older adults with CNP experienced approximately three times more falls than asymptomatic older adults. The reason why older adults with CNP fell more frequently may be because the motor task of walking performance in these individuals was more impaired. Consequently, similar types of motor tasks may increase the likelihood of falling during walking for older adults with CNP.

Humans have limited processing capacity, and cognitive ability is allocated to tasks in multitasking (28). Therefore, it is more challenging to perform multiple tasks simultaneously than to perform single tasks (29). In our study, similar to Sremakaew's study (12), there was no significant difference between the groups in terms of $TUG_{forward}$ and $TUG_{backward}$ durations during DT. However, the cognitive performance of older adults with CNP during DT was worse than that of older adults in the control group. This can be explained by the serial bottleneck model, which suggests that attention is selective and tasks occurring in a particular order are not independent (25). The completion of one task may affect another. In our study, we asked individuals to remember numbers (digit spans) and say them after completing the TUG. Therefore, older adults with CNP may have shared their cognitive resources with the primary motor task with which they had more difficulty, and this may have affected their cognitive performance later on.

In our study, the backward digit thresholds of the participants in the CNP group were worse than the forward digit thresholds. However, there was no difference in these individuals' backward and forward digit span performances during the dual task. This situation can be explained by the dual-task methodology we applied. We applied the digit span test on the digit thresholds in the dual task. In addition, we asked individuals for digit span answers after TUG. The fact that the application of TUG saves time for the participants and the digit threshold of backward application is lower may have eliminated the backward-forward difficulty and may have brought the difficulty level of the two tests closer to each other.

When investigating DT performance, the method typically focuses on walking performance. However, this approach can be misleading because

individuals may prioritize different tasks during DT. They may allocate more processing capacity to one task and care less about the other. Therefore, evaluating motor and cognitive performance during DT is important. Measuring cognitive performance, in addition to motor performance, can provide valuable information about attention sharing.

This study has some limitations. Typically, in the digit span task, the individual is asked to say the number sequences immediately at the end of the test. However, our study applied the digit span test with the TUG when evaluating the dual-task performance. As a result, there was a delay. This delay may have activated specific memory processes. Therefore, digit span test results applied with TUG may not reflect attention and short-term memory values in elderly individuals. The single-digit span test should be considered for attention and short-term memory. In addition, older adults may develop cognitive impairment due to depression, and depression can make the elderly more perceiving pain or suffering. In our study, the depression level of elderly individuals was not evaluated. In future studies, the effect of depression on dual-task and attention processes in elderly individuals can be investigated.

CONCLUSION

Our findings show that older adults with CNP have more difficulty in dual-task situations, such as walking while carrying a tray with glasses, compared to asymptomatic older adults. Since most daily activities involve performing multiple tasks simultaneously, gait assessment of older adults with CNP should include motor dual-tasking. When evaluating cognitive dual-tasking, relying solely on walking performance may yield misleading results. Therefore, assessing cognitive performance in addition to walking performance can provide crucial insights into the processing capacity of older adults with CNP.

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ORIGINAL ARTICLE

THE EFFECT OF FEAR OF FALLING OF OLDER STROKE SURVIVORS ON THEIR SELF-EFFICACY AND QUALITY OF LIFE: A CROSS-SECTIONAL STUDY

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Abstract

Introduction: The study was conducted to examine the effect of fear of falling on self-efficacy and quality of life in older stroke survivors.

Methods: A descriptive cross-sectional study design was used. One hundred and twenty-one older adults who had had a stroke and admitted to hospital between March and December 2021 were included. Data were collected using the Sociodemographic Characteristics Form, Stroke Specific Quality of Life Scale, Tinetti Falls Efficacy Scale, Stroke Self-Efficacy Questionnaire, Barthel Activities of Daily Living Index, and Standardized Mini Mental Test. Descriptive statistics, numbers, percentages, means, Pearson correlation analysis, and simple linear regression analysis were used.

Results: The mean age of participants was 74.19±6.66 years, Tinetti Falls Efficacy score was 47.67±17.38, Stroke Self Efficacy Questionnaire score was 22.49±7.64, and Stroke Specific Quality of Life Scale score was 3.13 ± 0.68. A statistically significant negative correlation was found between fear of falling and self-efficacy (r:-0.849; $p < 0.001$) and fear of falling and quality of life (r:-0.846; $p < 0.001$). The simple linear regression analysis indicates that Tinetti Falls Efficacy Scale had a statistically significant effect on Stroke Self Efficacy Questionnaire ($p < 0.001$). Tinetti Falls Efficacy Scale had a significant effect on Stroke Specific Quality of Life Scale ($p < 0.001$).

Conclusion: Fear of falling in older stroke survivors significantly affects their self-efficacy and quality of life. It is recommended that fear of falling should be evaluated in detail and comprehensively in older stroke survivors.

Keywords: Aged; Fear; Self Efficacy; Stroke; Quality of Life.

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INTRODUCTION

It is well known that improving self-efficacy and quality of life (QoL) levels is essential in the rehabilitation process of individuals who have had a stroke (1-3). Self-efficacy is a broad concept and a behavioural determinant. The perceived capacity of an individual who has had a stroke to perform a task also affects functional independence by affecting their performance of that task (4). A recent study reported that stroke survivors' participation in physical rehabilitation was affected by self-efficacy and that stroke survivors with high self-efficacy had faster motor development and increased mobility performance (2). It is known that high self-efficacy in stroke survivors improves the QoL, increases confidence in self-management, enables recovery, and supports rehabilitation (3). In addition, Ogwumike et al. (2021) reported that functional independence and exercise self-efficacy are the main determinants of QoL after stroke (4). QoL is an important concept in the stroke rehabilitation process. QoL is defined as the individual's perceptions, goals, expectations, standards, and concerns regarding their position in life in the context of the culture and value system in which they live (5).

In the stroke rehabilitation process, the concept of fear of falling (FoF) has become increasingly important, as have those of self-efficacy and QoL. It is well known that individuals who have had a stroke have a significantly higher incidence of falling and FoF than those who have not (6). The rehabilitation process is adversely affected in individuals whose activities are restricted due to FoF (7). Kamide et al. (2021) stated that self-efficacy decreases due to falls, and new falls may occur (8). It has been reported that the FoF seen in elderly individuals is a predictor of their QoL. FoF increases when an individual's physical functions are limited, and the presence of FoF decreases QoL and self-efficacy levels (9). Although the relationship between FoF and self-efficacy and QoL is known, more research is needed to reveal how strong the relationship is. In addition, although stroke is not an ageing problem, it has an increasing incidence with age (10), and no study has yet determined the effect of FoF on self-efficacy and QoL in older stroke survivors. With the aim of raising awareness of this issue, the present research was conducted to determine the effect of FoF on the QoL and self-efficacy of older adults who have had a stroke.

MATERIALS AND METHOD

A descriptive cross-sectional study design was used. Data were collected in face-to-face interview with individuals who had had a stroke and admitted to the neurology outpatient clinic of a university hospital between March and December 2021. The study was reported in accordance with the STROBE (The Strengthening the Reporting of Observational Studies in Epidemiology) checklist: cross-sectional studies (available at www.strobe-statement.org).

Sample

The sample consisted of individuals who met the inclusion criteria (over 65 years of age, Turkish-speaking, literate, having an ischaemic stroke, having a place and time orientation, having no aphasia, having a Standardized Mini-Mental Test Score above 24 and a Barthel Activities of Daily Living Index of 62 points and above). Due to the nature of the outpatient clinic where the data were collected, only elderly individuals with ischaemic stroke were included in the study. The sample comprised 121 individuals with older stroke survivors who voluntarily agreed to participate in the study. In the calculation of the sample size, the lowest regression coefficient was taken as 0.25 in order to obtain the highest sample size. The calculation made in the G-Power 3.1.9.4 programme (regression coefficient of 0.25, type I error based on 0.05, type II error (power) 0.80) indicated a sample size of 81. Individuals who were bed- and wheelchair-dependent, had severe vision

and hearing problems, and were experiencing an acute situation that would affect self-efficacy and QoL during the data collection process were not included in the study. As a result of the post hoc analysis, the power of the study was found to be 97% in the regression analysis performed with one independent variable in the G-power 3.1.9.4 programme, the effect size was found to be d = 0.15, the significance level was less than 0.05, and the sample number was 121.

Data Collection Tools

Data collection tools are described in Table 1 (11-16).

Analysis of Data

IBM SPSS Statistics Premium Academic Pack – Concurrent User V 25 was used to analyse the data. The data were analysed using descriptive statistics, number and percentage distributions, correlation

Table 1. Study Measures, Scoring, and Reliability

Measurement Tool	Number of Items	Description and (Example)	Scoring and Reliability
Sociodemographic Characteristics Form	11 items	It includes questions such as age, gender, marital status, date of diagnosis, chronic disease, and previous history of falling in older adults who have had a stroke.	-
Stroke-Specific Quality of Life (SS-QoL) (11)	48 items 8 sub-dimensions	It includes questions about activity, family and social aspects, energy, language, temperament, personality, thinking, and vision in the stroke survivor.	Likert type from 1-5. 1 = strongly agree 5 = strongly disagree Min-max: 1-5 (Cronbach's α: 0.97, in the current study: 0.97)
Tinetti Falls Efficacy Scale (T-FES) (12)	10 items	It evaluates the fear of falling experienced by individuals while performing activities of daily living.	Scoring from 1-10. 1 = I trust myself a lot 10 = I don't trust myself at all Min-max: 10-100 (Cronbach's α: 0.71, in the current study: 0.96)
Turkish version of the Stroke Self-Efficacy Questionnaire (T-SSEQ) (13)	13 items 2 sub-dimensions	It measures the self-efficacy judgments of stroke survivors in certain functional areas.	Likert type between 0-3. 0 = I don't trust myself at all 3 = I trust myself a lot Min-max: 0-39 (Cronbach's α activity 0.89, self-management 0.66, in the current study 0.95)
Barthel Activities of Daily Living Scale (BI) (14,15)	10 items	It consists of activity and self-management sub-dimensions.	Min-max: 0-100 The score of the item is between 5-15. (Cronbach's α: 0.93)
Standardized Mini Mental Test (SMMT) (16)	11 items	It determines the level of Independence in activities of daily living.	Min-max:0-30, For educated individuals, 22 points and below indicate cognitive impairment. (kappa value: 0.92)

analysis, and simple linear regression analysis. A value of $p < .05$ (95% confidence interval) was considered statistically significant.

Ethical Aspects of the Research

The necessary institutional permission and permission from the non-interventional research ethics committee (2021/10-14, 29.03.2021) were obtained for the implementation of the study and was conducted according to the World Medical Association Declaration of Helsinki. Participation in the research was voluntary, and written and verbal consent was obtained from the participants after they were informed of the purpose of the research.

RESULTS

The study participants' demographic characteristics were evaluated, and the results are given in Table 2. Descriptive statistics of the Stroke Self-Efficacy Questionnaire (T-SSEQ), the Stroke Specific Quality

Table 2. Distribution of Demographic Characteristics of Older Stroke Survivors (n=121)

Demographic Characteristics	n	%
Age (Min-Max / mean±SD)	65-92 / 74,19 ± 6,66	
Sex		
Female	52	43,0
Male	69	57,0
Marital status		
Married	79	65,3
Single	42	34,7
Educational status		
Primary education	91	75,2
High school	27	22,3
College-university	3	2,5
Diagnosis		
Less than 1 year	25	20,7
1-5 years	44	36,4
More than 5 years	52	43,0
Stroke frequency/number		
1 time	107	88,4
2 times	11	9,1
3 and more than 3	3	2,5
Getting help from someone for the care		
Yes	92	76,0
No	29	24,0
Having a chronic illness		
Yes	113	93,4
None	8	6,6
History of falling		
Yes	58	47,9
No	63	52,1
With whom he/she lives		
Lives alone	5	4,1
With his/her spouse	61	50,4
With spouse and children	16	13,2
With other relatives	39	32,2
Total	**121**	**100,0**

Table 3. The Effect of Fear of Falling on the Stroke Self-Efficacy and Quality of Life Scales of Stroke Survivors

	Stroke Self-Efficacy Scale								
	ß	**SH**	**Beta**	**t**	**p**	**F**	**Model (p)**	**R^2**	**Durbin-Watson**
Constant	40,302	1,079	-	37,344	0,000 [a]	308,107	0,000[a]	0,721	1,838
Fear of Falling	-0,374	0,021	-0,849	-17,553	0,000 [a]				
	Stroke-Specific Quality of Life Scale								
	ß	**SH**	**Beta**	**t**	**p**	**F**	**Model (p)**	**R^2**	**Durbin-Watson**
Constant	4,708	0,097	-	48,459	0,000 [a]	299,608	0,000 [a]	0,716	1,653
Fear of Falling	-0,033	0,002	-0,846	-17,309	0,000 [a]				

[a] p<0,001

of Life (SS-QOL), and the Tinetti Falls Efficacy Scale (T-FES) included in the study were evaluated. According to the results obtained, the mean T-SSEQ score of the older adults who had a stroke was 22.49 ± 7.64, the mean SS-QOL score was 3.13 ± 0.68, and the mean T-FES score was 47.67 ± 17.38.

There is a statistically significant negative and very strong relationship between the T-FES mean score and T-SSEQ (r:-0.849; $p < 0.001$) and between the T-FES mean score and SS-QOL (r:-0.846; $p < 0.001$). A simple linear regression analysis was conducted to investigate the effect of T-FES on T-SSEQ, and the results show that the established model is statistically significant ($F = 308,107$; $p < 0.001$). It was found that T-FES had a statistically significant 72% effect on T-SSEQ. A further simple linear regression analysis was performed to investigate the impact of T-FES on SS-QOL in older adult stroke survivors, and the results showed that the established model was statistically significant ($F = 299,608$; $p < 0.001$). It is seen that T-FES has a statistically significant 71% effect on SS-QOL in older stroke survivors (Table 3).

DISCUSSION

FoF

It was determined that the older stroke survivors included in the study had a moderate FoF, and nearly half had a previous history of falling. The FoF-related findings in this study are similar to those in the literature. Savcun et al. (2021) examined the relationship between balance and FoF in stroke patients and stated that stroke survivors with poor balance avoid activities and experience FoF (17). Fortini et al. (2021) stated that 40% of the participants in their study had a history of falling (18). Compared to the reported studies, it was observed that a slightly higher number of individuals in this study had FoF and a history of falling. The reason for this is thought to be that, unlike the other studies, the sample of this study consisted of older adults.

Self- Efficacy

Not only is FoF is common in individuals who have had a stroke, but it also triggers fear of moving (17).

In the literature, it is emphasised that self-efficacy is an important variable related to various factors, such as activities of daily living, perceived health status, and QoL after stroke (19,20). In our study, it was found that older adults who had had a stroke had a moderate self-efficacy perception.

Nott et al. (2021) studied the role of self-efficacy in stroke self-management and reported that stroke patients with high self-efficacy have higher occupational performance than those with low self-efficacy and that self-efficacy is a mediating variable in improving occupational performance (21). Although stroke self-management does not improve occupational performance in older adults who no longer work, it is thought that increasing an individual's level of self-efficacy will cause an increase in both their activities of daily living and their level of coping with the negativities experienced. In addition, it is thought that improvement of self-efficacy in older adults who have had a stroke will lead to a positive change in their cognitive and physical perceived health status.

QoL

In the current study, it was found that older adults who had had a stroke had a moderate QoL. Similar to our study, Ellepola et al. (2022) examined the relationship between QoL and physical activity in daily life in individuals with stroke. It was found that the QoL related to the sub-score of general health, pain, social functionality, and vitality was moderate (22). The limitations caused by stroke bring changes to the QoL of individuals. It is thought that determining the factors affecting the QoL of older adults who have had a stroke and implementing interventions to improve their behavioural and cognitive functions will contribute to their QoL.

FoF and Self-Efficacy

The current study found a significant negative and very strong relationship between the FoF scale mean score and the Stroke Self-Efficacy scale mean score of older adults who have had a stroke. Similarly, Sheikh and Hosseini (2022) examined the relationship between gait variability and fall self-efficacy in stroke survivors and stated that the self-efficacy of older adults who have had a stroke decreases due to FoF (6). In the literature, it has been stated that self-efficacy will decrease as a result of decreased mobility, and more FoF may be seen in individuals who have had a stroke (23). The finding of a relationship between FoF and self-efficacy was expected. At the same time, it is emphasised that self-efficacy is important in evaluating FoF, and the relationship between FoF and self-efficacy should be determined in patients with stroke survivors (17). As a result of this study, it is pointed out that FoF is an important variable in self-efficacy.

FoF and QoL

There is a significant and negative correlation between the mean score of the FoF scale and the mean score of the Stroke-Specific Quality of Life Scale of older adults who have had a stroke in this study. Park and Cho (2021) examined FoF and related factors during activities of daily living in chronic stroke patients and stated that the presence of FoF after a stroke would lead to a decrease in physical function, self-efficacy, activities of daily living, and QoL (24). Jönsson et al. (2021) reported that stroke survivors with a history of falling have less physical activity in daily life, are more dependent, and have a lower QoL and that there is a significant negative relationship between falls and QoL. It has been emphasised that individuals with stroke and FoF should be encouraged to participate in activities (25). As found by the current study, Jönsson et al. determined that FoF is an important variable in QoL (25).

CONCLUSION

The average score of FoF, self-efficacy, and QoL of older adults who have had a stroke is moderate. It was concluded that FoF in older adults who have

had a stroke is associated with, and significantly affects, self-efficacy and QoL. Rehabilitation services are essential for improving stroke survivors' independence and QoL. When these services are provided, it should not be forgotten that FoF is an important determinant of self-efficacy and QoL. It is predicted that raising awareness of the importance of evaluating FoF in older adults with stroke will prevent falls in this group and increase their self-efficacy and QoL.

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ORIGINAL ARTICLE

PROGNOSIS AND RISK FACTORS FOR GERIATRIC STROKE PATIENTS IN EACH DECADE

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Abstract

Introduction: We aimed to compare the demographic characteristics, stroke localizations, stroke risk factors, and prognoses of geriatric stroke patients in different age groups.

Materials and Methods: Geriatric patients who had a neurological consultation following an acute ischemic stroke were evaluated in the study. Patients were divided into age groups of 65–69, 70–79, 80–89, and 90 years and older. The demographic findings, the diseases of the patients, pre-stroke antiaggregant or anticoagulant treatment, previous history of cerebrovascular disease, presence of atrial fibrillation, laboratory data, imaging reports from initial presentation, Echocardiography and Carotid-Vertebral Doppler Ultrasonography results were recorded. Neurological deficits were evaluated using the National Institutes of Health Stroke Scale and the Modified Rankin Score.

Results: The study evaluated 298 patients (161 females, 137 males). Significant differences were found in all four age groups in terms of the presence of diabetes mellitus. In relation to infarct localization, there were no significant differences between the four age groups. Previous antiaggregant or anticoagulant treatments were similar in all age groups. There were significant differences between the groups in terms of the presence of atrial fibrillation at presentation. In the 90 years and over age group, the values for the National Institutes of Health Stroke Scale and Modified Rankin Score were significantly higher.

Conclusion: The incidence of stroke can be reduced by the regular evaluation of elderly individuals for modifiable risk factors and their management. In elderly individuals who had ischemic strokes, we recommend to comprehensive cardiac assessment, including procedures like a 24-hour Holter monitor and transesophageal echocardiography for cardioembolic origins.

Keywords: Stroke; Geriatric; Risk factors; Prognosis.

INTRODUCTION

Stroke is the second leading cause of death worldwide, and its global prevalence is increasing with the aging of the population (1). The proportion of populations that comprise the elderly is increasing throughout the world, particularly in developed countries. Ischemic stroke may occur at any age, but most patients are elderly. Age is the most important unmodifiable risk factor for all types of stroke. In people aged 65 or older (the geriatric age group), the prevalence of stroke varies from 46–71 per 1,000 people (2). Studies report that 75–89% of all strokes occur in people over the age of 65 (3). Changes that occur in the brain with advancing age result in older people being affected more severely by stroke. Symptoms of aging can be observed in cerebral vessels (4).

It is common knowledge that the incidence of stroke rises with age. However, when geriatric patients are evaluated independently, our information –especially regarding the impact of age on prognosis– is quite limited (5). In addition, there are large gaps in the information on the prevention and treatment of stroke in the elderly (1).

The present study aims to compare the demographic characteristics, stroke localizations, stroke risk factors, and prognoses of geriatric stroke patients in different age groups.

