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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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## From The Editor In Chief

The Universal Declaration of Human Rights, adopted by the United Nations General Assembly 75 years ago and considered to be a monumental document in the history of human rights, was written by representatives from all over the world with different legal, cultural and linguistic backgrounds.

This is the first document that expresses the basic human rights that should be universally protected.

This year, the theme of the International Day of the Elderly on October 1 has been announced as "Fulfilling the Promises of the Universal Declaration of Human Rights for Older Persons: Across Generations".

Undoubtedly, the elderly should live an equal and dignified life without discrimination. They should age with rights and dignity, their access to justice should be facilitated, and their exclusion from society should be prevented.

Secure, dignified and self-determined lives in old age should go beyond dreams, and they should be protected from social and economic inequalities.

In this context laws and policies are needed to recognize the elderly as equal members of society and strengthen accountability towards the elderly as rights holders.

Yeşim GÖKÇE KUTSAL

EDITORIAL ARTICLE

# THE DIGITAL DIVIDE IN THIS AGING WORLD

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Yeşim Gökçe KUTSAL

*"It is not age that is at fault but rather our attitudes toward it"*
Marcus Tullius Cicero

## INTRODUCTION

The United Nations General Assembly has designated the period between 2021 and 2030 as the "Decade of Healthy Ageing". The main topics in this perspective are: Examining the perspectives of societies on the concepts of old age and aging, taking measures against age discrimination, developing the ability of the elderly to participate and contribute to the society and communities in which they live. Dissemination of opportunities, and also dissemination of the concept of age-friendly environment. Providing integrated care and basic health services that respond to the needs of elderly people and the provision of access to long-term care for elderly individuals who need it (1).

The key words at this point are "Healthy Ageing" and telemedicine practice areas for the elderly are being used more and more often.

## TELEMEDICINE PRACTICE AREAS

Telemedicine practice areas are basicly;

1. Measurement and monitoring of life data-Weight, blood pressure, oxygen saturation, blood glucose, ECG, EEG, EMG, etc. The patient is monitored using devices that can be worn with accessories such as clothing or belts, watches, glasses.

2. Interactive systems-Computer-aided applications, sensors that warn against falls at home, phones that work with a sound sensor.

3. Devices that provide communication with medical personnel-Telephone, video conferencing, text messaging, etc (2).

**General Advantages:** The most effective telecare interventions are automatic monitoring of vital signs and telephone monitoring of nurses. It increases the chances of life in the home environment by providing ongoing support to patients and family members. Also

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reduces unnecessary hospitalizations and leads to a reduction in costs due to the absence of the need for transfers to the hospital. It can be useful not only for the elderly, but also for those who care for them. Health services are provided in a more affordable, accessible and convenient system (3).

**General Disadvantages:** The cost of using telemedicine systems can affect physicians. Incorporating telemedicine services into healthcare applications may require purchasing equipment. These practices are not completely suitable for the current health system or funding flow or reimbursement for now.Telemedicine applications may not always be covered by health insurance/ social security.

It may remain under cyber threats. In this context, data privacy and integrity should be taken into account in terms of security. Care should be taken when installing the software and operating system, and attention should be paid to using the necessary security programs.

As can be foreseen; telemedicine applications reduce face-to-face visits and interviews with physicians. It can cause important symptoms to disappear/be overlooked.

It is much more useful in the monitoring and treatment of ongoing, previously diagnosed conditions. If the patient is experiencing new symptoms, she/he should always see a physician. The telemedicine application is more useful in managing known problems rather than diagnosing new ones.

Also if the patient is experiencing unidentified symptoms, she/he should always plan to visit his physician in person. During a physical examination, these problems can be more easily evaluated and diagnosed. A patient experiencing an urgent health problem should always contact their doctor, relatives, or emergency response team (2).

Disadvantages for the elderly-Older people do not see the usage of technology as a very important and basic requirement. They do not feel strong/ adequate about the use of technology, and the elderly are relatively slow to adopt this new form of health. Seniors want to see telehealth as safe and reliable, and they need to believe that their personal health information will be kept confidential and secure. It is much more possible for them to try these applications with the recommendations of their physicians.

## FACTS TO CONSIDER

Some elderly people prefer traditional visits to their doctor. These visits are the best and most reliable method for the diagnosis and follow-up of the disease. Telemedicine applications can provide a support in terms of personal health protection. According to some critics; telemedicine can negatively affect the continuity of elderly health and care.

Continuity of care requires the establishment of a long-term partnership with the patient's primary physician so that the full health history of the elderly patient and the full spectrum of health problems are known. Since telehealth is a relatively new field, data on its effectiveness are still limited.

From the perspective of elderly health, telemedicine can be used as a complement to the usual routine health practices.

## TECHNOLOGY PLATFORMS

Existing technology platforms have become the only source of connection with the health system for many elderly people. All applications should be re-evaluated and restructured in terms of the use of older individuals. The unmet psychological, social or functional needs of older individuals can be monitored, problems can be detected without delay, possible complications can be prevented and hospital admissions can be controlled (2).



**Shift to Focus on Digital Tools:** During the pandemic process, many people have continued to socialize, work and access health services through digital tools. Except the seniors! In this context, a digital divide based on age has occurred (4).

**Age-Based Digital Divide:** This term identifies a long-standing disparity in access to new technology and the skills to take advantage of new technologies. The elderly have not been able to use most of the digital measures implemented to help people in the pandemic. They could not adapt to the changes in the world, and a "Digital Divide" formed.

Digital gap is a concept that "underlines the inequality" in access to new media and explains the differences between those who have access and those who do not, those who use information and internet technologies and those who do not.

It also refers to socioeconomic factors such as income, education, and differences between demographic factors such as gender, race, ethnicity, and age.

There are 3 digital divisions of different types:

1. "Global", which refers to the differences in internet access between industrialized and developing countries,

2. "Social", which refers to the gap between rich and poor people in terms of knowledge in each society,

3. "Democratic", which refers to the differences between those who use digital technology to participate in public life and to be included in the social sphere and those who do not (5).

**Barriers:** Barriers for older individuals who want to use digital technology can be summarised as;

1. Age-related disabilities; age-related issues such as visual impairment, problems with dexterity and mobility, difficulties in understanding and comprehension.

2. Technological features; usability problems associated with complex screens and small-point fonts, some technical concepts or system designs.

3. Attitude; the perception that digital technology is dangerous, very expensive, complex, confusing and very difficult to learn. Fear of choice, control, privacy issues, reduced social interaction.

4. Education and support issues; economic barriers to access to digital technology education and lack of educational opportunities.

5. Cost; inability to purchase, use or access technological products due to insufficient income (6, 7).

As age progresses, the ability to use new technology and familiarity decreases. From this point of view "Technical Obstacles and Psychological Barriers" are defined.

Technical Obstacles: The inability to use small phones comfortably, and distinguish images, the inability of elderly people with vision problems to read texts and the difficulty to use a keyboard due to physical disabilities.

Psychological Barriers: Seniors don't trust themselves and they think that new communication technologies is for young people and also they have prejudices against this technology. They have the idea that is injurious to the privacy of personal information of interception, and they have the fear of being ridiculed (8).

## DIGITAL NATIVE/ DIGITAL IMMIGRANT

As is known; the older age group was not born into a digital society or environment. For this reason, they are disadvantaged compared to the younger generation in terms of relations with digital devices and are defined as "Digital Immigrants" in the literature. According to digital natives, they are unfamiliar with the technical and social structure of computer and internet technologies. Although they do not know the digital language, they had to learn

and adopt it. Today, they have to be able to take advantage of the opportunities provided by visual and auditory media and not be subjected to virtual exclusion. It should also be taken into account that education serves as an important catalyst for such skills.

## DIGITAL EQUALITY FOR ALL AGE GROUPS

The main theme of the 1st October "International Day of Older Persons" 2021 has been announced by the United Nations as "Digital equality for all age groups". The Covid-19 pandemic, in which many services, especially health, are accessible via digital systems, has made the process even more complicated and difficult for the elderly who cannot access these services (9).