MATERIALS AND METHODS

All consecutive patients who presented to the emergency service of Ankara Bilkent City Hospital –which serves as the stroke reference center in Ankara Turkey– with suddenly developing focal or global cerebral dysfunction signs and symptoms between January 1, 2020, and December 31, 2020, and who, after neurological consultation, were diagnosed with acute ischemic stroke and admitted to the neurology ward or intensive care unit, were evaluated in the present study.

Patients under the age of 65, those who had an intraparenchymal hematoma, a transient ischemic attack (TIA), head trauma, or cerebral venous thrombosis, and those patients found to have COVID-19 at presentation were excluded from the study.

Overall, 298 patients were eligible for the study. Neurologists had kept medical records for these patients until their discharge, and these records were evaluated in detail for the study.

The geriatric patients included in the study were divided into age groups of 65–69, 70–79, 80–89, and 90 and older. The age and sex of the patients were recorded and, if present, their diseases prior to the stroke (hypertension, diabetes mellitus, hyperlipidemia), any pre-stroke antiaggregant or anticoagulant treatment, whether valve replacement had been carried out, any previous history of cerebrovascular disease, the presence of atrial fibrillation in their electrocardiography (ECG), laboratory data for stroke on initial presentation, and imaging reports during the presentation (CT and MRI) were also recorded. The infarct areas detected by the neuroimaging investigations were classified into lacunar (LACI), posterior (POCI), total anterior (TACI), and partial anterior (PACI) circulation infarcts, after hemorrhage had been ruled out (6, 7). For the quantitative measurement of neurological deficits associated with stroke at both admission and discharge, the National Institutes of Health Stroke Scale (NIHSS) (8) (1–4 mild, 5–15 moderate, 16–20 moderate to severe, and 21–42 very severe) scores were recorded, and for an assessment of the degree of functional neurological disability developing after the stroke, the admission and discharge Modified Rankin Score (mRS) (9) (1 and 2 independent, 3 and over dependent) were recorded.

Echocardiography and Carotid-Vertebral Doppler Ultrasonography (USG) results on admission for stroke were also recorded. According to the Doppler USG findings, patients were

divided into four groups: no stenosis, intima-media thickening, asymptomatic stenosis (under 70%), and symptomatic stenosis (70–99%). Whether the occlusion in the carotid artery was complete was also noted.

Statistical Analysis

The data were analyzed using the IBM SPSS 22 program. In the analysis, $p < 0.05$ was accepted as statistically significant. Descriptive statistics of categorical variables included percentage frequency values (%), and the descriptive statistics of numerical variables included min, max, mean, and standard deviations. The patients were divided into four age groups: 65–69, 70–79, 80–89, and 90+. Statistical interpretations of numerical fields for these age groups were examined with the Kruskal-Wallis independent samples test. The Kruskal-Wallis test was used because the sample size was more than 2. Pearson's chi square method was used for the relationship between age groups and categorical variables. The Ethics Committee of Ankara City Hospital granted approval for this retrospective data analysis with approval number E1-21-1483.

RESULTS

The distribution according to age groups of the 298 (161 female, 137 male) patients included in the study is illustrated in Table 1.

The previous presence of hypertension (HT) and a diabetes mellitus (DM) diagnosis are considered established risk factors for stroke. In the present study, no significant difference was found between the four age groups in terms of the presence of HT ($p = 0.986$). However, a significant difference was found between the groups in terms of the presence of DM (25 patients in the 65–69 age group, 58 patients in the 70–79 age group, 28 patients in the 80–89 age group, and two patients in the 90 and older age group) ($p = 0.028$)*.

Blood lipid profile and glycosylated hemoglobin (HbA1c) values, also considered stroke risk factors, are demonstrated in Table 2. It was observed that as age increased, HbA1c and triglyceride (TG) values decreased.

No significant differences were found between patients in the four geriatric age groups with respect to antiaggregant or anticoagulant treatment received prior to the stroke (acetylsalicylic acid, clopidogrel, warfarin, new-generation oral anticoagulants, and combined treatments).

No significant differences were found between patients in the four geriatric age groups regarding valve replacement history or a previous history of cerebrovascular disease ($p = 0.278$ and $p = 0.434$), respectively.

However, a significant difference was found between the four age groups in terms of the presence of atrial fibrillation (AF) on presentation. According to the ECG investigation ($p = 0.029$), in the age range 70–89, AF was present in 56 patients overall (28 patients between 70 and 79, and 28

Table 1. Distribution of patients according to age group

Gender	Age Groups				Totals
	65–69	70–79	80–89	90 and older	
Female	26	68	55	12	161
Male	30	65	40	2	137
Total	56	133	95	14	298

Pearson's chi-squared test was used.
($p = 0.046$)

Table 2. Blood lipid profiles and HbA1c values for the groups

	Age Groups			
	65–69	**70–79**	**80–89**	**90 and Older**
Low density lipoprotein (LDL) mg/dL	115,4	110,1	111,1	97,4
High density lipoprotein (HDL) mg/dL	38,9	40,8	40,3	46,3
Triglycerides (TG)* mg/dL	**147,3**	**135,6**	**123,2**	**99,1**
Hemoglobin A1c (HbA1c) ** **(%)**	**7,83**	7,11	**6,64**	6,46

Kruskal–Wallis test was used.
* p = 0.002
** p = 0.002

Table 3. Comparison of age groups according to admission and discharge stroke severity scores

		Age groups				Totals
		65-69	**70-79**	**80-89**	**90+**	
Admission NIHSS*	No symptom	5	9	4	**1**	19
	Mild	27	66	47	**3**	143
	Moderate	21	51	37	**7**	116
	Moderate–severe	2	6	3	**2**	13
	Very severe	1	1	4	**1**	7
Discharge NIHSS**	No symptom	4	19	7	**1**	31
	Mild	34	74	50	**3**	161
	Moderate	15	33	34	**8**	90
	Moderate–severe	2	4	1	**1**	8
	Very severe	1	3	3	**1**	8
Admission mRS***	Independent	27	65	39	4	135
	Dependent	29	68	56	10	163
Discharge mRS******	Independent	36	75	38	**4**	153
	Dependent	16	52	48	**7**	123
	Died	4	6	9	**3**	22
Totals		56	133	95	14	298

NIHSS: National Institutes of Health Stroke Scale; mRS: Modified Rankin Score
Monte Carlo chi-square test was used.
* p = 0.024 (statistically significant)
** p = 0.029 (statistically significant)
*** p = 0.075 (statistically not significant)
**** p = 0.000 (statistically significant)

patients between 80 and 89), in eight patients between the ages of 65 and 69, and in four patients aged 90 or older.

As mentioned, patients were separated into the following infarct localization groups according to the neuroimaging findings at the emergency service: LACI, POCI, TACI, and PACI circulatory infarcts. No significant difference was found between the four age groups in relation to infarct localization ($p = 0.544$).

The NIHSS and mRS values for all patients at both presentation and discharge and their statistical analyses are presented in Table 3. Admission–discharge NIHSS and discharge mRS values were significantly higher in the 90 and over age group than in the other age groups.

No significant differences were found between the four geriatric age groups in relation to stenosis as detected by carotid-vertebral Doppler ultrasonography or in relation to the presence of thrombus, as shown in the echocardiography ($p = 0.565$ and $p = 0.201$, respectively).

DISCUSSION

Stroke is one of the major causes of morbidity and mortality in the geriatric age group. The main factor increasing the prevalence of stroke is age. However, there are large gaps in the available information regarding the prevention and prognosis of strokes occurring in old and very old individuals (1). In our country, the prevalence of ischemic stroke has increased by 115% in the last 30 years. This increase is particularly evident over the age of 70. Likewise, the mortality rate tends to increase with age, regardless of gender (10). In United States the age distribution of the general population is shifting upwards and the average age at first stroke is expected to increase accordingly. In the year 2010, strokes affecting individuals over the age of 85 constituted 23% of all stroke cases in the United States. However, projections indicate that by the year 2050, this proportion is expected to rise to 34%, signifying that more than half of all stroke incidents will occur after the age of 75 (11). The determination and elimination of risk factors for stroke, particularly in geriatric age groups, is of primary importance in both developed and developing countries, so that the incidence and mortality of stroke, and the high costs associated with it, can be reduced. The aim of the present study was to compare the risk factors and prognosis of four different age groups (separated by decades) in geriatric patients 65 years of age and older.

The significant difference found between the different age groups in terms of sex distribution may be attributed to the markedly higher number of women in the 90 and older age groups (12 females, two males). As is known, average life expectancy is higher in women than in men (12, 13). Moreover, stroke can occur at a younger age in women than in men (3). It was assumed that the significant difference in sex distribution was associated with these facts.

While the effectiveness of hypertension treatment in lowering the risk of stroke has been demonstrated, the timeline at which this reduction in stroke occurrence becomes evident remains less certain. Conversely, the adverse effects associated with hypertension treatment, such as orthostatic hypotension, syncope, falls, and electrolyte imbalances, seem to manifest shortly after the commencement of treatment (14). Due to the addition of other risk factors with increasing age, the presence of HT is a less significant risk factor for older patients than for younger ones. Studies have established that HT loses its significance as a risk factor, particularly over the age of 90 (15). Similarly, in the present study, no significant difference was found between the four geriatric age groups in terms of the presence of HT. HT was detected at similar rates in all age groups, indicating that HT no longer influences the risk of stroke with advanced age.

The mean ages of the patients included in the studies Action to Control Cardiovascular Risk in Diabetes (ACCORD), Action in Diabetes and Vascular Disease Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE), and the Veterans Affairs Diabetes Trial (VADT), which are the three largest studies to have investigated the relationship between DM and cardiovascular diseases, were 62, 66, and 60, respectively (15). All three studies recommended that other risk factors (such as HT, dyslipidemia, smoking, sedentary lifestyle, etc.) should be considered in addition to DM to decrease microvascular risk (16). In another study, 11,140 type 2 DM patients over the age of 55 were followed for five years to evaluate the development of microvascular and macrovascular risks. Their mean age was 66 ± 6. In this study, no significant differences were found between the group whose blood sugar levels were intensively reduced and the group whose blood pressure (BP) was not reduced intensively in terms of the development of major macrovascular events (17). There is no evidence to indicate that an intensive blood glucose level reduction decreases the risk of stroke (16). However, elderly patients are seldom included in studies such as the aforementioned. Among elderly or frail patients with a higher risk of hyperglycemia or a shorter life expectancy, according to American Diabetes Association (ADA) guidelines, a higher glycemic target is recommended (18). Patients who experienced ischemic stroke faced an elevated risk of stroke recurrence within one year in association with prolonged diabetes duration (≥8 years), as opposed to cases of shorter-term diabetes duration (19). In the present study, of the four age groups, the DM rate was relatively lower in the 90 and over age group (two of 12 patients). This difference may be attributed to the fact that the number of patients was relatively lower than in the other groups and that this group refers at a lower rate to routine hospital controls or outpatient clinics.

In the literature, the relationship between cholesterol levels and the risk of stroke is controversial. In the Framingham cohort, no significant relationship was found between cholesterol levels and the incidence of stroke (20). In a study investigating the relationship between age and dyslipidemia in 2,074 ischemic stroke patients either under or over the age of 65, it was reported that in patients over 65, namely the geriatric group, total cholesterol, TG, and LDL levels were lower than those in the non-geriatric group (21). In that study, total cholesterol, TG, and LDL levels were found to be significantly higher in ischemic stroke patients between the ages of 50–59 and 60–69 than in those aged 80 and older. In the non-geriatric group, a more severe and common disturbance was found in the lipid levels. Similarly, in the comparison of the four age groups in the present study, it was established that as age increased, TG and LDL levels decreased, with the decrease in TG levels being statistically significant ($p = 0.002$). It was assumed that this difference might be due to decreased intake through diet as age increases.

For stroke prevention, recommendations based on clinical studies support the utilization of acetylsalicylic acid, clopidogrel, and combined antiaggregant treatments (22). However, there is limited evidence of the benefit/risk ratio of the prophylactic administration of combination treatments, especially in very old individuals. In a study by Arnett et al., entitled ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease, the initiation of routine, low-dose acetylsalicylic acid (75–100 mg) for the prevention of atherosclerotic cardiac diseases in individuals over the age of 70 was not recommended, since it increases the risk of bleeding (17, 18). Exploration into novel antiplatelet treatments like clopidogrel, ticagrelor, or prasugrel has not been conducted within the context of primary prevention, and thus, they should not be immediately regarded as substitutes for acetylsalicylic acid in this particular role (23). In

present study there was no significant differences between patients in the four geriatric age groups with respect to antiaggregant or anticoagulant treatment received prior to the stroke.

AF is the most common cardiac arrhythmia and a major risk factor for ischemic stroke. From the literature, it can be seen that AF prevalence increases two-fold with each decade of increase in age, reaching a rate as high as 9% in the age range of 80–89. In the Framingham study, the risk of stroke associated with atrial fibrillation was found to be 1.5% between the ages of 50 and 59, while it was 23.5% between the ages of 80 and 89 (24, 25, 26, 27). In the present study, and consistent with the literature, the prevalence of AF was found to be significantly higher in the age groups 70–79 and 80–89. In addition, of the 228 ischemic stroke patients between the ages of 70–89, 56 were established as having AF through an ECG at presentation. However, in this age group, only 25 patients were on anticoagulants (seven on warfarin, 18 on new-generation oral anticoagulants). The role of anticoagulant therapy in prophylactic management of stroke in patients with AF has been demonstrated in many studies. However, the present study indicated that prophylactic treatment for AF patients had not been administered to an adequate degree.

The most important study aimed at determining the etiology of stroke all over the world reported that over half of all stroke types occurred in individuals over the age of 75 (2). Studies have shown that, particularly in patients aged 80 and older, the risk profile for ischemic stroke is different from that of younger patients (25). As in other countries, the results obtained in the present study suggest that routine cardiac examination and ECG investigation in this age group, with changes to risk factors and proper anticoagulation measures in patients with AF, may lead to a marked drop in the incidence of stroke. In the present study of 228 ischemic stroke cases between the ages of 70 and 89, 15 died and 100 were discharged with dependency. In light of this, it is our suggestion that the addition of an ECG and Holter investigation to a control examination—even if the patient does not have a previous history of any cerebrovascular event—may be beneficial for decreasing the morbidity and mortality associated with ischemic stroke in this population.

In most studies on ischemic stroke, the very old group (age over 90) was generally excluded. These patients were included in our study. Both discharge NIHSS and discharge mRS were higher in patients over 90 years of age. Our study supports the need to be more careful when deciding on acute treatment (intravenous and intra-arterial) and secondary prophylaxis in patients aged > 90 years who applied in the acute period.

The main limitations of the present study are associated with its retrospective nature in a single center. Because we were unable to obtain all body mass index (BMI) and smoking figures accurately, we could not incorporate these factors into the study, and patient follow-up was carried out only until discharge. Information on dementia and malnutrition, which could affect discharge NIHSS and mRS scores, was missing. There was no left atrial dilatation information on transthoracic echocardiography, which is frequently associated with atrial fibrillation. In terms of long-term mortality, mRS information at day 90 was not noted.

CONCLUSIONS

The incidence of stroke, which increases markedly with age, and the morbidity, mortality, and high financial burden associated with it may be reduced by the regular evaluation of elderly individuals for modifiable risk factors (especially the ECG) and their management. When an etiologic cause cannot be found in elderly ischemic stroke patients, a detailed cardiac examination (such as 24-hour Holter, transesophageal echocardiography) should be performed.

Further studies with larger patient series are required to determine the changes in risk with interventions on modifiable risk factors and to follow patients for a longer period of time.

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ORIGINAL ARTICLE

ANALYSIS OF RISK FACTORS AFFECTING MORTALITY IN GERIATRIC PATIENTS OPERATED ON FOR HIP FRACTURES

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Abstract

Introduction: High mortality rates after hip fracture surgery are an essential health problem. We evaluated the factors affecting mortality in the postoperative 30-day period.

Materials and Methods: A total of 906 patients aged 65 years and over who underwent hip fracture surgery were included. The patients were divided into two groups: those who died within 30 days of surgery and those who survived. Demographic data, ASA classifications, comorbidities, method of anesthesia, length of stay in hospitals and intensive care units, and the effects of these parameters on postoperative 30-day mortality were analysed.

Results: The postoperative 30-day mortality of the patients was 8.6%. The mean age of the patients who died during this period was 83.49 ± 6.9 years, while the mean age of the survivors was 78.7 ± 7.6 years. In our study, age (OD: 1.091; CI 95%, 1.051–1.132), The American Society of Anesthesiologists (ASA) physical status classification (OD: 12.69; CI 95%, 1.074–150.17), coronary artery disease (OD: 0.521; CI 95%, 0.287–0.944), general anesthesia administration (OD: 0.305; CI 95%, 0.140–0.667), and creatinine values (OD: 1.045; CI 95%, 1.114–1.892) were determined to be independent risk factors.

Conclusions: Detailed examination of elderly hip fracture patients considering these risk factors and close perioperative follow-up will reduce mortality.

Keywords: Aged; Anesthesia; Hip Fractures; Mortality.

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INTRODUCTION

In most countries, the proportion of elderly individuals in the total population is increasing. In the US, the elderly accounted for 8.3% of the population in 2016, and this increased to 9.7% by 2021. This proportion is expected to increase to 11% in 2025, 22.6% in 2060, and 25.6% in 2080 (1).

The prevalence of hip fractures is also increasing. With the exception of distal radius fractures, hip fractures are the most common in older people. In younger people, hip fractures are usually the result of high-energy traumas, such as falling from a height or involvement in a traffic accident. Elderly individuals generally have lower bone density, and so hip fractures often occur due to low-energy traumas (2). In 1990, there were 1.66 million elderly hip fracture patients worldwide, and this number is expected to reach 6.25 million by 2050 (although the exact number will depend on changes in demographic characteristics of the population over the next quarter century). The one-month mortality rate of these patients varies from 4% to 14% (3).

Studies have shown that age, gender, ASA classification, comorbidities, anesthesia method, blood product transfusion, waiting time for surgery, hospitalisation time, and biochemical abnormalities affect mortality in elderly hip fracture patients. However, the extent to which these risk factors affect mortality is still debated. Accordingly, the purpose of this study was to determine the factors affecting the mortality of patients 65 years old and older in the first 30 days after surgery.

MATERIALS AND METHODS

Patient selection and data collection

Approval for this study was received from the Sakarya University Faculty of Medicine Non-Invasive Ethics Committee on 30 June 2022 (number 145950). Patients who had undergone surgery for hip fracture between 1 January 2015 and 1 June 2021 were retrospectively analysed. The study sample included 906 patients 65 years of age and older who had undergone surgery for a hip fracture. Patients with missing data, those who were younger than 65, or those who had received a massive blood transfusion were excluded.

The patients were divided into two groups. Group 1 (n=78) included patients who died within 30 days of hip fracture surgery, while group 2 (n=828) included patients who survived longer than 30 days. Demographic data available in patient files were recorded, including age and gender, ASA classifications, comorbidities, intraoperative anesthesia method, total hospitalisation time, waiting time for surgery, whether the patient was hospitalised in the intensive care unit, and length of stay (if any) in the intensive care unit. Routine preoperative and postoperative laboratory tests, including tests for haemoglobin (Hb), platelets (PLT), international normalised ratio (INR), aspartate aminotransferase (AST), alanine aminotransferase (ALT), urea, and creatinine were also examined. The data from the analysis of the two groups' files were compared, and a regression analysis was used to determine the factors affecting mortality.

Statistical analysis

The SPSS Statistics 20 package of programs was used to conduct a statistical analysis of the data. Qualitative data were expressed as numbers and percentages, and quantitative data were expressed as means ± standard deviations. Normality testing of continuous data was done using the Kolmogorov–Smirnov test. The two samples t-test was used to compare repeated measures of continuous variables. Student's t-test and the Mann–Whitney U test were used to compare continuous variables between the two groups. Factors affecting mortality were determined by logistic regression analysis. $P<0.05$ was considered to be statistically significant.

RESULTS

A total of 906 patients aged 65 years and over who had undergone hip fracture surgery were included in our study. The mean age of all patients was 79.1 ± 7.6 years. The mean age of the patients in group 1 (83.49 ± 6.9) was statistically higher than the mean age of the patients in group 2 (78.7±7.6) (p<0.001).

Of 906 patients, 63.9% (n = 579) were female, and 36.1% (n = 327) were male. While 64.1% (n = 50) of the patients were female and 35.9% (n = 28) were male in group 1, in group 2, 63.9% (n = 529) were female and 36% (n = 299) were male. There was no difference between the two groups in terms of gender distribution (p = 0.970).

Table 1. Demographic data

	All Patients n = 906	Group 1 n = 78	Group 2 n = 828	p Value
Age (Years)	79.1 ± 7.6	83.49 ± 6.9	78.7 ± 7.6	<0.001
Gender, n (%)				
Female	579 (63.9)	50 (64.1)	529 (63.9)	0.970
Male	327 (36.1)	28 (35.9)	299 (36.1)	
ASA classification				
I	6 (0.7)	0 (0)	6 (0.7)	
II	84 (9.3)	0 (0)	84 (10.1)	0.049
III	815 (90)	78 (100)	737 (89)	
IV	1 (0,1)	0 (0)	1 (0,1)	
Hemoglobin (gr/ dL)	11.5 ± 1.6	10.9 ± 1.9	11.5 ± 1.6	<0.001
Platelet (1000/ μL)	227.5 ± 80.8	215 ± 96	228 ± 79	0.217
INR	1.1 (0.9-1.2)	1.2 (1.2-1.3)	1.0 (0.9-1.1)	<0.001
Urea (mg/dl)	54 (42-76)	84 (45-170)	52 (40-71)	<0.001
Creatinine (mg/ dL)	0.9 (0.8-1.3)	1.5 (0.7-2.4)	0.9 (0.8-1.3)	0.083
ALT (U/L)	12 (9.2-16.7	11.5 (7-14)	12 (10-16)	0.206
AST (U/L)	23 (17.2-34)	23 (17-32)	26 (21-40)	0.545
General	67 (7.4)	12 (15.4)	55 (6.6)	0.005
Regional	839 (92.6)	66 (84.6)	773 (93.4)	
Comorbidities				
Hypertension	613 (67.7)	53 (67.9)	560 (67.6)	0.955
Chronicle renal failure	44 (4.9)	8 (10.3)	36 (4.3)	0.020
Asthma	46 (5.1)	7 (9.0)	39 (4.7)	0.101
COPD	102 (11.3)	7 (9.0)	95 (11.5)	0.504
Diabetes	257 (28.4)	19 (24.4)	238 (28.7)	0.411
Cerebrovascular accident	104 (11.5)	10 (12.8)	94 (11.4)	0.703
Epilepsy	8 (0.9)	0 (0)	8 (1.0)	0.383
Coronary artery disease	153 (16.9)	21 (26.9)	132 (15.9)	0.013
Alzheimer	118 (13.0)	16 (20.5)	102 (12.3)	0.040
Heart failure	158 (17.4)	26 (33.3)	132 (15.9)	<0.001

ASA classification: The American Society of Anesthesiologists physical status classification. INR: International Normalised Ratio. ALT: Alanine Aminotransferase. AST: Aspartate Aminotransferase. Regional anesthesia: Combined Spinal Epidural Anesthesia, Spinal Anesthesia, Peripheral Nerve Block, Epidural Anesthesia. COPD: Chronic Obstructive Pulmonary Disease. Data are given as n (%), mean ± standard deviation or median (25-75 percentile).

The ASA classification of all patients in Group 1 was ASA 3, and there was a significant difference between the two groups (p = 0.049). When the patients in group 1 and group 2 were compared concerning other diseases, group 1 was found to have significantly more patients with chronic renal failure, coronary artery disease, Alzheimer's disease, and heart failure (p = 0.20, p = 0.013, p = 0.40, p < 0.001, respectively). There was no difference between the two groups with regard to other comorbid diseases.

General anesthesia was applied to only 7.4% (n = 67) of the 906 patients in our study, while regional anesthesia was used in 92.6% (n = 839). When comparing the method of anesthesia applied, it was found that general anesthesia was applied to 15.4% (n = 12) of the patients in group 1 and 6.6% (n = 55) of the patients in group 2, and the difference was statistically significant (p=0.005) (Table 1).

Group 1 and group 2 were compared regarding length of hospital stay and waiting times for surgery, and no significant difference was found (p = 0.773 and p = 0.405). However, as might be expected, admission to the intensive care unit was significantly higher in group 1 (66.7%). vs. 24.3% p<0.001). No significant difference was found between the two groups in terms of patients followed in the intensive care unit (p=0.953) (Table 2).

Parameters with a statistically significant difference in mortality were analysed by multivariate

Table 2. Hospital and intensive care unit length of stay

	All Patients n = 906 (100)	Group 1 n = 78 (8.6)	Group 2 n=828 (91.4)	P Value
Length of Hospitalization (days)	9.3 ± 6.2	10.1 ± 7.2	9.2 ± 6.1	0.773
Surgery Waiting Time (days)	3.7 ± 2.4	4.4 ± 2.7	3.7 ± 2.4	0.405
Number of Patients Admitted to Intensive Care Unit (n,(%))	253 (27.9)	52 (66.7)	201 (24.3)	<0.001
Intensive Care Unit Hospitalization Time (days)	3 (2-4)	3 (2-4)	3 (1.2-4.7)	0.953

Data is given as n (%) or mean ± standard deviation and median (25-75) percentile .

Table 3. Logistic regression analysis of factors affecting mortality

	ODDS rate	95% confidence interval		P
Age	1,091	1,051	<0.001	<0.001
ASA Classification	12,690	1,074	0.044	0.044
Hypertension	1,303	0.736	0.364	0.364
Chronic renal failure	0.535	0.200	0.212	0.212
Chronic obstructive pulmonary disease	1,504	0.625	0.362	0.362
Coronary artery disease	0.521	0.287	0.032	0.032
General anesthesia	0.305	0.140	0.003	0.003
Insertion of blood product	0.920	0.525	0.771	0.771
Number of waiting days for surgery	1,062	0.959	0.247	0.247
Hemoglobin	0.871	0.744	0.087	0.087
Urea	1,006	0.999	0.102	0.102
Creatinine	1,045	1,114	0.006	0.006

logistic regression. Age (OD:1.09; CI: 95% 1.051–1.132), ASA classification (OD:12.690; CI: 95% 1.074–150.17), coronary artery disease (OD: 0.521; CI: 95%, 0.287–0.944), general anesthesia (OD: 0.305; CI: 95%, 0.140–0.667), and creatinine (OD: 1.045; CI 95% 1.114–1.892) were found to be independent risk factors for postoperative 30-day mortality ($p<0.001$, $p=0.44$, $p=0.032$, $p=0.003$, $p=0.006$, respectively) (Table 3).

DISCUSSION AND CONCLUSION

In this study, we aimed to determine the postoperative 30-day mortality rate and risk factors for mortality in elderly patients who underwent hip fracture surgery. The study included 906 patients, and the postoperative 30-day mortality rate was 8.6%. The independent risk factors affecting mortality were age, ASA value, coronary artery disease, administration of general anesthesia, and a high creatinine value.

Mortality rates after hip fracture surgery range from 4–14% in the literature (4). Moran et al. conducted a prospective observational study in 2011 including 2660 patients and found that the mortality rate was 9% in the first 30 days after hip fracture surgery (5). In another prospective observational study that included 728 patients, the 30-day mortality rate was found to be 5% (6). Similarly, the study of Palabiyik et al., which included 106 patients aged 80 and over, seven- and 30-day mortality rates were reported as 6.6% and 10.4% (7). In our study, which included 906 patients, the postoperative 30-day mortality rate was found to be approximately 8.6%, similar to the literature.

Advanced age is a risk factor in hip fracture operations. In addition to the main pathology, physiopathological changes occur in organ systems in elderly patients. This is important in the perioperative process. For this reason, we included patients aged 65 and over in our study in order to evaluate the elderly patient group within itself. There are many studies on this subject in the literature. In a study published in 2017, 168,087 patients over the age of 65 were divided into two groups for evaluation: 65–80 years of age and 81–99 years of age. Mortality was found to be 2.6% for the 65–89 age group and 4.4 % for the 81–99 age group (8). A cohort study by Frost et al. reported that advanced age affects in-hospital mortality in hip fracture patients (9). In our study, the mean age of the patients who survived was 78.7 ± 7.6 years, while the mean age of the patients who developed mortality was 83.49 ± 6.9 years. The age of the patients was among the independent risk factors affecting mortality. Similar to previous studies, our findings indicated that advanced age affects mortality.

Since our patients were of advanced age, most of them had comorbidities: hypertension, chronic renal failure, asthma, COPD, diabetes, cerebrovascular disease, epilepsy, coronary artery disease, Alzheimer's disease, heart failure, rheumatoid arthritis, thyroid gland disorders, Parkinson's, obesity, solid tumour, tuberculosis, and so on. ThΩe mortality and morbidity risks of elderly hip fracture patients are associated with comorbidities (10). When these other diseases were evaluated in our study, a significant difference was found for chronic renal failure, coronary artery disease, Alzheimer's disease, and heart failure, and coronary artery disease was found to be among the independent risk factors affecting postoperative 30-day mortality. Many studies have examined the impact of comorbidities on mortality. According to the cohort study of Ryan et al., which included 34,805 elderly hip fracture patients, obesity, COPD, and kidney failure were associated with mortality (11). In a study including 120 patients, comorbidities such as coronary artery disease, congestive heart failure, Alzheimer's, Parkinson's, and malignancy were reported to affect mortality (12). According to the cohort study of Frost et al., congestive heart failure, cerebrovascular disease, liver diseases, renal

diseases, and malignancy also affects mortality rates (8). In another cohort study, COPD, diabetes, and solid metastatic tumour occurrence were found to affect mortality, with COPD showing a substantial predictive value for mortality (13). Finally, a meta-analysis including 25,349 patients reported that lung diseases, diabetes, and cardiovascular diseases increased the risk of mortality (14).

According to most studies on patients who underwent hip fracture surgery, the ASA value is among the factors affecting mortality: The higher the ASA value, the higher the mortality rate (15,16). The majority of the patients who died in our study had high ASA values, and high ASA values were found to be an independent risk factor affecting mortality.

Overall, the impact of the anesthesia method on mortality in hip fracture patients remains controversial. In this study, we found that the mortality rate was higher in the general anesthesia group than in the regional anesthesia group, and general anesthesia was an independent risk factor for postoperative 30-day mortality. Similar results were reported in a retrospective observational study conducted by Radcliff et al., which included 5,683 hip fracture patients over 65 years of age (17). An extensive analysis, including 47 clinical trials and 35 reviews/meta-analyses, showed that the specific mode of anesthesia influences mortality and morbidity. Regional anesthesia is associated with reduced early mortality and morbidity (18). In contrast, a study by White et al., which included 65,535 patients with hip fractures, found no significant differences in 30-day mortality between the general anesthesia and neuraxial anesthesia groups (19). Similarly, a study by Basques et al., which included 9,842 patients, found no significant differences in 30-day mortality between the two anesthesia groups (20). However, Fields et al. reported that the risk of developing complications for 30 days was higher in patients who underwent general anesthesia in their retrospective observational study, which included 6,133 hip fracture surgery patients (21). Although Basque et al. worked with patients aged 70 and over, White and Fields did not include age restrictions in their study. We think that the advanced age patient group should be separated from the younger age patient group in terms of tolerability of hemodynamic changes.

The literature provides conflicting results regarding the waiting time for surgery in hip fracture patients. Some studies suggest that surgery performed earlier than 12 hours reduces short-term mortality, while surgery performed before six hours has no effect on mortality (15). Delaying surgery for more than 48 hours may be associated with in-hospital mortality but not with 30-day and one-year mortality (22). Another study reported no significant difference in mortality when surgery was delayed for up to four days, but mortality increased 2.5 times after surgery was delayed for more than four days (5). In the present study, the mean waiting time for surgery was 3.7 ± 2.4 days, and the mean waiting time for patients who died was 4.4 ± 2.7 days. However, the statistical analysis showed that the waiting time for surgery did not affect postoperative 30-day mortality. Prospective randomised studies have also reported that waiting time for surgery does not affect mortality when other factors, such as age, gender, ASA classification, and type of surgery, are considered (16,23). Longer waiting times may lead to prolonged hospital stays and increased postoperative complications and morbidity risk (16).

In our study, it was observed that Hb values were lower in the group that developed mortality in the 30-day postoperative period. According to the cohort study conducted by Ryan et al., which included 34,805 elderly hip fracture patients, 30-day mortality and rehospitalisation rates were higher in geriatric patients who were anaemic at presentation (11). Similarly, in another study that included 7,319 hip fracture patients, anaemia was observed in 42.9% of the patients, and low Hb value were found to increase mortality (24).

The most important limitation of the study is that it was not a randomised controlled trial. In conclusion, the findings are consistent with the literature, which has reported mortality rates ranging from 4% to 14% in elderly patients who undergo hip fracture surgery. Advanced age is a known risk factor, and comorbidities such as chronic renal failure, coronary artery disease, Alzheimer's disease, and heart failure also increase mortality risk. The ASA value is another factor affecting mortality, with higher ASA values associated with higher mortality rates. The type of anesthesia used also plays a role, with general anesthesia associated with higher mortality rates compared to regional anesthesia.

Overall, this study highlights the importance of identifying risk factors for mortality in elderly patients who undergo hip fracture surgery. By identifying these factors, we can mitigate the risk of postoperative mortality and improve patient outcomes.

Ethics Committee Approval: This study was approved by the Sakarya University Faculty of Medicine Clinical Research Ethics Committee (Date: 30.06.2022, No: 145950).

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ORIGINAL ARTICLE

EXAMINATION OF MENTAL SYMPTOMS, ANGER, AND DEATH ANXIETY IN ELDERLY CANCER PATIENTS

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Abstract

Introduction: Cancer is a disease that changes a person's expectations about death and life. The needs of elderly cancer patients differ according to other age groups. This study aims to reveal the relationship between psychological symptoms and death anxiety and anger expression in elderly patients diagnosed with cancer.

Methods: Scales assessing anxiety, depression, death anxiety, and anger were administered to patients over 65 years of age diagnosed with cancer. Patients were asked about the type of cancer, when it was diagnosed, and what treatment they received. They were also asked with whom they lived and with whom they came to check.

Results: Of the 201 patients included, 18.9% were diagnosed with anxiety disorder and 17.9% with depression. A high positive statistically significant correlation existed between anxiety and depression symptoms ($r=0.755$, $p<0.001$). There was a moderately positive and statistically significant correlation between anxiety symptoms and death anxiety ($r=0.599$, $p<0.001$) and state anger ($r=0.504$, $p<0.001$). A one-unit increase in state anger score increases the risk of developing depressive symptoms by 11%, while a one-unit increase in death anxiety increases the same risk by 10.6%. When we analyzed according to cut-off values, 124 (61.7% of the whole sample), participants had high death anxiety.

Conclusion: Psychological symptoms in elderly cancer patients seem to be associated with death anxiety and anger. Death anxiety should not be considered a natural consequence of getting cancer. Screening for mental symptoms during stressful times can help identify psychological needs and provide targeted psychological support for the elderly.

Keywords: Mental Health; Aged; Anger; Neoplasms.

INTRODUCTION

The second leading cause of death in 2018 was cancer and cancer incidence increases dramatically with age. Approximately 60% of all cancers occur in individuals aged 65 and older (1). After being diagnosed with cancer, patients experience severe mental health issues, such as anxiety and depression. The diagnosis of a fatal disease such as cancer is a negative stressor that severely affects patients' physical and mental health (2).

Cancer is considered a life-threatening disease synonymous with pain and suffering. Cancer diagnosis causes psychological distress, includes emotional problems for the patient and causes significant changes in social or family roles. Mood disorders, especially anxiety and depression, develop at a rate of approximately 30% in patients (3). Problems arising from physical illness and treatment-related side effects cause anger in patients. When the relationship between anger and cancer is examined, it has been reported that anger is the first emotion shown in response to a cancer diagnosis (4).

Advances in modern medical techniques prolong cancer patients' life span, but cancer is still synonymous with death. During this period, when patients can approach their last days, their fear of death also increases. Various studies on the effects of disease progression on death anxiety in patients with physical problems show that death anxiety becomes a critical problem, especially in a specific disease, such as cancer (5). It is essential to define, measure and control the predictors of death anxiety, related variables and the factors affecting anxiety in the elderly. In this context, the present study aims to determine the magnitude of mental problems in elderly cancer patients and reveal the effects of death anxiety, anger and anger expression styles on mental health.

MATERIALS AND METHODS

Study Design

Our study is a cross-sectional examination of elderly cancer patients. The study included 201 cancer patients who met the inclusion criteria and applied to the Medical Oncology outpatient clinic between May and June 2022. Before beginning, each participant was required to examine the purpose of the study and provide consent based on that understanding. Participants were also informed that their participation in the study was entirely voluntary and that they could disengage at any time. Participants were not compensated for their involvement in the research. The research was conducted by the Helsinki Declaration and with the Clinical Research Ethics Committee's approval (No. 9/223 of 19 Apr 2022).

Inclusion and exclusion criteria

The inclusion criteria for the study included being at least 65 years old, consenting to participate, and signing a consent form. Those under age 65, those with mental retardation, dementia, psychiatric diseases that impair discernment, and those with organic mental disorders were excluded.

Query variables

Sociodemographic and general information

Participants were questioned if they had a diagnosed chronic illness or mental health issue. Male or female was documented as the gender alongside the age. There were married, single, and divorced/widowed categories for marital status. They were requested to indicate the quantity and presence of their children. Participants were asked whether they resided in a city or a rural area. It was questioned with whom they live and with whom they come to the outpatient clinic controls. It was asked when they were diagnosed with cancer and what treatment they were currently receiving. The responses regarding the time of diagnosis were

categorized as first year, one to two years, three to five years, and over five years. Also, participants were asked whether someone in the family had been diagnosed with other cancer.

Assessment of Psychological Symptoms

The Hospital Anxiety and Depression Scale (HADS) comprised 14 items used in this study (6). The self-assessment scale was designed specifically for use in hospital settings, assessing the patient's anxiety and depression level and severity change. As a psychological screening instrument, it has been demonstrated that the scale yields clinically relevant results when applied to various diseases and clinical populations. The scale contains 14 items, including subscales HAD-A (seven questions) and HAD-D (seven questions) for anxiety and depression, respectively. Each item is rated on a 4-point Likert scale, and the maximum score for each sub-dimension is 21. Scores exceeding 10 indicate the possibility of psychological morbidity. Made were Turkish validity and reliability. The internally consistent reliability coefficients for the anxiety and depression subscales of the Turkish versions of the HADS were 0.85 and 0.78, respectively (7). The scale was also validated with cancer patients (8).

Assessment of Death Anxiety

Developed by Templer in 1970, the Death Anxiety Scale (DAS) is a 20-item self-report scale that assesses an individual's anxiety and fears about death (9). Sarıkaya conducted validity and reliability evaluations of the scale in Turkey in 2016 (10). On a Likert-type scale, questions have five answer options: never (0 points), rarely (1 point), occasionally (2 points), frequently (3 points), and always (4 points). The scale contains numbers between 0 and 80. High scores indicate a heightened fear of mortality.

Assessment of Anger

The State-Trait Anger Expression Inventory (STAXI) was used in our study as a standard measurement instrument for anger, emotion, and expression. Spielberger et al. devised the self-assessment scale in 1988, and Ozer adapted it to Turkish in 1994 (11, 12). It consists of four dimensions as a four-point Likert type (1: Never defines, 2: Some define, 3: Highly defines, 4: Defines) and a scale consisting of a total of 34 items, including State Anger (SA, ten items), Anger-in (AI, eight items), anger-out (AO, eight items), and anger-controlled (AC, eight items). High scores on the SA dimension indicate a high level of anger, high scores on the AI dimension indicate anger that is suppressed, and high scores on the AO dimension indicate that anger can be expressed readily. High scores on the AC dimension suggest that anger is controllable. The scores obtained in each size are added together, and the participants' scores are separately calculated for four sizes. Ozer conducted a reliability study and reported the following internal consistency coefficients for the scale: 0.79 for the SA dimension, 0.62 for the AI dimension, 0.78 for the AO dimension, and 0.84 for the AC dimension.

Statistical Analysis

Version 26 of the SPSS program was used to conduct the statistical analyses. Analytical methods (Kolmogorov Smirnov/Shapiro-Wilks test) were used to determine whether the variables had a normal distribution. Descriptive analyses employed medians and minimum and maximum values for non-normally distributed and ordinal variables. Categorical values were presented as frequencies, and continuous variables with normal distribution were presented as mean and standard deviation (percentages). Where applicable, the Chi-Square or Fisher exact test was used to compare the proportions of these variables between groups (when chi-square test predictions do not hold due to low predicted cell counts. The importance of pairwise differences was tested using the Mann-Whitney U test with Bonferroni correction to account for multiple comparisons. The Spearmen correlation test was used to measure the correlation coefficients and their importance when examining

the relationships between non-normally distributed and ordinary variables. A statistically significant result had a p-value of less than 0.05. The sample size calculation was calculated as 134 with a 95% confidence interval and an effect size of moderate effect size. ROC curves were calculated to determine a cutoff for anxious and depressive states in cancer patients. The area under the curve (AUC), sensitivity, and specificity, along with their respective 95% confidence intervals (95% CI), were calculated (13).