In this regard issues that need to be prioritized are:

1. Emphasizing issues such as availability, access, capacity development, infrastructure and renewal of digital opportunities in public and private areas,

2. Discrimination for the inclusion of the elderly in all these processes, etc. combating prejudices that cause situations,

3. Making full use of digital technologies in order to fully achieve the sustainable development goals,

4. Establishment of the necessary policies and legal frameworks to ensure the privacy and security of the elderly who use digital environments,

5. To support the continuation of the studies in the field of digitalization on the basis of human rights.

These applications offer a number of options for maintaining health and making care easier and more accessible. The older age group should be encouraged to use social media, communicate by phone and video links. In this way, social isolation will be prevented and cognitive stimulation will be provided (10).

**The Voice of Older Persons:** The issue of digitalization of services has been raised by the voice of older persons AGE platform Europe in Nov, 2022. In the declaration "Everyone has the right to access quality basic services, including water, sanitation, energy, transport, financial services and digital communications," was said (11).

Given the pace of changes in the digital technology sector, it is difficult to know what kind of tools will be used in the next 20 years! The educational background and financial situation of internet users and non-users also play a key role in unequal access to technologies. Older people are less capable due to the fact that their access to education and lifelong learning in digital environments is ignored. A question has been raised: Isn't this lack of interest also the result of an "Internalized Ageism"?

**Ageism / Age Discrimination:** Ageism is a key barrier affecting the design, adoption and use of digital technology. In the context of digital technology ageism takes place on 3 levels: 1-Macro (design and policy), 2-Meso (social and organizational environment), 3-Micro (individual). All three of these levels interact and influence each other (12).

### Last Words

A paradigm shift is needed. Questions that need to be answered are:1-What digital technologies do the elderly want and need? 2-What is the ability of the elderly to use digital technology? 3-Are the elderly included in the design process of digital technology and related policies? The elderly should definitely take place in all these processes (12).

The key message for socially healthy, successful, productive and active aging is: Don't plan "for" the elderly, plan "together" with the elderly. Because only they know what they're going through!

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INVITED REVIEW ARTICLE

# ARTIFICIAL INTELLIGENCE IN GERIATRICS

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## Abstract

The increasing elderly population globally presents challenges in geriatric healthcare, including better resources, unmet healthcare needs, and sustainability of health and social security systems. Artificial intelligence (AI) is being used to address these challenges, with studies focusing on socially assistive robots, humanoid robots, and robotic pets in elderly care.

This review aims to provide a comprehensive overview of the roles of artificial intelligence (AI) technologies in elderly healthcare by identifying the potential benefits and challenges in geriatric healthcare services. AI technologies can potentially improve care and health outcomes for older adults, promote healthy aging, and alleviate the burden on the healthcare system. Moreover, AI systems can assist healthcare providers in assessing potential drug interactions, identifying medication errors, and optimizing medication regimens to minimize side effects and enhance overall patient safety. In addition, AI-supported robots can provide caregivers personalized and efficient care while providing rehabilitation and mobility support for the elderly. Collaboration between healthcare professionals and artificial intelligence holds significant potential to facilitate more effective delivery of care, improve patient outcomes, and optimize health resources for the increasingly aging population.

***Keywords:*** Aging; Geriatrics; Artificial Intelligence; Healthcare.

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## INTRODUCTION

A significant demographic shift is occurring globally due to the increasing elderly population. The World Health Organization (WHO) predicts that by 2030, one in six people will be aged 60 or older (1). This change has brought forth many challenges and issues in geriatric healthcare. One of the most crucial problems is the need for more excellent healthcare resources to address the health issues faced by the elderly population (2). Additionally, the growing aging population brings about dynamic and uncertain demands that traditional elderly healthcare services find challenging to meet, leading to an inevitable increase in unmet healthcare needs and further burdening the existing healthcare system (3). Therefore, finding sustainable strategies, especially to promote care for the population aged 65 years and older, is crucial.

Another fundamental challenge in the health services of this age group is the sustainability of health and social security systems (4). As the elderly population grows, the burden of healthcare services and resources increases (2). Ensuring the continuity of healthcare services while bringing this burden to sustainable levels is paramount. It should be remembered that improvements in the effectiveness and quality of elderly care are needed during all these regulations.

Another challenge in geriatric science arises from the need for interdisciplinary care to address the complex healthcare needs of older adults (5). This involves collaboration among geriatricians, nurses, social workers, physiotherapists, and professionals from various medical disciplines. These professionals must collaborate to develop comprehensive care plans that consider the physical, mental, and social well-being of the elderly.

Innovative approaches and technological advancements are required to cope with these challenges and meet the aging population's needs. Artificial intelligence (AI) products have advanced rapidly, contributing to the fundamental reshaping of working environments and applications in various fields (6). This rapid transformation has significantly affected the healthcare sector, leading to the development of new software and wearable technology devices. In recent years, studies have been conducted on using specific types of AI technology, such as socially assistive robot technology, humanoid robots, and robotic pets in elderly care (7, 8). These studies provide in-depth insights into the potential benefits of AI technologies for serving elderly individuals. The overall application of AI technologies in healthcare for the elderly has rarely been evaluated using empirical evidence. Exploring the breadth and depth of the literature in this field can provide significant indicators of the future role of AI technologies in elderly healthcare and open up new possibilities for elderly healthcare services.

There is a need for research and advancement in geriatric clinical care, especially in the utilization of artificial intelligence systems. AI systems can assist in diagnosing, treating, and improving care for elderly individuals with chronic illnesses.

The aging global population, challenges in geriatric science and healthcare, need for more significant healthcare resources, improvements in care quality and effectiveness, interdisciplinary care, and advancements in technology and artificial intelligence systems pose substantial challenges (9). Therefore, an integrated, multidisciplinary approach is crucial for effectively addressing these challenges. One potential solution is the application of artificial intelligence in geriatrics.

Therefore, this review aims to provide a comprehensive overview of the roles of AI technologies used in elderly healthcare by identifying the potential benefits and challenges in elderly healthcare services.

## OVERVIEW OF ARTIFICIAL INTELLIGENCE (AI)

Artificial intelligence (AI) is a multidisciplinary approach in computer science and linguistics to create machines capable of performing tasks that typically require human intelligence. These tasks encompass learning, reasoning, problem-solving, natural language understanding, and communication. As a field within computer science, AI focuses on developing technologies that can mimic or replicate human intelligence (10).

AI systems are designed to learn from data, recognize patterns, make conscious decisions, and interact with humans and their environment. AI encompasses technologies such as machine learning, computer vision, natural language understanding, and natural language processing that allow machines to learn, adapt, reason, and interact with humans and their environments in a human-like manner (11, 12).

Innovative elderly healthcare products and services incorporating AI integration are considered a significant method for the future of geriatrics. In this field, artificial intelligence can be employed to create innovative elderly care products, services, or product-service systems (PSS), which are self-learning in addition to intelligent systems or platforms (13). Therefore, developments in AI applications are considered exciting for geriatric health services.

The utilization of artificial intelligence in geriatrics has the potential to enhance patient outcomes and revolutionize healthcare practices. Healthcare professionals in geriatrics can leverage AI technologies to improve diagnosis, treatment planning, and patient monitoring accuracy and efficiency. Additionally, AI can play a significant role in predictive analytics, identifying individuals at high risk for specific conditions and enabling proactive interventions. Moreover, AI can assist caregivers by developing assistive devices and identifying social isolation and loneliness in older adults (14). Integrating AI into geriatrics can improve the quality of care for older adults, promote healthy aging, and alleviate the burden on the healthcare system.