RESULTS

General Characteristics

A total of 201 people with cancer took part in the study. Of these, 94 (46.8%) were women, and 107 (53.2%) were men, while the median age was 70 (65-90) years. 76.6% (n=154) of the participants were married, and 23.4% (n=47) were single. 90.5% of participants graduated from primary school, 6.5% from secondary school, and 3% from university. There were various cancer types that the participants had. Most participants had gastrointestinal tumors (26%, or n=54), lung, urinary tract, and breast cancers (each 15.4%, n=31). Twenty-one participants (10.4%) had gynecological tumors, and 20 (10%) had head and neck tumors. Half of the people who took part lived in cities (n=101), and half (n=105) had a family cancer history. When examining who attended the controls, it was determined that the majority (90%) arrived with a family member, whereas 10% came alone. Whereas 137 (68.2%) participants had a chronic illness, 29 (14.4%) also had a psychiatric disorder. 31.8% of these participants had been diagnosed with cancer within the last twelve months, 29.9% in 1-2 years, 20.4% in 3-5 years, and 17.9% in 5 years and more. Those with a score of 11 or higher were the most likely to have experienced anxiety (18.9%) or depressive (17.9%) disorders. 53.7% (n=123) of the participants were patients whose treatment had been completed and attending check-ups, while 21% (n=48) had metastatic treatment. When the treatment type categorized individuals, 130 (53.9%) received chemotherapy, and 37 (15.4%) received radiotherapy.

When the demographical features were compared on the scales that DAS, HADS-A, HADS-D, there were only statistically differences between participants used smart drugs and HADS-A scale scores (p=0.021). For participants who were using smart drugs, HADS-A scores were significantly higher than the participants who did not use smart drugs. All the mean/median (min-max) scores and some sociodemographic data are shown in Table 1.

Comparing the state-anger and anger expression of the participants with their sociodemographic information revealed no significant differences by gender, type of cancer, presence of other chronic disease/psychiatric disease, use of chemotherapy or smart drug therapy, or with whom the patient lived and came the control. However, who took radiotheraphy had significantly higher scores of anger-out and anger-in (p=0.025; p=0.037) as shown in Table 2.

Correlations of All Scale Scores

The mean DAS score for the whole group was 23.17±18.69, and the mean HADS-A score was 6.97±4.64. HADS-D score was 7.69±4.54. There was a medium positive statistically significant correlation with HADS-A, DAS (r=0.599, p<0.001) and state-anger (r=0.504, p<0.001). As we know there was a high positive statistically significant correlation between HADS-A and HADS-D (r=0.755, p<0.001). There was a moderately negative correlation between state-anger and anger-control (r=-0.406, p<0.001). There was a weak positive statistically significant correlation between anger level and DAS (r=0.208, p=0.003). All correlations are shown in Table 3.

Logistic Regression Analysis

After the correlation, a Logistic Regression Analysis Backward: LR style was conducted to determine the

Table 1. Comparison of mean DAS, HADS-S, HADS-D results, and sociodemographic features

	DAS (mean±SD)		HADS-A (mean±SD)	p value	HADS-D (mean±SD)	p value
Gender						
Women	22 (0-62)	0.211	7.44±4.34	0.086	8.21±4.15	0.070
Men	20 (0-61)		6.56±4.87		7.22±4.83	
Marital Status						
Married	23.32±19.17	0.709	7.02±4.82	0.350	7.53±4.55	0.988
Single	17.22±2.51		6.81±4.05		8.19±4.52	
Educational Status						
Primary School	23.69±18.55	0.715	7.05±4.60	0.918	7.72±4.43	0.322
Secondary School	16.85±18.12		6.00±4.43		7.54±5.50	
University	21.17±24.73		6.67±6.56		7.00±6.57	
Diagnosis time						
0-12 months	24.69±19.98	0.929	7.09±4.81	0.541	8.03±4.95	0.913
1-2 years	22.02±18.17		7.02±4.56		7.50±4.33	
3-5 years	20.15±3.15		6.54±4.81		7.00±4.67	
5 years and more	22.25±15.82		7.17±4.42		8.17±4.05	
Type of Cancer						
Head & Neck	25.40±5.42	0.265	6.10±5.24	0.904	5.95±5.32	0.455
Gastrointestinal system	23.72±5.06		6.78±5.02		7.54±4.84	
Lung	23.58±5.13		7.29±5.35		7.97±5.17	
Urinary Tract	23.16±4.37		6.81±4.40		7.16±4.24	
Breast Cancer	22.52±4.66		6.74±3.94		7.84±3.92	
Gynecological	22.43±3.90		7.71±3.93		9.00±3.71	
Other	21.46±3.41		8.08±3.90		9.08±3.40	
Chronic Disease						
Yes	23.08±4.94	0.291	7.25±5.02	0.479	7.77±4.42	0.931
No	23.42±4.71		6.84±4.46		7.65±4.62	
Psychiatric Disease						
No	23.46±4.84	0.383	6.73±4.72	0.082	7.47±4.63	0.190
Yes	22.45±4.35		8.38±3.91		9.00±3.81	
Chemotherapy						
No	23.08±4.94	0.279	7.25±5.02	0.063	7.77±4.42	0.232
Yes	23.42±4.71		6.84±4.46		7.65±4.62	
Radiotherapy						
No	23.05±4.53	0.143	7.19±4.42	0.167	7.98±4.29	0.071
Yes	24.46±5.67		6.00±5.46		6.38±5.42	
Smart drug						
No	23.61±5.08	0.268	6.39±4.66	**0.021**	7.46±4.84	0.352
Yes	22.80±4.16		7.97±4.46		8.08±3.98	
Family Cancer History						
No	23.72±4.66	0.246	6.71±4.49	0.399	7.55±4.45	0.549
Yes	22.86±4.87		7.25±4.80		7.83±4.66	

DAS: Death Anxiety Scale, HADS-A: Hospital anxiety and depression scale, anxiety part; HADS-D: Hospital anxiety and depression scale, depression part

Table 2. Comparison of state-anger, anger-out, anger-in, anger-control and sociodemographic features

	State-anger	P	Anger-out	p	Anger-in	p	Anger-control	p
Gender								
Men	20 (10-40)	0.319	23 (8-32)	0.194	25 (9-36)	0.965	24 (11-32)	0.889
Women	19 (10-40)		21 (8-120)		25 (11-36)		23.5 (11-32)	
Educational Status								
Primary School	19 (10-40)		21 (8-120)		24 (9-36)		24 (11-32)	
Secondary School	25 (10-31)	0.578	2.46±6.06	0.168	26 (17-36)	0.336	23.54±6.02	0.258
University	24.00±10.41		24 (16-32)		26.00±7.04		25.83±3.31	
Place of residence								
City	19 (10-40)	0.648	23 (8-32)	0.194	26 (9-36)	0.198	24 (11-32)	0.070
Rural area	20 (10-40)		20.5 (8-120)		22.5 (9-36)		23 (11-32)	
Type of Cancer								
Head & Neck	18 (10-40)		22 (11-32)		24 (17-36)		24 (13-32)	
Gastrointestinal system	23 (10-40)		23 (9-120)		26 (9-36)		24 (11-32)	
Lung	22 (10-40)	0.430	22.23±6.75	0.147	25 (9-36)	0.479	24 (13-32)	0.265
Urinary Tract	18 (10-30)		20 (8-32)		23.77±6.36		23.16±4.37	
Breast Cancer	17 (10-40)		20.23±6.23		22 (14-36)		23 (14-32)	
Gynecological	21.38±9.16		17 (10-24)		21.76±5.59		23 (16-29)	
Other	20.86±9.05		23 (8-26)		22.54±5.36		21.46±3.41	
Chronic Disease								
No	19.5 (10-40)	0.686	20 (8-32)	0.669	22 (11-36)	0.540	22.5 (14-32)	0.291
Yes	20 (10-40)		23 (8-120)		25 (9-36)		24 (11-32)	
Psychiatric Disease								
No	19.5 (10-40)	0.733	22.5 (8-120)	0.819	25 (9-36)	0.914	24 (11-32)	0.383
Yes	20 (10-40)		20.79±5.14		22 (16-36)		23 (15-32)	
Chemotherapy								
No	20 (10-40)	0.733	24 (8-32)	0.374	26 (9-36)	0.459	23 (11-32)	0.279
Yes	18 (10-40)		20 (8-120)		22.5 (9-36)		24 (11-32)	
Radiotherapy								
No	19.5 (10-40)	0.689	21 (8-120)	**0.025**	24 (9-36)	**0.037**	23.5 (11-32)	0.143
Yes	20 (10-40)		24 (11-32)		27 (14-36)		24 (13-32)	
Smart drug								
No	18 (10-40)	0.119	21 (8-120)	0.974	25 (9-36)	0.922	24 (11-32)	0.268
Yes	20 (10-40)		23 (10-32)		25 (9-36)		23 (14-32)	
People attending check-up								
With Child	19.5 (10-40)		22 (8-120)		25 (9-36)		24 (11-32)	
With Spouse	20 (10-40)	0.640	22.5 (9-32)	0.220	24.5 (9-36)	0.201	24 (13-32)	0.824
With a person from family	18 (10-40)		17.46±6.02		21.00±4.78		22.85±4.62	
Alone			24 (8-32)		27 (14-36)		24 (16-32)	

Table 3. Correlations of all scale scores

	HADS-A	HADS-D	State-anger	Anger-in	Anger-out	Anger-control	DAS
HADS-A	1						
HADS-D	0.755**	1					
State-anger	0.504**	0.419**	1				
Anger-in	-0.158*	-0.333**	0.137	1			
Anger-out	-0.186*	-0.322**	0.098	0.888**	1		
Anger-control	-0.386**	-0.443**	-0.406**	0.421**	0.511**	1	
DAS	0.599**	0.488**	0.208**	-0.184**	-0.218**	-0.287**	1

HADS-A: Hospital anxiety and depression scale, anxiety part; HADS-D: Hospital anxiety and depression scale, depression part; DAS: Death anxiety scale. *p<0.05 **p<0.001

Table 4. Logistic regression analysis for groups with and without anxiety and depression symptoms

Predictors for HADS-A	β	S.E	p	OR
Age	-0.064	0.031	0.037	0.938
State-anger	0.107	0.024	<0.001	1.113
Anger-control	-0.110	0.045	0.016	0.896
DAS	0.069	0.012	<0.001	1.072
Predictors for HADS-D				
Gender(1)	1.456	0.422	0.001	4.290
Place of Residence (1)	1.223	0.407	0.003	3.396
State-anger	0.125	0.032	<0.001	1.133
Anger-out	-0.078	0.042	0.061	0.925
Anger-control	-0.108	0.056	0.053	0.898
DAS	0.060	0.013	<0.001	1.061

HADS-A: Hospital anxiety and depression scale, anxiety part; HADS-D: Hospital anxiety and depression scale, depression part; DAS: Death anxiety scale; S.E: Standard Error; OR: Odds Ratio

anxiety and depression symptoms' predictors. The regression analysis included age, gender, educational status, cancer type, diagnosis time, with whom and where he lived, with whom attended the check-ups, presence of chronic disease and psychiatric disease, and all scale scores. Analysis results are shown in Table 4 and contain essential determinants of the last stage of the Retrospective style.

A unit increase in the State-anger score increased the likelihood of developing anxiety symptoms by 11%, whereas a unit increase in the DAS score increased the same risk by 10.6%. A one-unit increase in Anger-control increased the likelihood of developing symptoms by 10.2%.

Being female increased the risk of developing depressive symptoms by nearly 4.3 times, whereas

living in a rural area increased the risk by nearly 3.4 times. A unit increase in the State-anger score increased the risk of developing depression symptoms by 11%, whereas a unit increase in the DAS score increased the same risk by 10.6%. One unit increase in Anger-out and Anger-control scores was associated with a 7.5% and 10.2% increase in symptom occurrence, respectively.

ROC Analysis

The effectiveness of DAS and STAXI scores was assessed using Receiver Operating Characteristic (ROC) curves. The optimal cut-off value for the DAS was greater than 19 units. STAXI was greater than 22.5 (Figure 1). The AUC was 0.74 (95% CI 0.66–0.82), with a sensitivity of 92% and a specificity of 55% for DAS and the AUC was 0.77 (95% CI 0.70–0.84), with a sensitivity of 74% and a specificity of 66% for STAXI (Both $p<0.001$). When we analyzed according to the cut-off values, 83 (41.3% of the whole sample) participants had high anxiety, and 124 (61.7% of the whole sample), participants were high death anxiety.

DISCUSSION

The current study investigated the relationships between death anxiety, anger level and mental symptoms and focused on predictors for developing mental symptoms. Our study's analysis shows a connection between the psychological symptoms seen in cancer patients, death anxiety and anger. As death anxiety increases in elderly cancer patients, anger also increases. As the level of anger rises, it becomes more difficult to control one's anger. No studies have examined the relationship between mental symptoms, death anxiety, and rage in cancer patients over 65. As a result of the analysis, it has been shown that an increase in anger and death anxiety levels increases the probability of developing anxiety and depressive symptoms. It

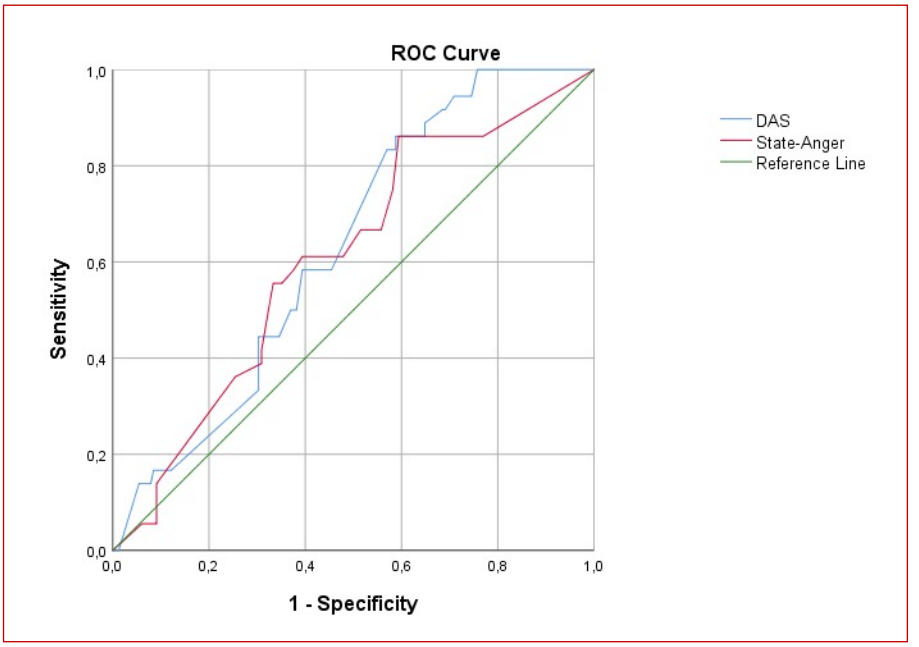

Figure 1. Roc curves of DAS and State-Anger
DAS: Death Anxiety Scale

has also been found that being a woman and living in a rural area increases the risk of developing symptoms of depression.

Relationship with Mental Symptoms and Cancer

In a study examining the mental health problems of elderly cancer patients and associated factors, 85.1% and 81.7% of patients exhibited anxiety and depression, respectively (14). The study's results, in which 159 cancer patients were analyzed, show that depression directly increased with age (15). In our sample of patients, all above the age of 65, 18.9% were diagnosed with anxiety disorders and 17.9% with depression. In our study, 14.4% of the participants had a history of psychiatric illness. There was no significant difference between those with and without a history of psychiatric disease regarding anxiety and depression symptoms occurring during cancer. Once mental health problems are identified, psychosocial interventions can reduce cancer patients' distress and improve their quality of life, regardless of their prognosis.

The current literature has no consensus regarding the extent to which gender can induce psychological distress in cancer patients. According to a large-sample study, the prevalence of clinically significant psychological distress was 43.8%, and there was no significant difference between the sexes (16). Similar to our research, in a study conducted with elderly cancer patients, no significant difference was reported between the two genders regarding the prevalence of psychological distress (17). More than half of our sample consisted of men, and when gender and anxiety and depression levels were compared, no significant difference was found between the two groups. However, the analysis concluded that being a woman increased the risk of developing symptoms of depression.

Mixed anxiety/depression symptoms were observed at higher rates in malignancies of the pancreas, gastric, head/neck, and lungs but at lower rates in breast cancer patients (18). Depression is strongly linked to lung, pancreatic, oropharyngeal, and breast malignancies. It has been reported that patients with lymphoma, gynecological, and colon malignancies experienced less depression (19). In our study, 26% of participants had cancer of the gastrointestinal tract, and there was no significant difference in psychological symptoms between cancer categories. Patients with gynecological cancer had a higher mean HADS-D score than patients with other cancer categories, but no significant difference existed between psychological symptoms and cancer types. Similar to our findings, studies have found no significant difference in psychological distress scores between patients based on cancer location and type (16, 17). The fact that the psychological distress of cancer patients depends on the location of the disease demonstrates that they should not be considered a homogenous group. Future research may emphasize psychological distress in patients with the same type of cancer but receiving various treatments.

Death Anxiety in Elderly Cancer Patients

The results of a meta-analysis designed to predict the rate of death anxiety in cancer patients and the factors influencing its occurrence revealed that death anxiety in cancer patients was moderate and influenced by sociodemographic factors, such as region, cancer type, gender, and marital status (5). In a study examining death anxiety and related factors in elderly cancer patients, 42% were found to have elevated death anxiety. Also, it was shown that men contemplated mortality more frequently than women, but women experienced more significant death anxiety than men (19). Similarly, 61.7% of our sample of elderly cancer patients exhibited high levels of death anxiety. In an investigation of racial and gender disparities in death anxiety, race, and gender were found to have a significant impact on

death anxiety. It has been established that death anxiety and psychological distress were more prevalent in women than males, both in the general population and among cancer patients (20). In our study, the ratio of women to men was almost equal among the participants. When the scores from the death anxiety scale were examined, the average scores of the women were higher, but there was no statistically significant difference between them. The results suggest that healthcare providers can effectively address the fear of death in elderly patients by tailoring their approaches based on race and gender. It is recommended that healthcare providers consider this approach when working with elderly patients to improve their patients' overall well-being.

There is a statistically significant correlation between death anxiety and marital status in elderly patients, as demonstrated. Married participants experienced significantly higher levels of death anxiety than single participants (5). Regarding this discovery, there have been contradictory findings. According to a different study, widowed women experienced more significant death anxiety than those whose spouses live (21). In our study, most of the patients were married, and death anxiety levels were higher in married people, but no statistically significant difference was found.

It has been shown that death anxiety increases with the duration of the illness. It has been reported that fear of recurrence was a significant predictor of death anxiety and was positively related (20). It has been reported that patients were relatively agitated, anxious, and restless in the first period after diagnosis and more stable after three months, and death anxiety recurred between 3 and 6 months. It has been found that the initial anxiety and tension reappeared due to stress (22). In our study, the death anxiety level was highest in the first year following the cancer diagnosis; it tended to increase again after five years. The result may be due to the progression of the disease, a longer duration of cancer, treatment side effects and chemotherapy, and patients' gradual exposure to the reality of their disease and dread of pain and suffering.

Although the mean scores obtained from the death anxiety scale of our study were the highest in head and neck cancers, no statistically significant difference was found when cancer types and death anxiety levels were compared. Breast cancer is scary and tragic for many women, so these patients show feelings of death, anxiety, and anger. It has been shown that patients with breast cancer experience high levels of depression, anxiety, anxiety about relapse, and fear of death. (23). A study investigating death anxiety in female cancer patients showed that patients with higher mental well-being had less anxiety about death (24). Reducing death anxiety in cancer patients should be considered in improving mental symptoms during cancer treatment.

The Relationship Between Cancer and Anger

Anger is one of the most common reactions, especially in the face of a physical illness that can cause death, such as cancer. It has been found that 9–18% of advanced cancer patients experience intense anger that causes clinical concern. Some research has shown that it may be helpful for patients to activate their anger to fight their cancer (4). In our study, according to cancer type, the highest anger level was reported in patients with gastrointestinal tumours, but there was no statistically significant difference. Considering the kind of treatment received, patients who received radiotherapy received high scores in the sub dimensions of suppressing and expressing anger compared to other treatment types. In a study of older women with breast cancer, lower anger/aggression scores in women with medium and high education levels were interpreted as having more advanced coping systems than women with low education levels (25). In our study, patients

with breast cancer had lower anger levels than other cancer types. Still, no statistically significant difference was found between anger levels and cancer type, including gender and education level. Longitudinal studies are needed to measure anger and other moods throughout the disease, showing the results of anger interventions.

Future research should account for the limitations of the present investigation. Due to the study's cross-sectional design, only a fleeting snapshot of cancer patients' moods at the time of measurement is presented. When a person receives a life-threatening diagnosis, even if they are ordinarily calm, tension can cause anger to surface. In contrast, after surviving a rigorous chemotherapy regimen or invasive surgery, a sense of calm and happiness may prevail. Second, a larger sample size would be beneficial to increase the statistical power and generalizability of the results. Given the small sample size and different types of cancer, some subgroups are underrepresented. One of the limitations of our study is that the participants were not asked about their experience in the hospital, where they had difficulty controlling anger during treatment.

Controlling levels of death anxiety and wrath may prevent the development of mental symptoms in elderly cancer patients. Assessing psychological distress during times of stress can aid in identifying psychological requirements, thereby facilitating targeted psychological support. Therefore, the study's results may improve understanding of individual responses in elderly cancer patients. Future studies should more specifically explore the role of gender, which is still unclear, and enhance the understanding of the relationship between mood symptoms, death anxiety, and anger expression. Longitudinal studies should be planned to determine whether changes in fear of death in cancer patients are related to psychological distress, anger, and disease course.

CONCLUSION

It is recommended that cancer patients be screened for psychiatric symptoms because of its association with non-adherence to treatment and poor prognosis. Individual, cultural, and social factors affect the death anxiety of cancer patients. It has been shown that the design and implementation of psychological interventions sensitive to these factors and targeting death anxiety positively affected patients. Screening for mental symptoms during stressful times can help identify psychological needs and provide targeted psychological support. This article may enable healthcare professionals to evaluate common psychiatric disorders such as anxiety and depression in elderly cancer patients, to realize the importance of fear of death in the elderly, and to understand patients' anger. The results will guide future efforts to improve the psychological health of older cancer patients.

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ORIGINAL ARTICLE

TREATMENT OUTCOMES IN BREAST CANCER PATIENTS AGED 65 AND ABOVE

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Abstract

Introduction: Despite the increasing number of elderly patients with breast cancer, optimal treatment options remain limited. This study aims to evaluate the clinical characteristics, treatment approaches, and survival outcomes of the patient group aged 65 and above who were treated for breast cancer at our clinic.

Materials and Methods: The data of breast cancer patients aged 65 and above who received treatment and follow-up at our clinic between 2012 and 2018 were retrospectively analyzed. Overall survival and disease-free survival analyses were performed using Kaplan-Meier analysis, and comparisons were conducted using the log-rank test.

Results: A total of 108 elderly female patients with breast cancer were included in the study. The median follow-up duration was 79.75 months (6.64 years), with a maximum follow-up of 133.49 months (11.12 years). At the end of this period, 88 patients (81.48%) were still alive. The 3-year overall survival rate was 93.5%, and the 5-year overall survival rate was 86.1%. The 3-year disease-free survival rate was 91.6%, and the 5-year disease-free survival rate was 88.7%.

Conclusion: When making treatment decisions for elderly breast cancer patients, factors such as performance status, comorbidities, toxicity, and post-treatment quality of life should be carefully considered alongside age. Treatment decisions should be based on comprehensive evaluations taking these factors into account.

Keywords: Breast Neoplasms; Treatment Outcome; Aged; Mastectomy; Drug Therapy; Radiotherapy.

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INTRODUCTION

Breast cancer is the predominant form of malignancy globally and exhibits the highest fatality rate among females. It ranks fifth in cancer-induced mortality across various tumor categories (1). As the population ages, the number of elderly individuals diagnosed with breast cancer has been increasing (2). The average age of breast cancer onset is around 61 years, with 45% of newly diagnosed breast cancer patients being aged 65 and above (3,4). Advanced age is considered a risk factor for breast cancer (5). In elderly patients, the diagnosis of breast cancer often occurs at a later stage, leading to 48% of patients being diagnosed with metastatic disease. Limited data is available to establish the standard treatment approach for elderly breast cancer patients. Despite comprising a significant proportion (40%) of cases, tumor biology and optimal treatment remain uncertain. The scarcity of randomized trials demonstrating the safety and efficacy of adjuvant therapies complicates treatment decision-making. Although the American Society of Clinical Oncology (ASCO) and the International Society of Geriatric Oncology (SIOG) encourage research in this age group, the conducted studies account for only 4% of the total (6,7,8). The discrepancy between chronological age and functional age should be taken into account when making treatment decisions, as it is an essential factor to consider. After diagnosis, a comprehensive geriatric assessment should be conducted for these patients. This approach allows for a more accurate evaluation of treatment tolerability, the need for hospitalization, and survival outcomes affected by comorbidities.

The aim of this study is to evaluate the clinical characteristics, treatment approaches, and survival outcomes of the patient group aged 65 and above who were treated for breast cancer at our clinic. Additionally, the study aims to contribute to the existing literature on elderly breast cancer patients.

MATERIAL AND METHODS

This retrospective study was conducted at a radiation oncology center in Turkey and approved by the local ethics committee (Approval No: E-19-2690, dated 09/05/2019). Data of breast cancer patients aged 65 and above, who underwent treatment and follow-up at the Department of Radiation Oncology between 2012 and 2018, were retrospectively examined. Patient information was collected from medical records, hospital information systems, and through telephone communication with the patients. Histopathological characteristics, stages, types of treatment, hormone receptor status, recurrence, metastasis information, and dates of follow-up visits were retrospectively recorded. This retrospective study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of our hospital.

A total of 108 breast cancer patients aged 65 and above were included in the study. The median age of the patients was 70 years (ranging from 65 to 90). The most common histopathological type was invasive ductal carcinoma, with the majority having grade 2 tumors. The patients were staged according to the AJCC staging system. Hormone receptor positivity was prevalent among the patients. The histopathological characteristics of the patients are presented in Table 1. Among them, 59 patients underwent breast-conserving surgery, while 49 patients underwent mastectomy. Axillary evaluation was performed for all patients surgically. Adjuvant chemotherapy consisted of 4 cycles of doxorubicin and cyclophosphamide (AC) followed by 12 weeks of paclitaxel. Neoadjuvant chemotherapy was administered to 18 patients with locally advanced disease.

All patients received adjuvant radiotherapy using the Varian Trilogy therapy unit. Hormone therapy, predominantly aromatase inhibitors, was administered to all hormone receptor-positive patients. Herceptin was given to patients with Her2 positive receptor types. The detailed primary

Table 1. Histopathologic features of patients

	Number of cases	Percent
Histopathology		
Invasive ductal carcinoma	85	7.8
Invasive lobular carcinoma	4	3.7
Mucinous	7	6.5
DCIS	5	4.6
Papiller	3	2.8
Other	4	3.6
Grade		
1	31	28.7
2	47	43.5
3	30	27.8
T stage		
is	5	4.6
1	36	33.3
2	48	44.4
3	9	8.3
4	10	9.3
N stage		
0	47	43.5
1	38	35.2
2	15	13.9
3	8	7.4
LVI		
Yes	34	31.5
No	74	68.5
PNI		
Yes	32	29.6
No	76	70.4
HR status		
Positive	92	85.2
Negative	16	14.8
Margin status		
Positive	2	1.9
Negative	106	98.1
HER2		
Positive	14	13
Negative	94	87
Triple negative	10	9.3
Ki 67- median (min-max)		13 (80-1)

DCIS: Ductal carcinoma in situ
LVI: Lymphovascular invasion
PNI: Perineural invasion
HR: Hormone receptor

treatment characteristics of the patients are presented in Table 2. The median follow-up period was 79.75 months (6.64 years), with a maximum follow-up of 133.49 months (11.12 years). At the end of this period, 88 patients (81.48%) were still alive.

Statistical Analysis: SPSS Statistics version 26.0 (IBM Corp., Armonk, New York) was used for the statistical analysis of the data. Patient characteristics and numerical variables were evaluated and presented in tabular form using descriptive statistics. Survival outcomes were examined using life tables. Overall survival and disease-free survival analyses between groups were performed using Kaplan-Meier analysis, and comparisons were made using the log-rank test. A p-value of ≤0.05 was considered statistically significant.

RESULTS

A total of 108 elderly female patients with breast cancer were included in the study. The median age of the patients was 70 (range: 65-90), and the mean age was 70.84±4.65. The median follow-up duration was 79.75 months (6.64 years), with a maximum follow-up of 133.49 months (11.12 years). At the end of this period, 88 patients (81.48%) were alive.

The most common histopathological type observed in the patients was invasive ductal carcinoma (78.7%), followed by mucinous carcinoma. Early-stage disease accounted for the majority of cases. The number of patients with pathological T2 stage was 48 (44.4%), while 36 patients (33.3%) had T1 stage, and 5 patients were diagnosed with ductal carcinoma in situ. The majority of patients were N0, accounting for 43.5%. Thirty-four patients had positive lymphovascular invasion (LVI). The hormone receptor positivity rate among the patients was 85.2%. Both hormone receptor-positive and HER2-positive patients accounted for 13% of the cases. There were 10 patients with triple-negative breast cancer.

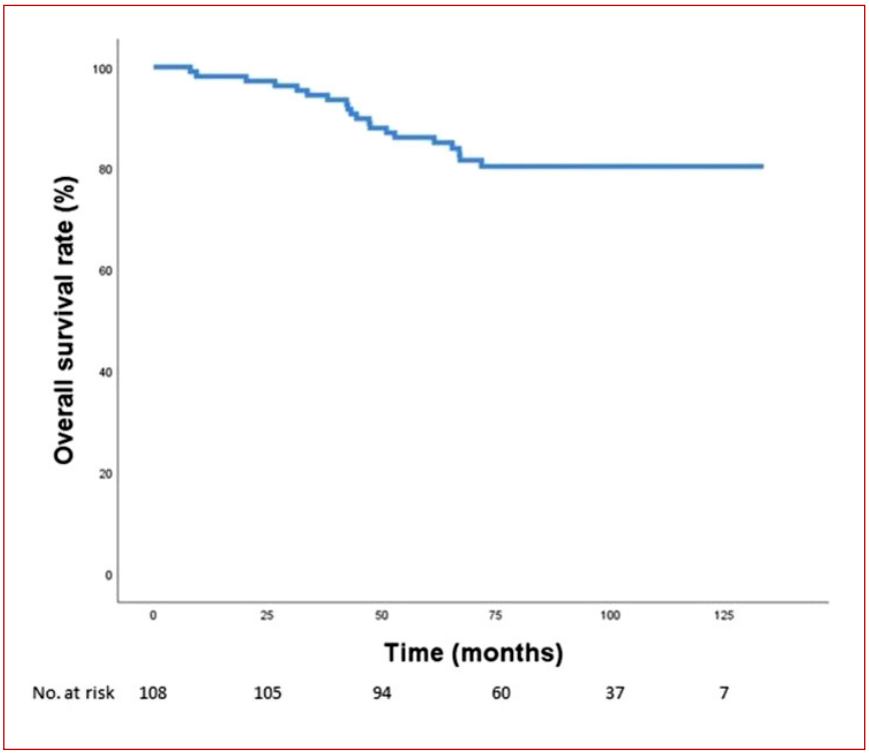

Figure 1. Overall survival (OS) analysis of 65 years of age and older breast cancer patients

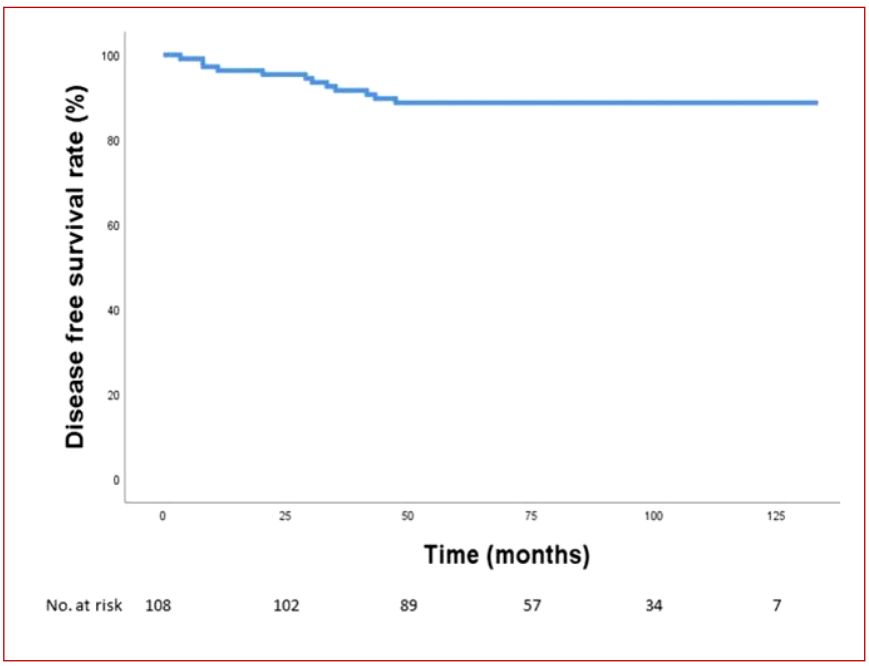

Figure 2. Disease-free survival (DFS) analysis of 65 years of age and older breast cancer patients

A total of 59 patients underwent breast-conserving surgery, while 49 patients underwent mastectomy. Sentinel lymph node biopsy (SLNB) was performed on 45 patients (41.7%), and axillary lymph node dissection (ALND) was performed on 48 patients (44.4%). The majority of patients received adjuvant chemotherapy, which consisted of 4 cycles of doxorubicin and cyclophosphamide (AC), followed by 12 weeks of paclitaxel. For locally advanced cases, 18 patients received neoadjuvant chemotherapy followed by surgery and radiotherapy. All patients who received breast-conserving surgery received a total of 50 Gy radiation to the whole breast and 10 Gy additional dose to the tumor bed, while seven patients received an additional 16 Gy dose to the tumor bed. Postmastectomy radiotherapy was administered to patients with T3-T4 or N2-N3 disease, delivering 50 Gy to the entire chest wall and regional lymph nodes. Hormone receptor-positive patients received hormone therapy, predominantly with aromatase inhibitors. All patients with HER2-positive tumors received trastuzumab.

The 3-year overall survival (OS) rate was 93.5%, and the 5-year OS rate was 86.1% (Figure 1).

Disease-free survival (DFS) at 3 years was 91.6%, and at 5 years it was 88.7% (Figure 2). Among the 20 patients who died, 11 died from causes unrelated to cancer. The median age at diagnosis for non-cancer-related deaths was 76 (range: 69-84), and the median OS was 44.4 months (95% CI: 33.71-56.93). For patients who died due to cancer, the median age at diagnosis was 71 (range: 66-90), and the median OS was 43.2 months (95% CI: 25.66-56.99).

Three patients experienced local recurrence (2.7%) at the 8th, 11th, and 47th months, all of whom had received breast-conserving surgery. None of these patients had positive surgical margins, and two of them had triple-negative tumors. All three patients are currently alive without disease after receiving adjuvant chemotherapy and undergoing treatment for local recurrence.

Table 2. Treatment characteristics of patients

	Number of cases	Percent
Type of surgery		
Breast conserving surgery	59	54.6
Mastectomy	49	45.4
Regional lymphatics		
SLND	45	41.7
ALND	48	44.4
SLND+ALND	15	13.9
Neoadjuvant chemotherapy		
Yes	18	16.7
No	90	83.3
Adjuvant chemotherapy		
Yes	62	57.4
No	46	42.6
Trastuzumab		
Yes	13	12
No	95	88
RT treatment dose		
50	50	46.3
60	51	47.2
66	7	6.5
Lymphatic irradiation		
Yes	59	54.6
No	49	45.4
Hormone therapy		
Yes	92	85.2
No	16	14.8

SLND: Sentinel lymph node dissection
ALND: Axillary lymph node dissection

Eight patients (7.4%) developed distant metastasis, and all of them had a fatal outcome. The median time to distant metastasis was 31.85 months (range: 3.52-43.20). In patients with distant metastasis, the median survival after metastasis detection was 9.46 months (range: 1.31-28.06).

Table 3. Trastuzumab, TNB and HT features; recurrence and death status according to adjuvant CT in T1-2 N0 staged patients

	Adjuvant CT group	No CT group	Total
Number of cases	15	20	35
Hormone therapy			
Yes	12	20	32
No	3	0	3
Trastuzumab	0	0	0
Triple negative	2	0	2
Recurrence			
Local	2	0	2
Distant	0	1	1
Death			
Cancer related	0	1	1
Other causes	2	1	3

CT: Chemotherapy

Subgroup analysis was performed on a total of 35 patients, including 15 who received adjuvant chemotherapy and had T1-2 and N0 disease. A comparison of the chemotherapy and non-chemotherapy groups is presented in Table 3.

DISCUSSION

Elderly women constitute a significant portion of breast cancer patients. However, there is a scarcity of research data specifically focusing on this age group, leading to uncertainties in treatment options. Geriatric assessments, which evaluate the tolerability of different treatments for elderly patients, are still not widely used in clinical practice. In our study, we examined the tumor characteristics and treatments of 108 breast cancer patients aged 65 and above. All patients were able to undergo surgery, chemotherapy, and radiotherapy treatments. Consistent with the literature, the most common histopathological type observed was invasive ductal carcinoma (IDC) (9,10). The majority of patients were hormone receptor (HR) positive. In elderly breast cancer patients, the tumor biology predominantly consists of HR-positive, HER2-negative, and low Ki67 proliferation index patients (11,12,13). In our study, similarly to the literature, we observed a high number of HR-positive patients and a low number of HER2-positive patients.

In our study, all patients underwent surgical treatment. Various retrospective studies have shown that treatment approaches vary according to age, and less aggressive treatment options are chosen for elderly patients. Aggressive treatments are also avoided due to concerns about tolerability in these patients. In the past, the traditional treatment for geriatric patients was radical or modified radical mastectomy. Nowadays, breast-conserving surgery (BCS) has become prominent, although it is less preferred by patients due to the necessity of adjuvant treatments (14,15,16). In our study, 54.6% of the patients underwent BCS, while 45.4% underwent mastectomy. Patients tolerated the surgical treatment well, and there were no delays in initiating adjuvant treatments.

After surgical treatment, our patients received adjuvant chemotherapy based on tumor size and lymph node involvement. The ongoing randomized study by The Early Breast Cancer Trialist's Collaborative Group (EBCTCG) aims to investigate the effects of chemotherapy and hormone therapy on recurrence and 15-year survival. However, the study primarily includes patients aged between 60-69, and the number of patients aged 70 and above is limited (17). Therefore, although the effectiveness of treatment may be similar, the low number of older patients is concerning. Age alone should not be a barrier to receiving chemotherapy. The decision should be based on the patient's performance status and comorbidities (18,19) In our study, adjuvant chemotherapy was administered to 62 (52.4%) patients, while neoadjuvant chemotherapy was administered to 18 (16.7%) patients.

Therefore, it is worth noting that studies on postoperative radiotherapy after breast-conserving surgery in patients aged 70 and older, with negative lymph nodes and hormone receptor-positive tumors, suggest a reduction in local recurrence rates without significantly affecting overall survival. However, these studies are based on historical series from an era when radiotherapy technology was less advanced and associated with higher side effects (20,21). Clinical trials aim to explore the avoidance of postoperative radiotherapy in elderly breast cancer patients, but definitive indications for such practices are still not well-defined (22).

In our study, we administered whole breast radiotherapy to all patients who underwent breast-conserving surgery, along with an additional boost dose to the tumor bed. For patients who underwent mastectomy, we planned radiotherapy to the chest wall and regional lymph nodes for those with T3-T4 tumors or lymph node positivity. Our patients tolerated radiotherapy well.