## ROLE OF ARTIFICIAL INTELLIGENCE IN GERIATRIC CARE

As healthcare advancements continue, the recognition of artificial intelligence's (AI) potential role in geriatrics is increasing. This technology can significantly enhance patient outcomes and revolutionize health practices within this domain. AI technologies can assist physicians in diagnosing and deciding on treatment options and predicting, classifying, and optimizing efficiency for risks associated with geriatric diseases for both healthcare professionals and patients alike. AI algorithms, through the analysis of extensive datasets, can identify patterns and trends that clinicians may not immediately discern. This information can empower healthcare providers to make more informed decisions and provide personalized care to elderly patients.

In addition, AI-assisted devices and wearable sensors can continuously monitor the health status of elderly individuals, alerting healthcare professionals in abnormal changes or emergencies. Furthermore, AI facilitates remote monitoring and telehealth services, allowing elderly patients to receive care comfortably in their homes (15). By automating routine tasks and administrative processes, AI can alleviate the burden on healthcare providers, enabling them to use their time and resources more effectively.

AI can contribute to the management of medications in geriatric care. Polypharmacy, or the use of multiple medications, is a common issue among elderly patients who manage various health conditions (16). AI technology can aid healthcare providers in assessing potential drug interactions, identifying medication errors, and optimizing



medication regimens to minimize side effects and enhance overall patient safety.

Moreover, AI can potentially improve mental healthcare in geriatric patients. Prevalent mental health issues in older adults are often inadequately diagnosed or overlooked. AI can address this gap by accurately predicting who may require mental health treatment before symptoms worsen. AI algorithms can identify early indicators of changes in mental health status through analysis of daily behaviors and patterns, allowing healthcare providers to intervene and provide support at an early stage (17).

AI could be particularly effective in the early recognition and diagnosis of neurocognitive disorders such as dementia. Traditional diagnostic methods often produce results that overlap with normal cognitive function in older adults, limiting their clinical utility. However, AI enables healthcare providers to analyze large amounts of data from various sources, including medical records, brain imaging scans, and cognitive assessments. AI algorithms can detect subtle patterns and abnormalities in these data, facilitating more accurate and early diagnosis of neurocognitive disorders (18). In addition to diagnosis, AI can effectively treat and manage geriatric mental health conditions. For example, AI-supported tools that analyze speech patterns and facial expressions can enhance psychotherapy by providing insights into the patient's emotional state, enabling therapists to tailor their sessions accordingly.

Furthermore, AI can support caregivers by providing better care for elderly patients. Loneliness and social isolation are common among older adults and can exacerbate mental health issues. AI can analyze loneliness symptoms during qualitative interviews and understand gender differences and nuances in loneliness reporting processes to provide customized interventions, support and mitigate the harmful effects of social isolation (19).

AI technologies can also assist caregivers by providing tools and devices for dressing, hand washing, and fall detection. By automating these tasks, AI can reduce the workload on caregivers and enhance the overall quality of care provided to elderly adults. Overall, AI has the potential to significantly improve geriatric care by aiding diagnosis, predicting treatment outcomes, and enhancing treatment approaches.

## HEALTH MONITORING AND WEARABLE DEVICES

Health services based on wearable devices designed for health monitoring have garnered significant interest in the management of both physiology and psychology (20). Integrating artificial intelligence (AI) and wearable devices enables objective remote monitoring of daily life activities and fall incidents, offering a potential solution for elderly care and promoting independent living. These devices can support caregivers in dressing, handwashing, and fall detection, thus facilitating prompt and early intervention (11). However, the current evidence regarding their effectiveness is limited because these devices lack high-quality methodologies (15). To overcome these limitations, it is crucial to address challenges such as device loss, discomfort in usage, and lower battery life.

In geriatric care, AI in health monitoring and wearable devices allows healthcare professionals to access real-time data on patients' physiological and behavioral patterns, enabling personalized and proactive care. Additionally, the early detection of signs of health deterioration in older adults can lead to timely intervention, potentially reducing hospitalizations and healthcare expenditures and decreasing the need for frequent hospital visits, thereby contributing to a more efficient healthcare system (21).

In conclusion, AI health-monitoring technologies have the potential to significantly improve care and health outcomes in older adults (22). However, ethically designing and implementing these

technologies is crucial, considering factors such as privacy, autonomy, consent, and the social and emotional well-being of elderly individuals.

## PREDICTIVE ANALYTICS FOR DISEASE PREVENTION

An area where predictive analyses using artificial intelligence (AI) can be particularly beneficial is the prevention of geriatric diseases. Healthcare providers can analyze extensive patient data using AI algorithms and machine-learning techniques. These datasets encompassed medical records, genetic profiles, lifestyle data, and biometric measurements. These datasets enable the prediction of the likelihood of developing specific diseases in geriatric populations through analyses. As a result, researchers can identify risk factors and early signs of disease, enabling timely intervention and implementation of preventive measures (23).

Researchers have made significant efforts to develop AI-based prognostic models for predicting the onset of geriatric mental health disorders. AI algorithms can analyze data from multiple sources, including medical records, patient-reported symptoms, and genetic information, to identify patterns and risk factors indicating the development of mental health disorders, such as depression or cognitive decline. Following these identifications, AI-based approaches can predict individual therapeutic interventions in geriatric mental health, shaping applied therapeutic interventions by analyzing patients' treatment responses. This personalized health approach will lead to more effective treatment and better outcomes for geriatric patients. One of the challenges in geriatric mental health is the shortage of specialists. AI can help bridge this gap by providing accessible and timely interventions. For instance, developing chatbots that offer personalized and timely interventions can enable individuals to access mental health support when needed (24).

Predictive analyses conducted using AI technologies will play a significant role in disease prevention and management in geriatric populations in the future. AI technologies can use predictive analyses to analyze various data sources, such as electronic health records, wearable devices, and free-text clinical notes. These sources provide valuable information about an individual's health status and play a crucial role in identifying models and risk factors for disease development. By utilizing predictive analytics, healthcare providers can proactively identify individuals at a high risk of disease development in geriatric populations and intervene early to prevent or manage diseases.

## ROBOTICS IN ELDERLY CARE

Artificial intelligence (AI) and robotics in elderly care are promising opportunities for enhancing the quality of life of elderly adults. It is a rapidly advancing technological sector. The development of this technology seems poised to give rise to intelligent elderly care solutions worldwide. These solutions encompass aids in daily living areas, such as AI-supported care robots and intelligent companion robots, aimed at assisting in service provision, security monitoring, human-computer interaction, and entertainment (25). The integration of AI systems into assistive living technologies has the potential to address the challenges faced by the elderly care industry, especially in addressing shortages on the service supply side.

By utilizing AI-supported robots, caregivers can effectively manage the growing elderly population while providing personalized and efficient care. Moreover, as the global population ages, there is an increasing need for innovative approaches to healthcare. AI and robotics can assist caregivers in tasks such as dressing, handwashing, and fall detection (11). These devices can provide physical support to individuals, reduce the risk of accidents, and enhance the overall safety and well-being of the elderly.



Furthermore, AI-supported robots have the potential to revolutionize rehabilitation and mobility support for the elderly. Exoskeletons and rehabilitation robots can aid in physical therapy exercises and increase mobility and strength in older individuals (26). By offering personalized assistance and feedback, these technologies can help older adults regain independence and improve their quality of life.

In general, AI and robotics have the potential to enhance the quality of care for elderly adults in various ways, ranging from physical assistance to social support and health monitoring (27). AI and robotics can realize this impact through diverse means, including physical assistance, social support, and health monitoring.

## ETHICAL CONSIDERATIONS OF AI IN GERIATRICS

AI should complement human interaction, providing healthcare professionals with valuable insights to personalize and adapt care plans for each patient.

Artificial intelligence (AI) and machine learning in healthcare, especially in geriatrics, have ethical concerns (28). These concerns include data privacy and security, algorithmic fairness and biases, obtaining informed consent from users, and potential interventions in the doctor-patient relationship.