In a subgroup analysis of our study, which included 35 early-stage patients with T1-2 and N0 disease, no significant differences were observed in overall survival and disease-free survival between those who received adjuvant chemotherapy and those who did not. Considering the potential toxicity of chemotherapy in elderly patients with early-stage breast cancer, current guidelines recommend systemic adjuvant endocrine therapy for HR-positive patients. The survival benefit of chemotherapy in elderly patients remains uncertain. Therefore, in HR-positive, Her2-negative, lymph node-negative, or limited lymph node involvement (1-3 nodes) cases, prognostic scoring methods like Oncotype Dx or Mammaprint, which assess the risk of recurrence, are utilized. However, their widespread use is hindered by high costs (23).

Among our patients, 11 out of 20 deceased individuals passed away due to non-cancer-related causes, while 8 developed distant metastasis, leading to poor outcomes. The 5-year overall survival rate in our study was 86.1%. In a study by Joana et al., overall survival was evaluated in patients aged 65 and older, revealing a rate of 82.7% (24).

The limitations of our study include the lack of detailed information on comorbidities, data on the duration of hormone therapy in elderly patients, and the absence of comprehensive evaluations of treatment-related side effects as this is a retrospective study. Furthermore, due to the methodology of reaching out to non-responsive patients through telephone contact and gathering information from their relatives, specific details regarding aromatase inhibitors could not be ascertained. Additionally, considering the evolving nature of geriatric patient assessment scores and the ongoing refinement of their role in treatment decisions, our study spanned the past 10 years and treatment decisions were made based on outcomes from studies involving younger breast cancer patients. It's important to highlight that comprehensive information and widespread utilization related to patients' vulnerability scores and concurrent health conditions are even currently lacking.

The strengths of this study lie in its comprehensive evaluation of breast cancer treatment outcomes in a specific age group, shedding light on a population that has been understudied. The inclusion of a significant number of elderly patients and the examination of various treatment modalities, including surgery, chemotherapy, and radiotherapy, contribute to a more holistic understanding of their management. The study's attempt to address the limited research on elderly breast cancer patients and its contribution to the existing literature are also notable strengths. By examining both clinical characteristics and treatment approaches, the study provides valuable insights into the challenges and opportunities in managing breast cancer in this age group. Since the geriatric age group is examined, it is an article that may benefit geriatrics from an oncological point of view.

Importantly, this study underscores the significance of collaborative assessment and treatment decision-making involving both oncologists and geriatricians. The joint evaluation by these specialists is appropriate, as evidenced by the demonstration that while biological age alone may not hold complete significance, elderly patients can tolerate treatments despite their advanced years. Therefore, this research emphasizes the necessity of a nuanced approach that takes into account factors beyond chronological age.

In conclusion, this study not only highlights the importance of considering various factors, including performance status, comorbidities, and post-treatment quality of life, when making treatment decisions for elderly breast cancer patients, but also suggests that collaborative evaluation and treatment decision-making by oncologists and geriatricians would be beneficial. While providing valuable insights, the study also brings attention to the existing gaps in knowledge and the need for further research to optimize treatment strategies for this growing patient population.

CONCLUSION

When making treatment decisions for elderly breast cancer patients, factors such as performance status, comorbidities, toxicity, and post-treatment quality of life should be carefully considered alongside age. Treatment decisions should be based on comprehensive evaluations taking these factors into account.

As future suggestions; retrospective studies may lead to prospective studies and guidelines as they show feasible treatments and tolerability in elderly breast cancer patients.

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ORIGINAL ARTICLE

RISK FACTORS FOR PROLONGED INTENSIVE CARE UNIT STAYS IN ELDERLY PATIENTS AFTER CARDIAC SURGERY: A RETROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Introduction: With the increase in life expectancy and developments in surgical and anesthetic techniques, intensive care follow-up, and treatment methods, the number of patients undergoing open-heart surgery has increased.

Methods: The clinical files of 220 patients who underwent cardiovascular surgery were retrospectively reviewed. The patients were divided into two groups: group 1 (those who stayed for one day or less) and group 2 (those who stayed for more than one day). In addition, the reason for hospitalization for five days or more was investigated. The effect of patient variables on the length of stay in the intensive care unit was investigated by logistic regression analysis.

Results: Hemoglobin values, ejection fraction values, and intensive care unit hospitalizations were significantly lower ($p<0.05$) than those in the group with intensive care unit hospitalizations of <24 h. The sodium value was significantly higher ($p<0.05$) in the group with intensive care unit hospitalizations >24 h than in the group with intensive care unit hospitalizations <24 h. The pacemaker requirement rate in the group with intensive care unit hospitalizations >24 h was significantly ($p<0.05$) higher than the group with intensive care unit hospitalizations < 24 h. The sinus rhythm in the group with intensive care unit hospitalizations >24 h was significantly lower ($p<0.05$) than that in the group with intensive care unit hospitalizations <24 h. Intensive care transfusion of erythrocyte suspension, fresh frozen plasma, and platelet suspension were significantly higher ($p<0.05$) in the group with intensive care unit hospitalizations >24 h than in the group with intensive care unit hospitalizations <24 h.

Conclusion: In our study; We found that factors such as preoperative low ejection fraction (EF), hypernatremia, female gender, inotrope requirement, delirium, extubation time, intraoperative-postoperative transfusion, drainage revision affect the length of stay in the intensive care unit In the intraoperative period, methods to protect myocardial and kidney functions and provide hemostasis bleeding control reduce the duration of intensive care hospitalization

Keywords: Thoracic Surgery; Length of Stay; Critical Care; Aging.

INTRODUCTION

The prevalence of cardiovascular diseases has increased worldwide in recent years. Cardiovascular diseases (CVD), including coronary artery disease and stroke, are the most common mortal noncontagious diseases globally, accounting for an estimated 18.6 million deaths in 2019 (1). The burden of cardiovascular disease in an increasingly aging population has resulted in a shift in the demographics of cardiac surgery patients to include those who are older, increasingly frail, and have multiple comorbidities (2, 3). As a result, the number of patients undergoing cardiac surgery has been on the rise. Advanced age, female gender, decreased left ventricular function, arrhythmia, inotropic agent use, and the need for an intra-aortic balloon pump (IABP) have been identified as risk factors for prolonged intensive care unit (ICU) stays, and these variables have been found to prolong the length of stay in the ICU (4,5). However, the complex nature of these patients means that they face a longer and more complex postoperative process, which often requires a longer period of time. Long stays in the intensive care unit have been reported in 4–11% of cardiac patients, with some sources claiming as many as 36% (6,7). Therefore, it is critical to identify risk factors and closely monitor patients with these characteristics to shorten and minimize the length of stay in intensive care units (8). With this increase, the cost calculations for patients undergoing cardiac surgery have begun. Caring for critically ill patients requires significant expenditure of time, money, and resources, including specialist staff, one-on-one nursing care, and advanced equipment and treatments (9).

This study aimed to investigate the risk factors associated with prolonged ICU stay in patients who underwent cardiac surgery. Many factors affect the length of hospital stay of patients who have undergone open-heart surgery.

METHOD

Adult patients undergoing cardiac surgery between January 2012 and August 2021 were reviewed retrospectively after obtaining approval from the Clinical Research Ethics Committee (Date: April 27, 2021; Ethics Committee Number:2021/25).

Data were obtained by examining the anesthesia and surgery information obtained from the files of patients who were followed up in the Cardiovascular Surgery Intensive Care Unit (CVS ICU), intensive care follow-up forms, and hospital epicrisis reports. Demographic characteristics, American Society of Anesthesiologists (ASA) scores, and comorbidities (hypertension [HT], hyperlipidemia [HL], diabetes mellitus [DM], chronic obstructive pulmonary disease [COPD], peripheral arterial disease [PAD], renal dysfunction, and left ventricular ejection fraction [LVEF]) were examined during preoperative evaluation. The intraoperative anesthesia method, cardiopulmonary bypass, aortic cross-clamp, operation times, and type of operation (emergency or elective) were evaluated. In the postoperative period, the amount of drainage, need for inotropic support, use of an intra-aortic balloon pump (IABP), re-exploration for bleeding, amount of blood product used, time to intubation, prolonged mechanical ventilation (>24 h), respiratory system complications (pneumonia), neurological events (stroke, transient ischemic attack), renal failure requiring dialysis, atrial fibrillation (AF), permanent pacemaker requirement, presence of delirium are evaluated. The Richmond Agitation-Sedation Scale (RASS) was used to evaluate agitation and sedation routinely in our hospital. The RASS scores range from -5 (unrousable) to +4 (very agitated), with 0 representing a state of calmness. This assessment aids in understanding patient disposition and its impact on ICU stay duration. Moreover, lactate levels were recorded before the operation, when the patient first came to the ICU after the operation, and at the 24th hour.

Laboratory parameters were recorded before and after surgery. The laboratory parameters evaluated were HbA1C, hemoglobin (Hb), hematocrit, sodium, calcium, potassium, glomerular filtration rate (GFR), blood urea nitrogen (BUN), and creatinine levels. The lowest and highest GFR values were also recorded in the ICU. Using these parameters, we determined whether there was a difference between young (65–74 years) and very elderly (>75 years) patients. Using the G*Power (v3.1.9) program for sample size determination and power analysis, we employed the data provided by Demir et al. (10) concerning various age groups. The calculation was grounded in the length of intensive care stay percentage effects, resulting in a determined effect size of w=0.326. Consequently, we achieved 80% power at an α=0.05 significance level. The analysis indicated a necessity for a minimum of 182 cases, In accordance with this, our study encompassed a total of 220 cases.

Intensive Care Management

A mechanical ventilator with a tidal volume of 8–10 mL/kg was set to 40% FiO2 in the volume- or pressure-controlled ventilation mode. Routine blood gas analyses were performed, and FiO2 and respiratory frequency settings were adjusted to ensure that PaO2 was greater than 80 mmHg and PaCO2 was 35–45 mmHg. The patients were warmed up so that their stable temperature reached 37 °C. Normothermic patients with controlled pain and no excessive bleeding (>80 ml/h) were extubated.

Statistical Method

For the descriptive statistics of the data, the mean, standard deviation, median, lowest/highest frequency, and ratio values were used. The distribution of variables was measured using the Kolmogorov-Smirnov test. The Mann-Whitney U test was used to analyze independent quantitative data. The Chi-square test was used to analyze independent qualitative data, and the Fisher's test was used when the Chi-square test conditions were not met. The effect level was investigated using single and multivariate logistic regressions. We used the SPSS 28.0 program for the analysis.

RESULTS

Female patients admitted to the intensive care unit for more than 24 hours had a significantly higher rate ($p<0.05$) than female patients admitted for less than 24 hours. Hemoglobin (Hb) values, ejection fraction (EF) values, and ICU hospitalizations were significantly lower ($p<0.05$) in the group with > 24 hours of ICU hospitalization than in the group with < 24 hours of ICU hospitalization. (Table 2)

Postoperatively, the lowest GFR, highest BUN, Creatinine, aortic clamp time, and HbA1c values were observed in groups with ICU hospitalization for less than or more than 24 hours. The sodium level was significantly higher ($p<0.05$) in the group with >24 hours of ICU hospitalization than in the group with <24 hours of ICU hospitalization. (Table 3)

Pacemaker requirements were significantly higher ($p<0.05$) in the group with ICU hospitalization >24 hours than in the group with ICU hospitalization <24 hours. The sinus rhythm (SR) rate in the group with >24 hours of ICU hospitalization was significantly lower ($p<0.05$) than that in the group with <24 hours of ICU hospitalization. (Table 3)

When intensive care inotropic support was compared, the adrenaline dopamine (DA) and noradrenaline (NA) ratios were significantly higher ($p<0.05$) in the group with ICU stay >24 hours than in the group with ICU stay <24 hours. (Table 3)

When comparing the use of blood products in the ICU, the use of erythrocyte suspension (ES), fresh frozen plasma (FFP), and platelet suspension was significantly higher ($p<0.05$) in the group with >24 h of ICU hospitalization than in the group with <24 h of ICU hospitalization. Intraoperative ES transfusion was significantly ($p<0.05$) higher in the

Table 1. Demographic values

		Min	-	Max	Median	Mean	±	SS /n-%
Age		65.0	-	84.0	70.5	71.3	±	4.7
Age	< 75(65-74)					164		74.5%
	> 75(75-84)					56		25.5%
Gender	Female					87		39.5%
	Male					133		60.5%
ASA (American Society of Anesthesiologists)	II					23		10.5%
	III					141		64.1%
	IV					56		25.5%
HT (Hypertension)						176		80.0%
DM (Diabetes mellitus)						127		57.7%
Goiter						27		12.3%
COPD (Chronic obstructive pulmonary disease)						52		23.6%
Elective						215		97.7%
Urgent						5		2.3%

group with >24 h of ICU hospitalization than in the group with <24 h of ICU hospitalization. (Table 4)

The postoperative first-day drainage was significantly higher ($p<0.05$) in the >24 h ICU hospitalization group than in the <24 h ICU hospitalization group. (Table 4)

The revision rate and postoperative agitation rate were significantly higher ($p<0.05$) in the group with a duration of >24 hours in the intensive care unit than in the group with a duration of <24 hours. The extubation time and time of stay in the ICU were significantly higher ($p < 0.05$) in the group with >24 h in the intensive care unit than the group with <24 h (Table 4).

Patients with respiratory failure, SVO, kidney failure, sepsis, IABP, arrhythmia, and an ejection fraction <35% stayed in the ICU for ≥ 5 days (Table 5).

Regression Analysis Results

Multivariate logistic regression analysis was performed to determine the factors affecting long hospitalization (>1 d). The model obtained from the analysis performed using the backward elimination method was statistically significant [2 = 147.887, P <0.001]. In the model, the variables of extubation time, drainage on the first day, and erythrocyte suspension during intensive care follow-up were significant ($p<0.001$) (Table 6).

Table 2. Preoperative blood and background information of patients hospitalized in cardiovascular surgery intensive care for more than 24 hours and less

		ICU Stay ≤ 24 h				ICU Stay > 24 h				P	
		Mean	±	SD/n-%	Median	Mean	±	SD/n-%	Median		
Age		70.6	±	4.5	70.0	71.6	±	4.7	71.0	0.113	m
Age	< 75	54		80.6%		110		71.9%		0.173	x^2
	> 75	13		19.4%		43		28.1%			
Gender	Female	19		28.4%		68		44.4%		0.025	x^2
	Male	48		71.6%		85		55.6%			
ASA Score	II	7		10.4%		16		10.5%		1.000	x^2
	III	43		64.2%		98		64.1%			
	IV	17		25.4%		39		25.5%			
HT		53		79.1%		123		80.4%		0.826	x^2
DM		34		50.7%		93		60.8%		0.165	x^2
Goiter		8		11.9%		19		12.4%		0.921	x^2
COPD		11		16.4%		41		26.8%		0.095	x^2
Elective		67		100.0%		148		96.7%		0.181	x^2
Urgent		0		0.0%		5		3.3%		0.326	x^2
Preoperative Laboratory Values											
Hb		13.0	±	2.1	12.9	12.4	±	2.0	12.2	0.034	m
Hematocrit		38.4	±	5.8	38.3	37.3	±	5.6	37.4	0.174	m
GFR		77.6	±	22.2	77.5	69.5	±	20.7	70.6	0.052	m
BUN		19.0	±	5.5	18.0	22.7	±	13.8	19.0	0.100	m
Cr (Creatinine)		1.0	±	0.2	0.9	1.1	±	0.7	0.9	0.899	m
Na (Sodium)		136.1	±	4.1	135.0	135.2	±	4.5	136.0	0.489	m
K (Potassium)		4.4	±	0.4	4.4	4.3	±	0.6	4.4	0.933	m
Lactate Pre-anesthesia		1.1	±	0.4	0.9	1.0	±	0.4	0.9	0.107	m
Lactate ICU First ABG		1.6	±	0.6	1.5	1.5	±	0.6	1.4	0.250	m
Lactate ABG After 24 Hours		1.8	±	0.7	1.7	2.2	±	1.7	1.8	0.148	m
Preoperative EF (Ejection Fraction)		54.6	±	9.3	60.0	51.4	±	10.3	55.0	0.021	m

[m] Mann-Whitney U test / [X²] Chi-square test

ABG: Arterial Blood Gas; ICU: Intensive Care Unit; GFR: Glomerular Filtration Rate; BUN: Blood Urea Nitrogen; HT: Hypertension; DM: Diabetes Mellitus.

Table 3. Postoperative laboratory values of patients hospitalized more than 24 hours and less in cardiovascular surgery intensive care unit.

	ICU Stay ≤ 24 h			ICU Stay > 24 h			p	
	Mean ± SD/ n-%		Median	Mean ± SD/ n-%		Median		
ICU 24-Hour Laboratory Values								
Hb	9.5 ± 1.2		9.3	9.1 ± 1.0		9.2	0.198	m
Hematocrit	27.9 ± 3.7		28.1	27.2 ± 3.1		27.5	0.373	m
GFR (Glomerular filtration rate)	70.9 ± 19.0		69.6	65.1 ± 20.4		66.3	0.140	m
BUN (Blood Urea Nitrogen)	20.0 ± 6.1		20.0	22.9 ± 11.8		21.0	0.104	m
Cr	1.0 ± 0.2		1.1	1.2 ± 0.8		1.0	0.708	m
Na	141.3 ± 3.3		142.0	144.1 ± 9.3		143.0	0.001	m
K	4.4 ± 0.7		4.3	4.4 ± 0.6		4.4	0.250	m
Lowest postoperative period GFR	62.1 ± 22.7		64.1	55.2 ± 23.4		55.1	0.068	m
Highest postoperative period GFR	81.5 ± 19.5		88.2	77.4 ± 24.3		85.4	0.393	m
Aortic clamp Time	141.2 ± 181.3		72.0	166.1 ± 239.6		82.0	0.422	m
HbA1c (Hemoglobin A1C)	7.3 ± 1.9		6.5	7.0 ± 1.6		6.4	0.725	m
ICU Rhythm Yok	1	1.5%		0	0.0%		0.305	x^2
ICU Rhythm Var	66	98.5%		153	100.0%			
AF (Atrial fibrillation)	1	1.5%		7	4.6%		0.268	x^2
PACE	1	1.5%		22	14.4%		0.004	x^2
SR (sinus rhythm)	53	80.3%		90	58.8%		0.002	x^2
PR (PACE rhythm)	1	1.5%		8	5.2%		0.204	x^2
SB (Sinus Bradycardia)	6	9.1%		5	3.3%		0.070	x^2
ST (Sinus Tachycardia)	4	6.1%		19	12.4%		0.159	x^2
SVT (Supraventricular Tachycardia)	0	0.0%		1	0.7%		1.000	x^2
SNT (Sinus node tachycardia)	0	0.0%		1	0.7%		1.000	x^2

[m] Mann-Whitney U test / [X²] Chi-square test

CPB: Cardiopulmonary Bypass, EFLV: Ejection Fraction of the Left Ventricle

Table 4. Causes of patient hospitalization for more than 24-hours and less in intensive care

	ICU Stay ≤ 24 h				ICU Stay > 24 h				
	Mean	**±**	**SD/n-%**	**Median**	**Mean**	**±**	**SD/n-%**	**Median**	
Intensive Care Transfusion									
ES (Erythrocyte suspension)	0.55	±	0.78	0.00	2.37	±	2.70	2.00	0.000 [m]
FFP (Fresh Frozen Plasma)	0.58	±	1.07	0.00	1.48	±	2.12	1.00	0.001 [m]
Apheresis	0.03	±	0.25	0.00	0.23	±	0.82	0.00	0.018 [m]
Intraoperative Transfusion									
ES	0.57	±	1.05	0.00	0.81	±	0.99	0.00	0.034 [m]
FFP	0.29	±	0.70	0.00	0.52	±	1.01	0.00	0.121 [m]
Apheresis	0.03	±	0.17	0.00	0.05	±	0.25	0.00	0.582 [m]
Drainage Day 0	444.5	±	224.0	400.0	499.3	±	377.9	400.0	0.870 [m]
Drainage Day 1	102.2	±	111.6	100.0	309.6	±	231.7	250.0	0.000 [m]
Intensive Care Inotrope Support									
Adrenaline	6		9.0%		33		21.6%		0.024 x^2
NE (norepinephrine)	1		1.5%		38		24.8%		0.000 x^2
DA (Dopamine)	27		40.3%		95		62.1%		0.003 x^2
Dobutamine	0		0.0%		4		2.6%		0.316 x^2
Revision	2		3.0%		22		14.4%		0.013 x^2
Agitation	0		0.0%		13		8.5%		0.014 x^2
Extubation / Hour	9.2	±	3.0	8.0	21.9	±	21.2	17.0	0.000 [m]
Service Release Day	1.0	±	0.0	1.0	5.2	±	6.7	3.0	0.000 [m]

[m] Mann-Whitney U test / X^2 Chi-square test

DISCUSSION

Advancements in surgical and anesthesia techniques, coupled with innovations in extracorporeal circulation mechanisms and comprehensive monitoring, have notably curtailed intensive care unit stays. This has rendered open-heart surgery a viable and accessible treatment across all age groups. However, the prevalence of cardiac diseases remains substantial, entailing considerable morbidity and mortality. The majority of these procedures involve cardiopulmonary bypass (CPB). Despite considerable strides in recent years, postoperative morbidity and mortality rates in cardiac surgery persist, spanning from 5% to 75% contingent upon the specific procedure, patient comorbidities, and frailty factors (11). In patients following cardiac surgery complications that develop lead to deterioration in the quality

of life of patients and, in some cases, mortality. In this study, the factors that prolonged the length of stay in the intensive care unit of 220 patients who underwent open-heart surgery were investigated. 80% and 57.7% of the patients were diagnosed with hypertension and DM, respectively. In addition, although the length of stay on a mechanical ventilator and the length of hospital stay due to DM-related complications did not increase significantly, it was observed that they had an increased length of hospital stay (Table 1).

A recent study by Herman et al. (12) of 3489 patients who had undergone CABG surgery at a Canadian hospital concluded that a history of renal failure was among the independent predictors of prolonged hospitalization in the ICU setting. The study revealed that a higher creatinine level, which is a sign of renal failure, is an indicator of a longer ICU stay; however, age alone was not a negative factor in the evaluations made according to different age groups.

Cislaghi et al. (13) found that in a large study with 5123 patients who were followed up, the ventilation time was prolonged 2.2 times more in patients with an EF of 30%. In our study, we found that having an EF of <35% or poor LV function increased both the duration of ventilation and the length of stay in the intensive care unit (Table 2).

One of the factors that prolongs stay in the intensive care unit is the use of a cardiac pacemaker postoperatively. Pacemakers are effective treatments for symptomatic bradycardia and are widely used in modern cardiology (14). The length of stay in the intensive care unit was found to be longer in patients who required pacemakers (AF: 3.7%; PACE: 10.5%; SR: 65%, sinus bradycardia: 11%; sinus tachycardia: 23%; and supraventricular tachycardia: 1%). Patients with SR remained in the intensive care unit less frequently (Table 3).

Hein et al. (7) stated in their retrospective study involving 2683 patients that 26% of the patients stayed in the intensive care unit for more than 3 days. Advanced age, renal failure, respiratory failure, heart failure, and re-exploration were associated with prolonged intensive care. In our study, prolonged intensive care hospitalization was defined as ≥ 24 h. The routine stay in the intensive care unit of our hospital was 24 hours. A total of 220 patients were discharged to the inpatient ward: 67 on the first day and 177 on the fourth. The reason for the prolonged hospitalization may be that very complicated patients were admitted, and these patients were older. We found that 27.6% of the patients were hospitalized for more than three days (Table 4). We divided patients whose hospitalization period was prolonged into two groups: those who were hospitalized for more than one day and those who were hospitalized for five or more days. We found that the majority of patients hospitalized for five days or more were due to renal failure, arrhythmia, low ejection fraction, and respiratory failure (Table 5).

In contrast, Osinaike et al. (15) discovered that staying in the intensive care unit for more than four days increased the risk of pulmonary hypertension, mean CPB time, inotropic agent use, and surgical re-exploration; however, inotropic agent use remained the only independent variable in the multiple regression analysis. Garcia-Delgado et al. (16) stated that cardiac surgery causes widespread lung damage and respiratory distress by triggering an intense systemic inflammatory syndrome and increasing lung capillary permeability. Extubation and weaning times from the mechanical ventilator are prolonged in these patients, and exit from the intensive care unit and hospital is delayed. In our study, an increase of 1h in extubation time increased the probability of prolonged hospitalization by 1.361 times. An increase of 1 unit in the value of the erythrocyte suspension given in the intensive care follow-up increased the probability of prolonged hospitalization by 2.946 times, and a 1 unit increase in the drainage value on the first day increased the probability of prolonged hospitalization by 1.010 times.

Table 5. Those who stayed for five days or more

	Respiratory Failure	CVO	Kidney failure	Sepsis	IABP	Arrhythmia	EF: under %35 (20 out of 220 patients ≤ %35)
CABG: 5 patients	0	0	4	2	1	0	3
CABG+1 (Valve): 8 patients	3	1	5	1	0	2	1
CABG+ 2: 9 patients	4	1	3	2	0	2	
CABG+3 and more: 7 patients	3	0	2	1	1	1	4
Re-operated valve: 2 patients	2	0	1	1	1	1	1
1 valve: 1 patient	0	0	1	1	0	1	0
2 valves: 7 patients	6	1	5	3	0	2	3
3 valves: 4 patients	3	0	3	0	1	2	2

CABG: Coronary Artery Bypass Grafting; SVO: Cerebrovascular Disease; IABP: Intra-aortic Balloon Pump

Table 6. Results of the regression analysis

	OR (95 % GA)	Wald	P value
Constant	-	36.513	<0.001*
Extubation time	1.361 (1.202, 1.541)	23.564	<0.001*
ICU ES	2.946 (1.746, 4.969)	16.400	<0.001*
Drainage 1st day	1.010 (1.006, 1.014)	23.887	<0.001*

Gender remains a controversial variable in postoperative complications. Some studies have shown that women undergoing CABG are at a higher risk of morbidity and mortality than men (17). In our study, women stayed in intensive care longer than men, even after controlling for other disease factors.

Postoperative delirium, which is common in elderly patients, has been shown to be associated with poor outcomes, with delirium being 1.8 times more common in frail patients. Factors that accelerate the risk and development of delirium include advanced age and basic cognitive impairment (18). In our study, it was observed that the length of stay in the intensive care unit of patients with delirium increased.

In a study published by De Bruin et al. (19) in 2019, with the participation of 947 intensive care physicians, 53% of the participants stated that there was a transfusion protocol established by their hospitals and that the threshold Hb value for transfusion in the intensive care unit was 7 g/dL. A study conducted on Intensive Care transfusion rates found that ES, FFP, and apheresis platelet suspension were significantly higher ($p<0.05$) in the group hospitalized in the ICU for more than 24 h than in the group hospitalized for less than 24 h. Intraoperative transfusion of ES was significantly higher ($p<0.05$) in the groups with ICU hospitalizations of less than or more than 24 hours (Table 4).

Hypernatremia is a common problem, defined as a serum sodium concentration >145 mmol/L. Hypernatremia leads to an increase in serum osmolality and a loss of water from cells. An increase in serum sodium concentration manifests as a negative water balance. It may develop as an iatrogenic complication in elderly patients with a poor general condition or during hospitalization. It has the potential to be fatal (20). In our study, the Na value in the group with more than 24 h of ICU hospitalization was significantly higher ($p<0.05$) than that in the group with less than 24 h of ICU hospitalization.

Based on these findings, it was determined that open-heart surgery within the "65 years and older" patient cohort exhibited no impact on hospital stay length. This conclusion was drawn considering the thorough assessment of patient comorbidities, elective surgery circumstances, utilization of suitable anesthesia and surgical methodologies, and the potential for enhanced survival rates through meticulous intensive care monitoring.

This study has some limitations. This study used a theory-driven approach to identify risk factors and was evaluated in two stages at a research institute. Although the first stage examined the reasons for longer stays (>24 hours) in the ICU and the second used stratified random sampling to represent the prevalence rate of 5-day or longer stays in the ICU, the findings may be center-specific based on the data.

Conflict of Interest

The authors have no financial conflicts of interest and have nothing to disclose.

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ORIGINAL ARTICLE

PRE-ASSESSMENT CRITERIA FOR THE NEEDS OF PATIENTS IN PALLIATIVE CARE: THE ROLE OF PALLIATIVE CARE BY AGE GROUPS

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Abstract

Introduction: We aimed to define the characteristics of patients hospitalised in a palliative care unit and evaluate the role of palliative care services in the geriatric age group. The priorities and treatment approaches needed according to age groups were also evaluated.

Materials and Methods: The records of patients aged 18 years and older who followed up with palliative care between 01/2020-12/2021 were reviewed retrospectively. Patients aged 18-64 were defined as "group-1", patients aged 65-75 as "group-2", patients aged 76-90 as "group-3", and patients aged 91 and over as "group-4". The patient's age, sex, diagnosis, comorbidities, length of stay in the clinic, prognosis, pressure ulcers and immobilisation status were recorded and compared according to age groups.

Results: A total of 560 patients were included. The mean age was 73.14±14.22 years, and 53.2% were women. 48.2% of patients were transferred to the palliative care unit from the intensive care unit. Groups-1, 2, 3, and 4 consisted of 139 (24.8%), 129 (23%), 254 (45.4%), and 38 (6.8%) patients, respectively. When patients were examined according to age group, there was a statistically significant difference between the groups in terms of sex, pressure ulcers, immobilisation, mean hospital stay in the palliative care, and prognosis (p=0.026, p≤.001, p=0.006, p≤.001, p≤.001). While 72% of patients were discharged from the palliative care unit, 28% died during admission. The prognosis was better in group-1 compared to other groups.

Conclusion: Geriatric age and presence of chronic disease were the primary groups receiving palliative care. Access and integration of these patients to palliative care must be expanded.

Keywords: Palliative Care; Geriatrics; Critical Care; Chronic Diseases; Health Services Accessibility.

INTRODUCTION

Regardless of age, diagnosis, or prognosis, palliative care (PC) is a patient and family centred care setting that offers complete management of incurable diseases; the goal is to improve quality of life by foreseeing, preventing, and treating suffering (1). PC involves social needs as well as prevention, early detection, evaluation, and management of physical, psychological, and mental symptoms, according to the International Association of Hospice and PC definition and attempts to enhance the standard of living of caregivers, families, and patients. It can positively affect the course of the disease and can be applied at all healthcare levels (2-4).

The World Health Organization (WHO) estimated that globally, 56.8 million patients require PC per year, of which 25.7 million are in the terminal stage of disease (5). Only 14% of these individuals receive PC, and the need for PC continues to increase globally. Today, in the United States of America (USA), the majority of patients receiving PC are geriatric patients aged > 65 (6). Patients of any age and severe disease stage are eligible to receive PC (7), but different patient populations require different approaches (8). The requirements for the younger age group and the older age group are very different (9). There are significant differences in complaints, symptoms and treatment, as well as in needs and expectations, between older and younger age groups (6, 9, 10). Based on the limited literature available, we would have assumed that there would be differences in PC processes between very old, elderly, old and young age groups. Therefore, in our study, we evaluated the patients according to age groups.

This study aimed to define the characteristics of patients hospitalised in the PC unit, to determine their care priorities and the approaches needed according to age groups, as well as to evaluate the role of PC services in the geriatric age group. We aimed to comparatively emphasize the importance of the geriatric age group in the PC process by including all patients over the age of 18 in our study. Instances where PC service cannot be broadly provided were identified, including in the most developed high-income countries, and methods to raise awareness about PC among health service providers and professionals are discussed.

MATERIALS AND METHOD

Patients

All patients aged 18 years and older who followed up in the PC unit of Ankara City Hospital between January 2020 and December 2021 were included in the study retrospectively.

Patients with a hospitalisation period of less than two days in the PC unit, all repeated hospitalisations other than the first hospitalisation of patients with repeated hospitalisations, and patients with missing data were excluded from the study (Figure 1).

Study Design

Age, sex, diagnosis, comorbidities, duration of hospitalisation, prognosis (discharge or death), endoscopic gastrostomy, tracheostomy, pressure ulcers, and immobilisation status of each patient who met the inclusion criteria and the units for which consultation was requested in the PC unit were collected anonymously and recorded using Excel. Data were obtained electronically from patient records using Hospital Information Management System Software (HBYS, Ankara, Turkey).

The median age value of the patients included in the study, the geriatric age definition value and the "very old" patient age definition value were taken as cut-off values in the classification of the patients according to age groups. Geriatric age group was considered to be over 65 years of age (first cut-off value) (11). The mean age of all patients in our study was 73.14±14.22 years and the median age value was 76 years (second cut-off value) (first quartile age value 65, compatible with the accepted first cut-off value; second quartile age value 84). The

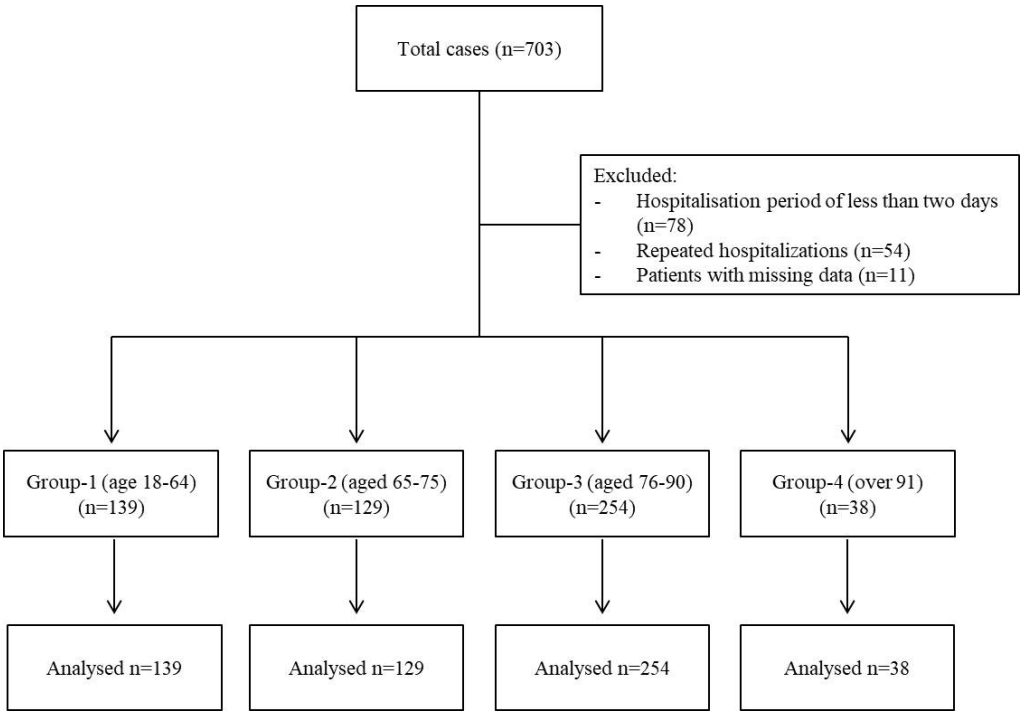

Figure 1. Flow charts of the patients

definition of the "very old" patient group is unclear in the literature. Some of studies recognise very old persons as those over 80 or 85 years of age (12-14), while some studies in the literature consider subjects aged 90 years and older to be very old, given the increasing proportion of elderly patients receiving medical services (15, 16). The only consensus in the literature for the "very old" patient group is that patients over 90 years of age have a poor survival prognosis in the short term after hospital discharge (16-20). Since the patient group over 90 years of age had a poor survival prognosis after hospital discharge, we thought that this patient group needed more PC services, and we considered the patient group over 90 years old as the "very old" patient group (third cut-off value). In our study, based on these literature data, patients aged 18-64 were defined as "group-1", patients aged 65-75 as "group-2", patients aged 76-90 as "group-3", and patients aged 91 and over as "group-4".

Ethics Statement

This study was approved by the Ankara City Hospital Ethics Committee (Approval Date and No:01.09.2021/E2-21-769). Ankara City Hospital Ethics Committee did not require informed consent because the study was retrospective. All procedures were performed in accordance with the guidelines outlined in the Declaration of Helsinki.

Outcome Criteria

The primary outcome of our study is the change in the characteristics, primary needs, care processes and prognoses of patients admitted to the PC unit according to age groups. The secondary outcome is the proportion of the geriatric age group in the PC process. The tertiary outcome is the impact of patient characteristics and place of residence on access to PC.

Sample Size

Patients who met the criteria admitted to the PC unit within a two-year period were included in our study. The two-year period was chosen at random.

Statistical Analysis

The statistical package program Statistical Package for the Social Sciences 24.0 (SPSS Inc., Chicago, IL, USA) was used to analyse the acquired data. The Shapiro-Wilk Test was used to assess the distribution of the obtained data. Mann-Whitney U and Student's t-tests were used to compare binary groups in accordance with the data distribution results. The Pearson Chi-Square test was used to compare categorical data between groups. Statistical significance was defined as $p < 0.05$. The number of cases (n), percent (%), mean ± standard deviation (±SD), or median (quarter 1, quarter 3), as well as the minimum value (min) and maximum value (max) were used to convey descriptive statistics. Categorical and demographic information are presented as percent (%) and number of cases (n).

When comparing the four groups, statistical significance was considered as <.008 after significant values were corrected using the Bonferroni correction for multiple tests.

RESULTS

Patient demographic and clinical characteristics are presented in Table 1. This study included 560 patients hospitalised in a PC unit. In 2020, 246 of these individuals were hospitalised, and 314 in 2021. Among all participants, 298 (53.2%) were female. The mean age was 73.14±14.22 years in all participants, 74.02±14.74 years in women, and 72.15±13.55 years in men (p=0.497).

Regarding place of residence, 14.3% of patients were admitted from a city other than Ankara, and 85.7% resided in the province of Ankara. When the settlements in their provinces of residence were viewed, it was determined that 83.2% of them lived in the city centre (Table 1). Admission to palliative services from the city centre was significantly higher.

Hypertension and diabetes mellitus were present in 52.5% and 29.6% of patients, respectively, while 28.4% of patients had some form of cancer (Table 1).

Prior to admission to the PC unit, 48.2% of the patients were transferred from intensive care units (ICU) and 12% from emergency rooms. Of these patients, 24.5 % (n=137) were admitted directly to the PC unit because of the inability of their relatives or caregivers to provide home care services (Table 1). Patients taken over from ICUs constituted the first rank in patient admission to the PC unit. The three most common requested consultations for patients in the PC unit were clinical nutrition (92.0%), physical therapy (91.8%), and infectious disease (45.9%) (Table 1).

When the additional clinical conditions of the patients were examined (Table 1), 280 (50%) had pressure ulcers, and 157 (28%) were immobilised.

Group-1 consisted of 139 (24.8%), group-2 129 (23%), group-3 254 (45.4%) and group-4 38 (6.8%) patients. The number of patients in Group-3 (76-90 years) was significantly higher than that in the other groups.

Considering the sex distribution by age group, there was a statistically significant difference between the groups (p=0.026) (Table 2). When the causes of the differences between the groups were investigated, a substantial sex difference was discovered only between Groups 1 and 4 (p=0.004). While the proportion of males was higher under the age of 65 years, the proportion of females was statistically higher over the age of 90 years.