Addressing ethical concerns is crucial before fully embracing AI in geriatric clinical practice. One of the primary ethical concerns is data privacy and security. To safeguard the privacy, integrity, and confidentiality of medical data, it is crucial to implement stringent security measures and access controls when AI systems collect and analyze patient-generated data. This becomes even more critical when cloud-based data storage and retrieval systems are used. Adherence to higher data privacy standards ensures patient information safety and protection.

Another ethical concern is algorithmic fairness and bias. Training AI systems on large datasets pose the risk of unfair or discriminatory outcomes due to biases in the data. Addressing this concern will require diverse datasets that account for the demographic characteristics and needs of the elderly. Regularly monitoring and evaluating AI algorithms for any bias or unfairness in decision-making processes is necessary. Additionally, regular audits and reviews of AI algorithms can help to identify and eliminate biases, ensuring fair and equal treatment for all patients (29)

Transparency and explainability of AI recommendations and decisions are vital ethical considerations. AI systems should provide clear and understandable suggestions and conclusions. This is particularly crucial in geriatric care, where elderly adults may have a limited understanding of AI technology and its outcomes (30).

Obtaining informed consent is an ethical responsibility and a legal requirement. This allows patients to make informed decisions about using their data and respecting their autonomy. It is essential to explain AI systems' goals, benefits, and potential risks and obtain detailed consent before using their data.

As the use of AI in geriatrics increases, there is concern about the possibility of interference in the doctor-patient relationship. Increased trust in AI systems may reduce direct interaction between patients and healthcare professionals, potentially diminishing the quality of the doctor-patient relationship. This could impact patient autonomy, confidence, and the outcomes of personalized care (31).

In addition to addressing ethical concerns regarding the use of AI in geriatrics, it is crucial to consider the potential benefits and risks associated with its implementation. The purpose of using AI systems in geriatric care is to provide effective and efficient healthcare services to the elderly (29, 30). AI can potentially enhance diagnostic accuracy, treatment outcomes, and overall patient care.

However, it is essential to carefully weigh potential risks, such as errors or incorrect recommendations by AI systems, which could have severe consequences for the health of elderly adults. Moreover, we should be mindful of the potential lack of human interaction and personalized care when using AI in geriatric care.

Integrating artificial intelligence into geriatric care has the potential to revolutionize elderly adult healthcare services, ensuring that ethical considerations take precedence in its implementation (30). Despite the significant potential of AI and robotics, addressing ethical concerns and maintaining a balance between human interaction and technology usage is critical. Elderly adults' emotional well-being, which is dependent on human touch and companionship, should never be replaced without careful consideration.

## COLLABORATION BETWEEN HEALTHCARE PROFESSIONALS AND ARTIFICIAL INTELLIGENCE

By harnessing the power of artificial intelligence, healthcare professionals can utilize the capabilities of machine learning to analyze large datasets and identify patterns in geriatric care. This deeper understanding can lead to more personalized and effective treatment plans for older adults by considering individual needs and preferences (32).

The integration of artificial intelligence into clinical settings requires collaboration between healthcare professionals and AI experts, inclusive working examples, and rigorous evaluation. This ensures that AI technologies developed for geriatric care can be used reliably, accurately, and safely in the elderly. Collaboration between healthcare professionals and artificial intelligence has the potential to facilitate more effective delivery of care, improve patient outcomes, and optimize health resources for the increasingly aging population. It is also essential to consider the social and environmental factors that can impact the well-being of older adults in designed AI technologies (33).

Geriatric collaboration between healthcare professionals and artificial intelligence holds significant potential to change mental health assessments, diagnoses, treatment decisions, and monitoring. This can assist clinicians in making more informed treatment decisions and customizing interventions to meet the specific needs of each individual (23).

Collaboration between healthcare professionals and artificial intelligence is critical for developing and implementing accurate and reliable AI technologies. This collaboration enables healthcare professionals to interpret the data generated by the developed AI algorithms and seamlessly integrate them into clinical practice. Moreover, it allows healthcare professionals to analyze AI-generated data to ensure alignment with best practices in geriatric care. Collaboration between healthcare professionals and artificial intelligence in geriatrics can generally transform mental health assessments, diagnoses, treatment decisions, and monitoring (23)

## CONCLUSION

In conclusion, integrating artificial intelligence in geriatrics has the potential to revolutionize health care for older adults. By harnessing the power of AI algorithms, healthcare professionals can gain valuable insights from the data generated and make more informed decisions regarding assessments, diagnoses, treatment plans, and monitoring. This collaborative approach between human expertise and artificial intelligence can ultimately lead to improved outcomes and enhanced quality of life for geriatric patients. However, it is essential to acknowledge the ethical considerations and potential limitations of AI in geriatric care, and further research and development are needed to ensure its responsible and effective use. Ethical



considerations include patient privacy, consent, and the potential for bias in AI algorithms. Additionally, the limitations of AI in geriatric care include the lack of emotional intelligence and the inability to provide personalized care that takes into account individual preferences and values. Therefore, it is crucial to continue researching and developing AI technologies in geriatric care to address these concerns and ensure that AI is used responsibly and effectively to improve older adults' lives.

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ORIGINAL ARTICLE

# INVESTIGATION OF THE FACTORS AFFECTING THE MORTALITY OF PATIENTS OVER 80 YEARS OF AGE DIAGNOSED WITH ACUTE PULMONARY THROMBOEMBOLISM

## Abstract

**Introduction:** To investigate the factors affecting the 30-day mortality of patients over 80 years of age diagnosed with acute pulmonary thromboembolism.

**Materials and method:** This descriptive, retrospective, and single-center study reviewed the medical records of patients over 80 years of age who were admitted to the hospital with a diagnosis of acute pulmonary thromboembolism between January 1, 2008, and April 30, 2023. The factors associated with mortality in patients who had died were examined. The recorded values of factors considered to be the determinants of 30-day mortality were also determined.

**Results:** This study included 113 patients, with a mean age of 83.7 ± 2.7 years, and comprised of 68 (60.2%) females. During the one-month follow-up period, 30 patients (26.5%) died of acute pulmonary thromboembolism or related complications. No statistically significant difference in age and gender was observed between the exitus and non-exitus groups ($p > 0.05$). Moreover, no significant difference was observed between the two groups in terms of hypertension and diabetes ($p > 0.05$), whereas other comorbidities were statistically significantly higher in the exitus group ($p < 0.05$). In the linear regression analysis, heart failure ($p < 0.001$), D-dimer level ($p = 0.019$), partial arterial oxygen pressure ($p < 0.001$), systolic pulmonary artery pressure ($p < 0.001$), and recent history of major surgery ($p = 0.021$) were found to be factors that affected the mortality.

**Conclusion:** The presence of comorbidities, poor hemodynamic findings, poor oxygenation, high pulmonary artery pressure, and high D-dimer levels may be mortality indicators in acute pulmonary thromboembolism patients over 80 years of age.

***Keywords:*** Pulmonary Embolism; Mortality; Ages.

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## INTRODUCTION

Sudden blood flow interruption in the pulmonary artery and/or its branches is defined as acute pulmonary embolism. The condition that causes a sudden blood flow interruption is usually a thrombus originating from the lower extremity veins (1). The estimated annual incidence is 60–120 per 100,000 (1). Acute pulmonary thromboembolism (APT) is a cardiovascular disease that requires urgent diagnosis and could have a high mortality rate. The clinical presentation of patients with APT may range from asymptomatic to cardiogenic shock and sudden cardiac death (1–2). The most common presenting complaints include dyspnea, chest pain, syncope, hemoptysis, and an impaired general condition. APT can be observed in any age group; however, studies have revealed that its incidence increases with advancing age (2). The number of patients with APT is expected to increase due to prolonged life expectancy in the society and higher elderly patient population every year. The mortality rate of APT is much higher among elderly patients than in young patients and this increase is directly correlated with age (3). However, elderly patients may have a large number of comorbidities that may mimic these symptoms, thereby making the diagnosis difficult (3–4). After the diagnosis is made, high-risk patients should be identified and appropriate treatment should be initiated to prevent mortality and morbidity (1–2). To date, numerous laboratory as well as clinical parameters and scoring systems have been identified to diagnose high-risk patients. However, almost all these studies have been conducted in the normal patient population. No studies have specifically investigated the relationship of these parameters and scoring systems with short- and long-term mortality in elderly patients over 80 years of age. Therefore, this study aimed to investigate the factors affecting the 30-day mortality in patients over 80 years of age diagnosed with APT.

## MATERIALS AND METHOD

The study was designed as a retrospective, single-center study. The records of patients with a diagnosis of APT and followed up at Baskent University Adana Dr. Turgut Noyan Training and Research Hospital between January 1, 2008, and April 30, 2023 were reviewed. Among these patients, patients aged ≥80 years and diagnosed with APT were included in the study.

Records of 1477 patients with an APT prediagnosis were accessed in the specified date range. The APT diagnosis could not be confirmed in 239 of these patients. Of the remaining 1238 patients, 1089 were excluded because they were under 80 years of age at the time of the event. The records of the remaining 149 patients were analyzed. However, 23, 11, and 2 patients were excluded because of incomplete file

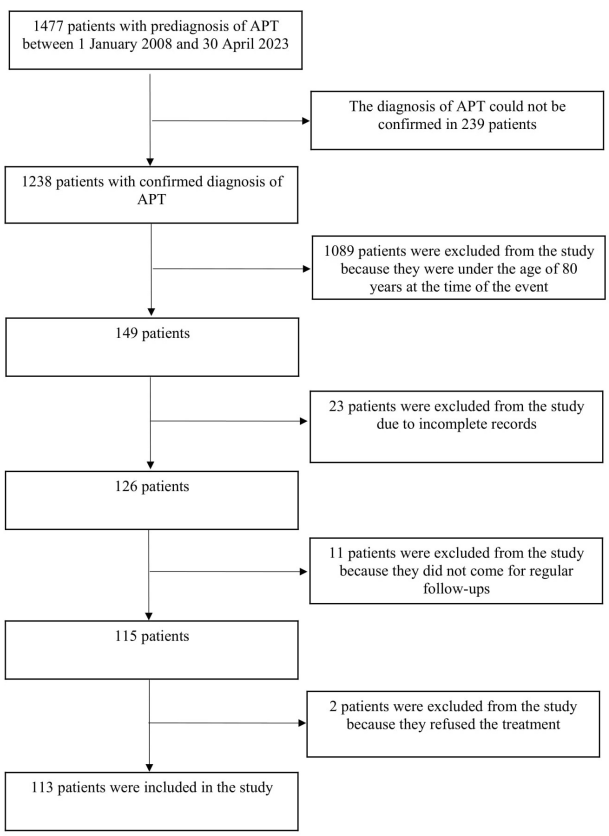



**Figure 1.** Study Design



records, because they did not attend regular follow-up visits, and because they refused treatment and left the hospital without permission, respectively. Finally, the remaining 113 patients were included in the study. The study design is depicted in Figure 1. Among all these patients, the APT diagnosis was confirmed only if thoracic computer tomography pulmonary angiography revealed filling defects in the main pulmonary artery and/or its branches.

The baseline demographic characteristics, vital signs, presenting complaints, comorbidity (diagnosed cancer, heart failure, chronic lung disease, chronic renal failure, or diabetes mellitus [DM]), the presence of deep vein thrombosis (DVT) by Doppler ultrasonography, and the recent history of major surgery were recorded. Partial arterial oxygen pressure ($PaO_2$) and oxygen saturation ($SaO_2$) in arterial blood gas, D-dimer, troponin positivity, hemoglobin, white blood cell (WBC) and platelet counts, and creatinine values were recorded. Echocardiographic evaluation was performed in accordance with the guidelines and ejection fraction (5). The estimated systolic pulmonary artery pressure (sPAP) and the presence or absence of right ventricular (RV) failure were evaluated based on the criteria in the guidelines. If RV failure was present, patients were classified into mild, moderate, and severe right heart failure based on the guidelines (5). An ejection fraction of <40% was considered to indicate heart failure. Further, chronic obstructive pulmonary disease (COPD), asthma, bronchiectasis, and pulmonary fibrosis diagnosed in accordance with the guidelines were considered to indicate a chronic lung disease.

Pulmonary embolism severity index (PESI) scores of all patients were calculated and recorded. In the PESI score, patient age and male gender were assigned 10 points; cancer was assigned 30 points; presence of heart failure or lung disease was assigned 10 points; pulse rate of ≥110 bpm was assigned 20 points; systolic blood pressure (SBP) of <100 mm Hg was assigned 30 points; respiratory rate of >30/min was assigned 20 points; body temperature of <36°C was assigned 20 points; mental status change was assigned 60 points; and SaO2 of <90% was assigned 20 points. All scores were summed. A total score of ≤65 was defined as class 1 (mild), 66–85 as class 2 (mild–moderate), 86–105 as class 3 (moderate), 106–125 as class 4 (moderate–heavy), and >125 as class 5 (severe) APT (1). At the 30-day follow-up, it was determined whether the patients were exitus due to APT or APT-related complications. It was also investigated whether laboratory and clinical values differed between the exitus as well as non-exitus patient groups, respectively. The recorded values that can be considered determinants of 30-day mortality were also evaluated.

### Study exclusion criteria

Patients whose APT diagnosis could not be confirmed by computed tomography, whose file records could not be accessed, who did not undergo echocardiographic evaluation in their hospitalization records, who left the hospital voluntarily after admission, who were noncompliant and refused treatment, who were under 80 years of age, who did not attend regular follow-up within 30 days post-discharge, who were noncompliant and refused treatment post-discharge, and who had missing records of the abovementioned clinical or laboratory values were not included in the study.

### Statistical analyses

SPSS computer program (Windows; SPSS, Inc., Chicago, Illinois, USA) was used to all statistical analyses. Kolmogorov-Smirnov test was used to evaluate whether the continuous variables conformed to the normal distribution. The values were expressed as mean ± standard deviation if they display the normal distribution, and as median and interquartile range [IQR] if they do not display the normal distribution. Proportion was used to

display categorical data. Chi-square test was used to compare categorical data. Unpaired t test was used to compare continuous variables that display the normal distribution while Mann–Whitney U-test was used to compare continuous variables that did not display the normal distribution. Standard multiple linear regression analysis was performed to identify independent predictors of mortality.

## RESULTS

The study included 113 patients. The mean age was 83.7±2.7 years and 68 (60.2%) of the patients were females. At the 1-month follow-up period, 30 patients (26.5%) died of APT or APT-related complications. The most common comorbidity was hypertension in 60.2% (68) of patients. No patients had end-stage renal failure or liver failure. The median PESI score was 104 (IQR = 29.5), and 23 (20.4%) of the patients were classified in the high-risk group based on the PESI score; no patient was classified in the low-risk group. Echocardiography revealed normal RV function in 61 (54%) patients, whereas 4 (3.5%) patients had severe RV failure. The most common presenting complaint was dyspnea in 94.6% (107) of patients. Further, two patients (1.7%) presented with cardiogenic shock. The baseline demographic, clinical, and laboratory data of the patients are summarized in Table 1. No statistically significant difference in age and gender was observed between the exitus and non-exitus groups (p>0.05). No significant difference in comorbidity such as hypertension and DM was observed between the two groups (p > 0.05), whereas other comorbidities were statistically significantly different between the two groups (p < 0.05). Similarly, in terms of laboratory values, the creatinine, hemoglobin, WBC, and platelet counts were similar between the two groups (p < 0.05). The comparison of laboratory, clinical, and demographic characteristics of patients with and without exitus is summarized in Table 2. According