There was a statistically significant difference between the age groups when pressure ulcers were analysed (p=0.001) - 33.8% of the patients in group-1, 54.3% in group-2, 55.1% in group-3, and 60.5% in group-4 (Table 2). The proportion of pressure ulcers did not differ significantly between groups 2,

Table 1. Patients' demographics and medical conditions

Features	Total (n=560)
Age (year, mean ± SD)	**73,14 ±14,22**
Gender, n (%)	
Male	262 (46.8)
Female	298 (53.2)
Place of Residence, n (%)	
City Centre	466 (83.2)
District Centre	64 (11.4)
Village	30 (5.4)
Is the place of residence in a different province other than Ankara? n (%)	
Yes	80 (14.3)
No	480 (85.7)
Comorbidities, n (%)	
Hypertension (HT)	294 (52.5)
Diabetes (DM)	166 (29.6)
Cancer (CA)	159 (28.4)
Cerebrovascular Diseases (CVH)	131 (23.4)
Coronary Artery Disease (CAD)	90 (16.1)
Alzheimer's Disease	77 (13.8)
Congestive Heart Disease (CHF)	48 (8.6)
Dementia	42 (7.5)
Chronic Kidney Disease (CKD)	40 (7.1)
Atrial Fibrillation (AF)	36 (6.4)
Parkinson's Disease	35 (6.3)
Benign Prostatic Hypertrophy (BPH)	31 (5.5)
Epilepsy	26 (4.6)
Hypothyroidism	20 (3.6)
Morbid Obesity	3 (0.5)
Clinic transferred at admission, n (%)	
Intensive Care Unit	270 (48.2)
Admission to Palliative Direct Admission	137 (24.5)
Emergency Medicine Clinic	67 (12.0)
Internal Medicine Clinic	29 (5.2)
Oncology Clinic	21 (3.8)
Neurology Clinic	13 (2.3)
Gastroenterology Clinic	4 (0.7)
Neurosurgery Clinic	4 (0.7)
Urology Clinic	4 (0.7)
Infection Clinic	3 (0.5)
Nephrology Clinic	3 (0.5)
General Surgery Clinic	2 (0.4)

Table 1 continued

Table 1. Patients' demographics and medical conditions

Endocrinology Clinic	1 (0.2)
Chest Diseases Clinic	1 (0.2)
Orthopedics Clinic	1 (0.2)
Additional clinical status, n (%)	
Pressure Ulcers	280 (50.0)
Immobilisation	157 (28.0)
PEG	132 (23.6)
Urine Catheter	32 (5.7)
Gastroenterostomy	1 (0.2)
Cystostomy	1 (0.2)
Colostomy	6 (1.1)
Ileostomy	4 (0.7)
Nephrostomy	1 (0.2)
The first seven units for which consultation was requested during the admission process, n (%)	
Clinical Nutrition Unit	515 (92.0)
Physical Therapy Clinic	514 (91.8)
Infectious Diseases Clinic	257 (45.9)
Stoma Wound Care Unit	179 (32.0)
Chronic Wound Unit Polyclinic	153 (27.3)
Neurology Clinic	144 (25.7)
Psychiatry Clinic	122 (21.8)

3, and 4 (group 2 versus 3, p=0.874; group 2 versus 4, p=0.495; group 3 versus 4, p=0.531). Group-1 did have significantly fewer pressure ulcers compared to the other groups (group 1 versus 2, p<0.001; group 1 versus 3, p<0.001 and group 1 versus 4, p=0.003). The wounds of 206 (73.5%) patients with pressure ulcers were located in the sacral region, and in terms of progression of all pressure ulcers, 35.0% were stage 1, 32.7% were stage 2, 25.7% were stage 3, and 5.8% were stage 4. The distribution of pressure ulcers according to their stage and localisation is summarised in Table 3.

One hundred and fifty-seven patients (28%) were bedridden (immobilised), which was statistically significantly different between the groups according to age (p=0.006, Table 2). The proportion of immobilisation in groups 1, 2, 3, and 4 were 18.7%, 24.8%, 33.1%, and 39.5%, respectively. There was a statistically significant difference in immobilisation between groups 1 and 3, and between groups 1 and 4 (p=0.002 and p=0.007, respectively). Immobilisation was significantly less common in group-1 than in groups 3 and 4.

The mean number of hospitalisation days in the PC unit was 17.84 ± 10.71 days. Considering the days of hospitalization according to the age group, there was a statistically significant difference (Fisher's ANOVA, p<.001). The mean hospital stay in group-1 was 13 days (SD=10.4), 4.69 days less than in group-3 (mean:19.5, SD:9.56, p<.001), and in group-4 it was less than 7.26 days (mean:22.1, SD:16.0, p<.001), and the difference was statistically significant when compared with both groups (post-hoc Tukey test, Figure 2). The mean hospital stay in group-2 was 16.4 days (SD=10.4), 3.09 days less than in group-3 (mean:19.5, SD:9.56, p=0.005), and in group-4 it was

Table 2. Distribution of Gender, Pressure Ulcers, Immobilisation and Prognosis by Age Groups of the Patients

			Gender		Total	p*
			Male	Female		
Age Groups	Age 18-64	(n)	73	66	139	0,026
		(%)	52,5%	47,5%	24,8%	
	Age 65-75	(n)	65	64	129	
		(%)	50,4%	49,6%	23,0%	
	Age 76-90	(n)	114	140	254	
		(%)	44,9%	55,1%	45,4%	
	Over 91	(n)	10	28	38	
		(%)	26,3%	73,7%	6,8%	
Total		(n)	262	298	560	
		(%)	46,8%	53,2%	100,0%	
			Pressure Ulcers		Total	p*
			Yes	No		
Age Groups	Age 18-64	(n)	47	92	139	<,001
		(%)	33,8%	66,2%	24,8%	
	Age 65-75	(n)	70	59	129	
		(%)	54,3%	45,7%	23,0%	
	Age 76-90	(n)	140	114	254	
		(%)	55,1%	44,9%	45,4%	
	Over 91	(n)	23	15	38	
		(%)	60,5%	39,5%	6,8%	
Total		(n)	280	280	560	
		(%)	50%	50%	100,0%	
			Immobilisation		Total	p*
			Yes	No		
Age Groups	Age 18-64	(n)	26	113	139	0,006
		(%)	18,7%	81,3%	24,8%	
	Age 65-75	(n)	32	97	129	
		(%)	24,8%	75,2%	23,0%	
	Age 76-90	(n)	84	170	254	
		(%)	33,1%	66,9%	45,4%	
	Over 91	(n)	15	23	38	
		(%)	39,5%	60,5%	6,8%	
Total		(n)	157	403	560	
		(%)	28%	72%	100,0%	

Table 2 continued

Table 2. Distribution of Gender, Pressure Ulcers, Immobilisation and Prognosis by Age Groups of the Patients

			Prognosis		Total	p*
			Discharge	Exitus		
Age Groups	Age 18-64	(n)	120	19	139	<0,001
		(%)	86,3%	13,7%	24,8%	
	Age 65-75	(n)	90	39	129	
		(%)	69,8%	30,2%	23,0%	
	Age 76-90	(n)	171	83	254	
		(%)	67,3%	32,7%	45,4%	
	Over 91	(n)	22	16	38	
		(%)	7,9%5	42,1%	6,8%	
Total		(n)	403	157	560	
		(%)	72%	28%	100,0%	

*Pearson Chi-square test, p<0.05 was considered significant.
Significance between groups p<0.008 was significant according to Bonferroni correction.

less than 5.66 days (mean:22.1, SD:16.0, *p*=0.003), and the difference was statistically significant when compared with both groups (post-hoc Tukey test, Figure 2). No statistically significant differences were found between group-1 and group-2 (*p*=0.099) and between group-3 and group-4 (*p*=0.082).

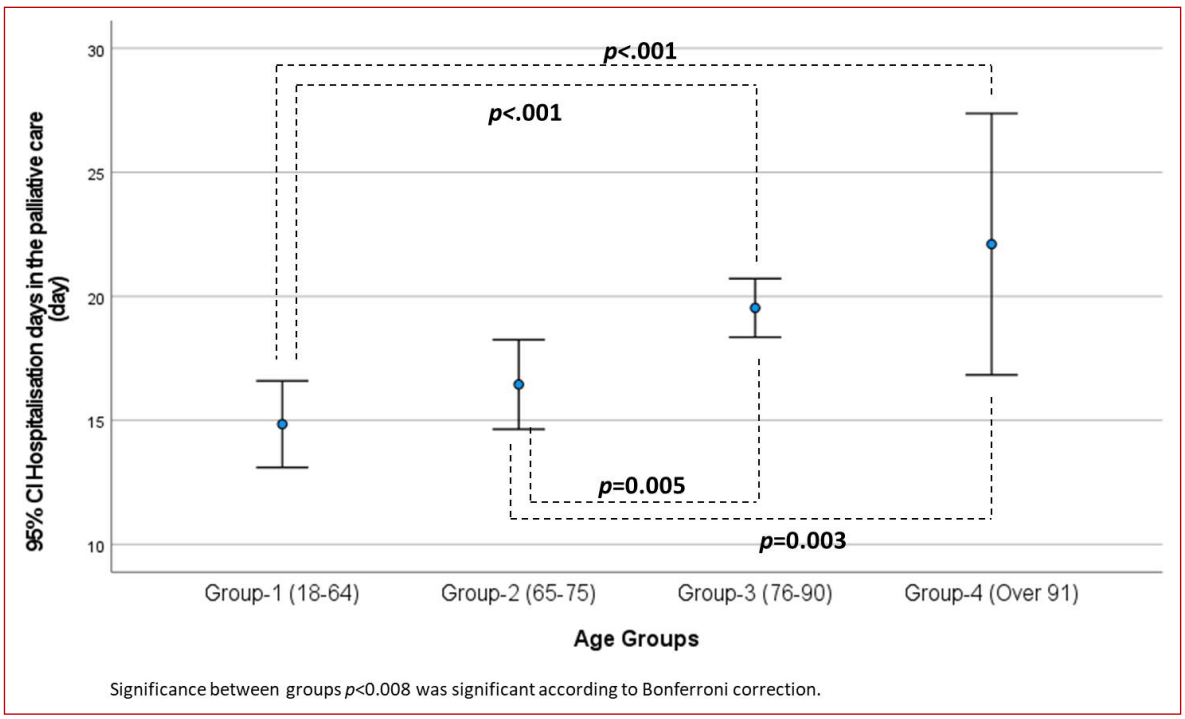

Figure 2. Hospitalisation days in the palliative care

Table 3. Distribution of pressure ulcers by stage and localization

Anatomical Localisation	Phase	Total
Sacrum	Phase 1	63 (30.6%)
	Phase 2	58 (28.2%)
	Phase 3	70 (34.0%)
	Phase 4	13 (6.3%)
	Unphasible	2 (1.0%)
	Total	206 (100.0%)
Gluteal	Phase 1	11 (18.0%)
	Phase 2	35 (57.4%)
	Phase 3	10 (16.4%)
	Phase 4	4 (6.6%)
	Unphasible	1 (1.6%)
	Total	61 (100.0%)
Heel	Phase 1	34 (72.3%)
	Phase 2	8 (17.0%)
	Phase 3	5 (10.6%)
	Total	47 (100.0%)
Trochanter	Phase 1	11 (35.5%)
	Phase 2	10 (32.3%)
	Phase 3	8 (25.8%)
	Phase 4	2 (6.5%)
	Total	31 (100.0%)
Leg	Phase 1	8 (29.6%)
	Phase 2	11 (40.7%)
	Phase 3	6 (22.2%)
	Phase 4	2 (7.4%)
	Total	27 (100.0%)
Ankle	Phase 1	6 (60.0%)
	Phase 2	1 (10.0%)
	Phase 3	2 (20.0%)
	Phase 4	1 (10.0%)
	Total	10 (100.0%)
Coccyx	Phase 1	2 (40.0%)
	Phase 2	2 (40.0%)
	Phase 4	1 (20.0%)
	Total	5 (100.0%)
Back	Phase 1	1 (20.0%)
	Phase 2	3 (60.0%)
	Phase 3	1 (20.0%)
	Total	5 (100.0%)
Arm	Phase 2	1 (100.0%)
	Total	1 (100.0%)
Hand	Phase 1	2 (66.7%)
	Phase 2	1 (33.3%)
	Total	3 (100.0%)
Toe	Phase 1	1 (100.0%)
	Total	1 (100.0%)
Total	Phase 1	139 (35.0%)
	Phase 2	130 (32.7%)
	Phase 3	102 (25.7%)
	Phase 4	23 (5.8%)
	Total	397 (100.0%)

A statistically significant difference was found when the PC unit lengths of stay in the patient groups with and without pressure ulcers or immobilisation were compared. The mean hospital stay for patients with pressure ulcers was 19.0 days (SD=10.2), and 16.7 days (SD=11.1) for without patients (p=0.009). The mean length of stay for immobilised patients was 19.3 days (SD=10.1), and 17.3 days (SD=10.9) for mobile patients (p=0.038).

In addition, 72% (n=403) of the patients were discharged from the PC unit and 28% (n=157) died during their stay in the unit. When prognosis was compared according to age group, a statistically significant difference was found between the groups (p<.001, Table 2). Death was observed in 13.7% of group-1 patients, 30.2% of group-2 patients, 32.7% of group-3 patients and 42.1% of group-4 patients during their PC unit stay. When the reason for the difference between the groups was examined, the mortality rate was significantly lower in group-1 than in the other groups (group 1 versus 2, p=0.001; group 1 versus 3, p<0.001; group 1 versus 4, p<0.001). Mortality rate and discharge were not statistically significantly different between the other three groups (group 2 versus 3, p=0.627; group 2 versus 4, p=0.171; group 3 versus 4, p=0.252).

DISCUSSION

In this study, access to PC services differed significantly according to patient characteristics. First, 75.2% the cohort (n=421) were geriatric patients aged 65 years and over. The geriatric patient group also needed more PC, and this patient group required further healthcare during PC. Access to PC services was significantly higher for patients living in large provinces and provincial centres. When hospitalisations in the PC unit were examined, 48.2% of the patients were admitted from the ICUs. The aforementioned shows that PC provides the integration of patients in ICUs into home care processes, and patient drainage from ICUs. Patient discharge from ICUs, which constitutes the majority of the health care cost of, is enabled

by PC services. Moreover, 24.5% of hospitalised patients were admitted directly to the PC unit. This group consisted of patients whose were care was too complicated for home services from their relatives or caregivers and were admitted to the PC unit for direct needs. This indicates that PC units are essential not only for patients, but also for families and caregivers. PC units assume this service when relatives are unable to provide home care. Pressure ulcers were present in 50% of the patients admitted to the PC unit, and 28% were immobilised. The presence of pressure ulcers and immobilisation of patients significantly prolonged PC hospitalisation time. Patients with pressure ulcers or those who are immobilised require more PC services because their care is more complex and has more requirements.

Rosenwax et al. determined that an increase in PC access rates was associated with living in big cities, having a partner, living in a private residence, and was higher for female patients (2). In our study, 85.7 % (n=480) of patients hospitalised in our PC unit resided in the province where the hospital is located. In addition, 83.2% (n=466) of the patients lived in the city centre and 53.2% were female, consistent with previously reported data. Our research indicates that this is primarily due to the inability of patients residing in districts or villages to reach PC centres, which are mainly located in provincial centres. Additionally, patients residing in districts or villages may not be aware of such services due to the low number of applications in larger central hospitals.

The PC team's main responsibilities are detailed symptom assessment and treatment suggestions for severely ill patients (7, 21). Geriatric comorbidities are special cases to be considered in the care of elderly patients with serious illnesses (22). Older patients with medical comorbidities are also predicted to be hospitalised more often (23). In our study, 90.9% of the patients (n=509) had one or more comorbidities. Thirty-eight of the 51 patients without comorbidities were aged < 65 years. The most common comorbidities were hypertension (52.5%), diabetes (29.6%), cancer (28.4%), cerebrovascular disease (23.4%), coronary artery disease (16.1%) and Alzheimer's disease (13.8%). Therefore, we speculated that geriatric patients with comorbidities are more likely to have significant care needs that are appropriate for PC services.

Regardless of age, diagnosis, or prognosis, PC attempts to provide a comprehensive therapy for patients with incurable diseases. PC also emphasises treatment of problems such as distress (physical, psychological, and spiritual), communication for shared decision making, and alleviating the strain on caregivers (24, 25). In patients with severe critical illness, intensive care (IC) attempts to sustain vital functions to reduce mortality and prevent morbidity (26, 27). Clinicians in ICUs lack knowledge and skills in many areas such as stopping/withdrawing interventions and providing end-of-life care in general (24, 28). These include using treatments to reduce pain, having effective conversations with family members, and knowing how to handle ethical dilemmas. Moreover, ICU admission is an unpleasant experience for patients at the end of life (29, 30). Expectedly, PC and IC can be opposite ends of care; PC is known as "conversing medicine" and IC is known as "technical medicine". However, there are similarities between the two types of treatments, as they can work together to help patients receiving IC. The already existing relationship between IC and PC will become stronger as ideologies blend, treatment cultures are normalised, and opportunities for collaboration present themselves (1). Due to this significant association, patients who need PC are generally followed up in ICUs because of their clinical processes and can be referred for PC, especially in the end-of-life period. In our study, we found that 48.2% of patients were admitted from ICUs, 12.0% from emergency services, and 24.5% were admitted directly to PC and hospitalised. These rates are consistent with previous data. We believe that PC will become increasingly important for patients being discharged from ICUs. In this regard, we support the idea that the number of

hospitals with PC units and beds should increase to accommodate for the aging population.

PC is a multidisciplinary team-based care approach that involves physicians, advanced practice clinicians, nurses, pharmacists, clergy's, and social workers and is distinct from other healthcare services (7). In our study; PC patients were consulted to many clinics after hospitalization and evaluated by several teams. The clinics that needed consultation the most were nutrition (92%), physical therapy (91.8%), infectious disease (45.9%), stoma wound care (32%), chronic wound care (27%), neurology (25.7%), and psychiatric (21.8%). Specialties including nutrition, physical therapy, pain management, infectious diseases, wound care, neurology and psychiatry are a priority in the PC process. Based on this, the PC process should involve multidisciplinary teamwork.

PC deals with patients of all ages with unique requirements related to death in a broad sense (31). By preventing and treating symptoms rather than illnesses in the care of patients until they pass away from a severe and life-threatening condition, PC seeks to enhance the quality of life and lessen suffering. Most patients receiving PC are > 65 years of age (6). Aging patients' requirements and characteristics shape PC needs (10). Therefore, we advocate the idea that it is crucial to group patients according to age in the PC process and provide services accordingly. In our study, we divided patients into four groups. We divided geriatric patients over 65 years of age into lower age groups because life expectancy and geriatric age group limits are the subject of discussion owing to newly developed medical treatments and technologies. In a study by Ersin et al. (32), it was found that 48.2% of patients receiving PC were female, 14.5% of all patients were between the ages of 60-69, 20.5% were between the ages of 70-79, and it was shown that 39.2% were between the ages of 80-89, while 25.8% were aged 90 years and over. In our study, 53.2% of all patients were female, and 75.2% were geriatric patients aged > 65 years. The geriatric age group had the highest number of patients hospitalised in the PC unit. We strongly argue that geriatric patients should be integrated into the PC process earlier in the disease course. There was a statistically significant difference between the age groups in terms of sex (p=0.026). While the male sex was higher in those under 65 years of age, the female sex was statistically higher in those over 90 years of age (p=0.004). We believe that the high number of female patients aged > 90 years is because female patients have a longer life expectancy than male patients. Pressure ulcers were less in group-1 (18-64 years) than in the other groups, indicating a significantly higher prevalence of pressure ulcers was in the geriatric age group. Immobilisation was statistically lower in group-1 than in group-3 and group-4. We think that in the patient group over 75 years of age, attention should be paid to immobilisation and its complications. In addition, in the PC unit, the mean hospital stay for pressure ulcers was 2.3 days (p=0.009), and immobilisation prolonged the mean hospital stay by two days (p=0.038). Studies have found that geriatric patients are more likely to apply to a hospice or skilled care facility and are less likely to be discharged home (10). In our study, the mean number of hospitalisation days in the PC unit was 17.84±10.71 days which was statistically significantly different by age between the groups (Fisher's ANOVA, p<.001). The mean PD hospitalisation times of patients in group-1 and group-2 were less than those in group-3 and group-4 patients. This result has not been examined in the literature before, and we suggest that patients over 75 years of age have more PC need and that early integration into PC should be provided to this patient group. We consider this group of patients as the cornerstone of PC services.

Limitations

Our study included a number of limitations. First of all, it was a single-center retrospective analysis with a limited patient population. Larger sample size investigations should back up our findings.

Our hospital is located in the city center and has the largest bed capacity of Ankara. For this reason, the accessibility of our hospital is high in the city center and patient demographic data includes the population of the region where our hospital is located. It may not be correct to generalize to all PC units and the population. Second, there were no data on how long it takes for patients to start PC from the time of diagnosis, and more detailed studies are needed for PC planning, especially for patients with chronic diseases including cancer. Single patients admitted to the PC unit and their first hospitalisations were evaluated; since the number of patients with more than one hospitalisation was not sufficient for evaluation, patients with more than one hospitalisation were not included in the evaluation. As this was a retrospective study, and the data were accessed through an electronic recording system, more extensive data (laboratory, treatment, etc.) from patients who received PC could not be obtained. In addition, the effect of care on the end-of-life indicators of patients could not be measured, and the rate of PC use could not be calculated.

CONCLUSION

PC service is most essential in the geriatric age group. Access to and integration into PC in this age group should be expanded. The connection between IC units and PC units continues to grow daily, and this connection becomes indispensable with the aging population. Identifying patients with critical PC needs is necessary for the effective use of resources and the future in line with the expected increase in care burden.

Even today, access to a PC is insufficient, and must be increased in particular for geriatric patients and patients living in rural areas. Chronic diseases should be confronted with the PC discipline as soon as possible as a standard approach, and even at the time of diagnosis if possible. The sooner a holistic approach is provided, the more opportunities may arise to capture foreseeable risks before maintain functional independence is impaired. Regardless of age, individuals with chronic diseases must have access to PC inpatient services at an appropriate time. To increase access, health professionals must have adequate government policies, programs, resources, and PC training.

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