**Table 1.** Baseline clinical, demographic, and laboratory values of the study population

| | |
|---|---|
| **Age, years** | 83.7 ± 2.7 |
| **Female gender n (%)** | 68 (60.2) |
| **SBP <100 mm Hg n (%)** | 10 (8.8) |
| **Heart rate ≥110 bpm n (%)** | 32 (28.3) |
| **Respiratory rate >30** | 10 (8.8) |
| **Active cancer n (%)** | 17 (15) |
| **Deep venous thrombosis n (%)** | 45 (39.8) |
| **Major surgery n (%)** | 14 (12.3) |
| **Hypertension n (%)** | 68 (60.2) |
| **Diabetes mellitus n (%)** | 23 (20.4) |
| **Coronary artery disease n (%)** | 35 (31) |
| **Smoking n (%)** | 12 (10.6) |
| **Heart failure n (%)** | 16 (14.2) |
| **Chronic lung disease n (%)** | 25 (22.1) |
| **Temperature <36°C n (%)** | 9 (7.9) |
| **Altered mental status n (%)** | 5 (4.4) |
| **Arterial oxygen saturation <90 n (%)** | 46 (40.7) |
| **Positive Troponin n (%)** | 92 (81.4) |
| **PESI points** | 104 (IQR = 29.5) |
| **PESI groups** | |
| Low risk n (%) | 0 (0) |
| Intermediate–low risk n (%) | 24 (21.2) |
| Intermediate risk n (%) | 36 (31.9) |
| Intermediate–high risk n (%) | 30 (26.5) |
| High risk n (%) | 23 (20.4) |
| **D-dimer (µg/L)** | 8170 (IQR = 4550) |
| **Ejection fraction (%)** | 53.1 ± 8.1 |
| **sPAP (mm Hg)** | 33 ± 11.7 |
| **Right ventricle functions** | |
| Normal n (%) | 61 (54) |
| Mild depressed n (%) | 33 (29.2) |
| Moderate depressed n (%) | 15 (13.3) |
| Severe depressed n (%) | 4 (3.5) |
| **Creatinine (mg/dL)** | 0.9 ± 0.5 |
| **Hemoglobin (gr/dL)** | 13.8 ± 1.5 |
| **WBC (/mm$^3$)** | 7525 ± 2293 |
| **Platelets (100/mm$^3$)** | 274 (IQR = 86) |
| **Dyspnea n (%)** | 107 (94.6) |
| **Chest pain n (%)** | 65 (57.5) |
| **Cough n (%)** | 47 (41.5) |
| **Syncope n (%)** | 19 (16.8) |
| **Fatigue n (%)** | 15 (13.2) |
| **Vomiting n (%)** | 11 (9.7) |
| **Cardiogenic shock n (%)** | 2 (1.7) |

IQR—interquartile range; PESI—pulmonary embolism severity index; SBP—systolic blood pressure; sPAP—systolic pulmonary artery pressure; WBC—white blood cell



**Table 2.** Comparison of baseline clinical, demographic, and laboratory values between the with exitus and without exitus groups

| | Exitus (n = 30) | No exitus (n = 83) | p |
|---|---|---|---|
| **Female gender n (%)** | 17 (56.7) | 51 (61.4) | 0.647 |
| **Age (years)** | 83.3 ± 2.2 | 83.9 ± 2.9 | 0.273 |
| **Active cancer n (%)** | 11 (36.7) | 6 (7.2) | <0.001 |
| **Heart failure n (%)** | 10 (33.3) | 6 (7.2) | <0.001 |
| **Chronic lung disease n (%)** | 13 (43.3) | 12 (14.5) | 0.001 |
| **Hypertension n (%)** | 17 (56.7) | 51 (61.4) | 0.647 |
| **Diabetes mellitus n (%)** | 5 (16.7) | 18 (21.7) | 0.558 |
| **Smoking n (%)** | 7 (23.3) | 5 (6) | 0.008 |
| **Coronary artery disease n (%)** | 15 (50) | 20 (24.1) | 0.009 |
| **Deep venous thrombosis n (%)** | 18 (60) | 27 (32.5) | 0.008 |
| **Major surgery n (%)** | 8 (26.7) | 6 (7.2) | 0.006 |
| **Saturation (%)** | 83.1 ± 5.3 | 91.9 ± 3 | <0.001 |
| **PESI point** | 140.5 (IQR = 75.5) | 93 (IQR = 25) | <0.001 |
| **D-dimer (µg/L)** | 10040 (IQR = 3675) | 7890 (IQR = 5450) | 0.001 |
| **Systolic blood pressure (mm Hg)** | 108.1 ± 17.5 | 134.8 ± 16.8 | <0.001 |
| **Oxygen (mm Hg)** | 71.8 ± 4.7 | 82.6 ± 8.1 | <0.001 |
| **sPAP (mm Hg)** | 46 ± 13.8 | 28.3 ± 6 | <0.001 |
| **Creatinine (mg/dL)** | 1.1 ± 0.7 | 0.9 ± 0.4 | 0.129 |
| **Hemoglobin (gr/dL)** | 14.2 ± 1.2 | 13.7 ± 1.5 | 0.1 |
| **WBC (/mm$^3$)** | 7232 ± 2250 | 7631 ± 2313 | 0.417 |
| **Platelets (100/mm$^3$)** | 272 (IQR = 70.7) | 274 (IQR = 88) | 0.876 |

IQR—interquartile range; PESI—pulmonary embolism severity index; sPAP—systolic pulmonary artery pressure; WBC—white blood cell

**Table 3.** Multiple linear regression analysis of mortality with clinical variables

| | Beta coefficient | p | 95% confidence interval | |
|---|---|---|---|---|
| | | | Lower | Upper |
| **Age** | -0.058 | 0.364 | -0.029 | 0.011 |
| **Gender** | 0.048 | 0.458 | -0.071 | 0.157 |
| **Active cancer** | 0.137 | 0.155 | -0.065 | 0.403 |
| **Heart failure** | 0.231 | <0.001 | 0.134 | 0.451 |
| **Chronic lung disease** | -0.002 | 0.980 | -0.149 | 0.146 |
| **PESI score** | -0.127 | 0.370 | -0.004 | 0.002 |
| **D-dimer** | 0.201 | 0.019 | 0.000 | 0.000 |
| **Arterial oxygen pressure** | -0.305 | <0.001 | -0.024 | -0.007 |
| **sPAP** | 0.584 | <0.001 | 0.014 | 0.030 |
| **Positive troponin** | 0.121 | 0.075 | -0.014 | 0.290 |
| **Diabetes mellitus** | 0.036 | 0.569 | -0.098 | 0.178 |
| **Hypertension** | -0.062 | 0.328 | -0.169 | 0.057 |
| **Smoking** | -0.78 | 0.304 | -0.327 | 0.103 |
| **Coronary artery disease** | 0.086 | 0.230 | -0.053 | 0.218 |
| **Deep venous thrombosis** | -0.28 | 0.680 | -0.149 | 0.098 |
| **Major surgery** | 0.198 | 0.021 | 0.042 | 0.489 |

PESI—pulmonary embolism severity index; sPAP—systolic pulmonary artery pressure

to the linear regression analysis, heart failure ($p < 0.001$), D-dimer level ($p = 0.019$), PaO2 ($p < 0.001$), sPAP value ($p < 0.001$), and a recent history of major surgery ($p = 0.021$) were found to be factors that influenced mortality. All regression analysis results are summarized in Table 3.

## DISCUSSION

The results of our study revealed that the 30-day mortality rate of patients over 80 years of age with an APT is 26.5%. The comorbidity rate was significantly higher in the exitus group. The presence of comorbidity, high PESI score at presentation, poor hemodynamic findings, poor oxygenation, high sPAP, and high D-dimer levels may be indicators of mortality in patients over 80 years of age.

The incidence and prevalence of APT and DVT were found to increase with age. The APT mortality was rather variable depending on the patient group investigated and ranged between 1% and 60% (6–7). A few studies that aimed to determine which patients are at higher risk have been conducted mostly in the young patient population. In a retrospective study by El Ghoul et al. with 100 patients, hypotension, the presence of cancer, RV dysfunction on echocardiography, and severe hypoxemia were found as predictors of in-hospital mortality (8). They obtained similar results to those of our study. Another study conducted by Friz et al. revealed that patients over 80 years of age had a 30-day mortality of 18.9% and a 90-day mortality of 29.7%. According to the results of the same study, the negative predictive value of the PESI score was found to be 94.1% as an indicator of the 30-day mortality and 88.2% as an indicator of the 90-day mortality. In conclusion, that study concluded that better risk scoring systems are required for the elderly patient group (9). In our study, the mortality rate was found to be 26.5%. This rate is compatible with the findings in related literature. In another study conducted by Gupta et al., with 183 patients (mean age 63 years in this study), the presence of cancer, age, WBC count, the presence of DM, the presence of liver disease, female gender, and the presence of massive APT at baseline were found to be independent predictors of long-term mortality (mean, 4.1 years) (10). Another study conducted by Keller et al., with 129 patients, demonstrated age as an independent risk factor for mortality and mortality that increases with increasing age (11). In all mortality studies, identifying high-risk patients is extremely important in terms of preventing mortality.

Further, poor hemodynamic findings, impaired RV function, and elevated sPAP are expected to be associated with mortality. Ammari et al., with 32 patients with submassive APT, revealed that high brain natriuretic peptide (BNP) level, impaired function, and high RV pulmonary artery pressure may be indicators of mortality (12). Moreover, acute RV dilatation and RV failure that develop in acute APT decrease the cardiac output in the left ventricle. The resulting hypotension causes organ hypoperfusion and increases mortality (13). The effects of these hemodynamic mechanisms in the young patient population are well known. Considering that the elderly patient population has lower cardiac reserve, it is likely to be affected more by this hemodynamic disturbance.

D-dimer is a fibrin formation and degradation biomarker. A high D-dimer level is associated with recurrent DVT, APT risk, and mortality (14). Since an increased D-dimer level indicates high thrombus burden, it is expected to be associated with mortality. Our study is consistent with the literature in this respect.

The effects of DM on the mortality rate of APT is unclear. In a large-scale study by Schmitt et al. (1,174,196 pulmonary embolism patients, 53.8% aged ≥70 years, 53.5% women, and among these, 219,550 [18.7%] patients with DM were included), mortality was reportedly higher in patients with DM compared to those without DM in patients with APT.

In this study, DM was reported as an independent risk factor for in-hospital mortality (15). In another large-scale registry study, DM was not found to be an independent risk factor for mortality (16). It must be noted that these studies were conducted in a normal patient population.

### Study Limitations

One of the greatest limitations of this study is that it was conducted retrospectively with file records. Further, the small number of patients and lack of a standardized treatment strategy in patients included in the study is additional important limitations. In future research, the findings need to be supported by multicenter studies with a large number of patients and standardized treatment protocols.

## CONCLUSION

Patients aged >80 years with APT had a high mortality rate. A high number of comorbidities, poor hemodynamic findings at presentation, RV failure, high sPAP, poor oxygenation, and high D-dimer levels may be associated with mortality.

**Conflict of Interest:** None declared

**Ethical Approval:** All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration. This study was approved by Baskent University Institutional Review Board (Project no: KA 23/294) and supported by Baskent University Research Fund.

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ORIGINAL ARTICLE

# EPIDEMIOLOGY, DEMOGRAPHIC CHARACTERISTICS AND FINAL VISUAL CONSEQUENCES OF OPEN GLOBE INJURIES IN GERIATRIC PATIENTS

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## Abstract

**Introduction:** Eye trauma is an important preventable cause of blindness. Decreased visual acuity of geriatric patients due to diseases such as cataracts, diabetic retinopathy, glaucoma, and retinal vascular diseases also cause eye trauma.

**Materials and Method:** In this study, the files of 29 patients aged > 65 years who were treated for open-globe injuries at the eye diseases outpatient clinic of Akdeniz University (Antalya, Turkey) between January 2013 and November 2022 were retrospectively analyzed. Patient age, sex, location of injury, characteristics of injury, other accompanying findings, hospital admission time after injury (less than 12 h or > 12 h), and final visual acuity of the traumatized eye at admission and after treatment were recorded in addition to the visual acuity of the healthy eye at admission.

**Results:** The most common causes of injuries were tree branches (48.3%) and hard objects (31.0%). A total of 51.7% of eye injuries occurred at home and 48.3% occurred outdoors. Blunt and penetrating incisive injuries were observed in 65.5% and 34.5% of the patients, respectively. However, the most common injuries were penetration (75.9%) and perforations (20.7%). Injuries were mostly observed in zones I (58.6%) and III (31.0%). Visual acuity in the affected eye was less than 20/200 in 79.3% of the cases.

**Conclusion:** Precautions should be exercised to prevent eye trauma that reduces vision or results in legal blindness, especially in individuals over the age of 65 years. Furthermore, post-traumatic rehabilitation is very important.

***Keywords:*** Geriatrics; Trauma; Blindness.

## INTRODUCTION

Eye trauma is a major and preventable cause of blindness worldwide. Mechanical trauma of the eye is divided into open- and closed-globe injuries by the Birmingham Eye Trauma Terminology (BETT) and the Ocular Trauma Classification Group (1). An open-globe injury can be defined as a full-thickness injury to the sclera, cornea, or both. Several studies on the epidemiology and prognosis of the aforementioned two types of injuries are present (2–4). The epidemiology and prognosis of eye trauma may differ in geriatric populations aged >65 years (5). Decreased visual acuity of geriatric patients due to diseases such as cataracts, age-related macular degeneration, diabetic retinopathy, glaucoma, and retinal vascular diseases also contribute to eye trauma. Several studies have demonstrated that open- globe injuries are associated with more hospitalizations and worse visual prognoses than closed-eye injuries in geriatric patients (5–6).

The aging process naturally leads to restrictions in daily activities, and the decrease in vision with age also contributes to these limitations. A decrease in vision with age may be a cause of trauma, however, vision loss due to trauma may make daily life even more difficult for older patients with limited daily activities, which may lead to a vicious circle. According to a United Nations report, the geriatric population will constitute 21% of the world's population by 2050 (7). To improve the quality of life of geriatric patients and their participation in daily life, maintaining a certain level of vision, and preventing possible trauma, and related vision loss is important.

Studies on eye trauma in the geriatric population compared to the normal population are limited (5,6,8–10). In particular, if considered a public health problem, geriatric patients with ocular trauma should be further examined.

In this study, we retrospectively analyzed the causes of open globe injuries, the characteristics of injuries, and their effects on vision in geriatric patients and discussed possible measures to prevent the traumas.

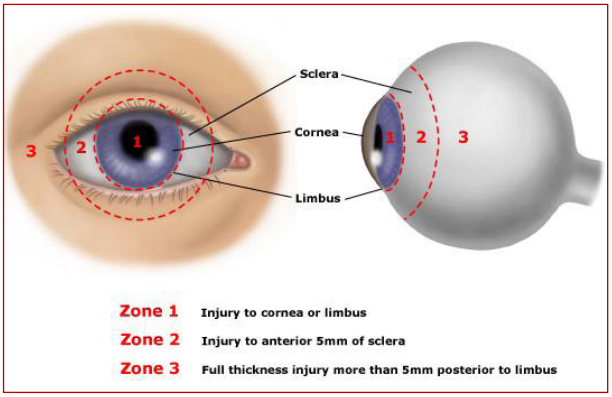



**Figure 1.** Open globe injury zones

## MATERIALS AND METHOD

In this study, the files of patients over the age of 65 years with open globe injury who visited the eye disease outpatient clinic of Akdeniz University (Antalya, Turkey) between January 2013 and November 2022 were retrospectively analyzed. Patient age, sex, location of injury, characteristics of injury, other accompanying findings, hospital admission time after injury (less than 12 h or >12 h), and final visual acuity of the traumatized eye at admission and after treatment were recorded in addition to the visual acuity of the healthy eye at admission. We recorded whether the injuries were penetrating, punctured, or ruptured according to the BETT system (1).

Ocular trauma scores were calculated and classified for each patient. The ocular trauma score has a very important prognostic value in predicting the final visual outcome in patients presenting with open globe injury. The ocular trauma score was divided into five groups of 100 points as follows; grade 1:0–44 points, grade 2:45–65 points, grade 3:66– 80 points, grade 4:81–91 points, and grade



5:92–100 points. The higher the ocular trauma score, the better the final visual acuity.

Primary repair was performed in patients in whom anatomical integrity was achieved with primary suturing. Patients with traumatic cataracts underwent intraocular lens implantation with scleral fixation along with traumatic cataract extraction surgery. Patients with traumatic retinal pathology who had a surgical indication underwent pars plana vitrectomy. Best-corrected visual acuity 1 year after surgery was considered as final visual acuity.

We grouped our patients with a final visual acuity greater than 20/200 (the legal limit of blindness) as good or worse and examined the factors affecting this outcome (11).

### Ethics Approval

This retrospective study was conducted by the ethical standards of the Declaration of Helsinki, with the approval of the Clinical Research Ethics Committee of Akdeniz University Hospital Medical Faculty.

## RESULTS

The mean age of 29 patients included in the study was 68.8 ± 5.1 years (65–85 years). The male-to-female ratio was 2.2/1 and the injured eye was the left eye in 58.6% of cases. The most common causes of injury were tree branches (48.3%) and hard objects (31.0%). Moreover, a total of 51.7% of eye injuries occurred at home and 48.3% occurred outdoors. Blunt and penetrating incisive injuries were observed in 65.5% and 34.5% of the patients, respectively. However, the most common injuries were penetration (75.9%) and perforations (20.7%). Injuries were mostly observed in zones I (58.6%) and III (31.0%). The incision length was > 5 mm in 69% of the cases. Moreover, visual acuity in the affected eye was less than 20/200 in 79.3% of the cases, whereas visual acuity was >20/200 in 86.2% of the cases in the fellow eye. The mean ocular trauma score was

**Table 1.** Characteristics of patients and injuries

| FEATURE | FREQUENCY N (%) |
|---|---|
| Age† | 68,8 ± 5,1 (65-85) |
| Sex | |
| Female | 9 (31,0) |
| Male | 20 (69,0) |
| Side | |
| Right | 12 (41,4) |
| Left | 17 (58,6) |
| Injury-tool | |
| Wood-tree branch | 14 (48,3) |
| Hard object | 9 (31,0) |
| Other | 6 (20,7) |
| Injury place | |
| House | 15 (51,7) |
| Outdoor | 14 (48,3) |
| Injury mechanism | |
| Blunt | 19 (65,5) |
| Sharp | 10 (34,5) |
| Injury type | |
| Penetrating | 22 (75,9) |
| Perforating | 6 (20,7) |
| Rupture | 1 (3,4) |
| Injury zone | |
| Zone I | 17 (58,6) |
| Zone II | 3 (10,3) |
| Zone III | 9 (31,0) |
| Size of injury | |
| ≤5 mm | 9 (31,0) |
| >5mm | 20 (69,0) |
| Traumatic eye VA | |
| ≤20/200 | 23 (79,3) |
| >20/200 | 6 (20,7) |
| Traumatic eye VA (logmar) † | 2,36 ± 0,92 |
| Fellow eye VA | |
| ≤20/200 | 4 (13,8) |
| >20/200 | 25 (86,2) |
| Follow-up time (month) †† | 16 (1-84) |
| Traumatic eye final VA | |
| ≤20/200 | 18 (62,1) |
| >20/200 | 11 (37,9) |
| Traumatic eye final VA (logmar) † | 2,03 ± 1,11 |
| Ocular Trauma Score† | 62,9 ± 19,0 |
| Grade I | 3 (10,3) |
| Grade II | 12 (41,4) |
| Grade III | 8 (27,6) |
| Grade IV | 6 (20,7) |
| Grade V | 0 |
| Evisceration | 2 (6,9) |
| First application time | |
| <12 hours | 21 (72,4) |
| >12 hours | 8 (27,6) |

†Average±Standart Deviation, ††: Median (min-max),
N: Number, VA: Visual Acuity

62.9 ± 19.0 with evisceration required in two cases. In the first 12 hours after injury, 72.4% of the patients presented to the hospital emergency department (Table 1).

The most common findings accompanying ocular trauma were uveal tissue prolapse (58.6%), conjunctival incision (48.3%), hyphema (24.1%), and traumatic cataracts (17.2%) (Table 2)

**Table 2.** Findings accompanying ocular trauma

| Finding | Frequency N (%) |
|---|---|
| **Uveal tissue prolapse** | 17 (58,6) |
| **Conjunctival laceration** | 14 (48,3) |
| **Hyphema** | 7 (24,1) |
| **Traumatic cataract** | 5 (17,2) |
| **Fibrin membrane** | 4 (13,8) |
| **Hemorrhagic coagulum** | 4 (13,8) |
| **Lens dislocation** | 3 (10,3) |
| **Vitreous at the wound** | 3 (10,3) |
| **Lid laceration** | 2 (6,9) |

N: Number

The demographic and clinical features of patients with a final visual acuity <20/200 and above were compared. Patients with a final visual acuity of <20/200 had a high initial visual acuity (p= 0.001) and a low ocular trauma score (p <0.001). However, no statistically significant differences were observed between the ages of the patients (Table 3).

The ocular trauma score was grade I in 16.7% of the cases, with a final visual acuity below 20/200; grade II in 66.7%; grade III in 11.1%; and grade IV in 5.6%. Of those with visual acuity greater than 20/200, 54.5% were grade III, and 45.5% were grade IV (p <0.001). The initial visual acuity value was low in patients with a final visual acuity of <20/200 (p= 0.001). However, no differences were observed between the final visual acuity groups in terms of age, sex, affected side, injury type, localization, injury size, or time of presentation (Table 4).

Of the 29 patients, 19 had diabetes, 13 had hypertension, and 11 had hyperlipidemia. Two of the patients had diabetic retinopathy, which caused a decrease in visual acuity in the non-traumatic eye. Among our patients, there is no known orthopedic, rheumatological or neurological disease that would reduce mobility.

The most common anterior segment findings in the unaffected eye were cataracts (79.3%) and pseudophakia (3.4%), while the most common fundus findings were diabetic retinopathy (6.9%), glaucoma-related optic atrophy (6.9%), and age-related macular degeneration (6.9%) (Table 5).

### Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows version 25. Categorical data are expressed as numbers and percentages, normally distributed continuous variables as mean and standard deviation and abnormally distributed median and minimum- maximum values. After distribution tests, normally distributed continuous

**Table 3.** Analysis of patient characteristics according to final visual acuity (quantitative variables)

| Feature | Final VA ≤20/200 (N=18) | | Final VA >20/200 (N=11) | | p value |
|---|---|---|---|---|---|
| | Mean ± SD | Min-max | Mean ± SD | Min-max | |
| **Age** | 69,1 ± 4,4 | 65-81 | 68,2 ± 6,2 | 65-85 | 0,657† |
| **Inıtial VA (logmar)** | 2,90 ± 0,27 | 2,60-3,20 | 1,49 ± 0,96 | 0,40-2,60 | 0,001† |
| **Ocular trauma score** | 51,9 ± 14,4 | 26-90 | 80,9 ± 9,4 | 70-90 | <0,001† |

†Student t test, VA: Visual Acuity, N: Number, SD: Standart Deviation



**Table 4.** Analysis of patient characteristics by final visual acuity (categorical variables)

| Feature | Final VA ≤20/200 (N=18) | Final VA >20/200 (N=11) | p value |
|---|---|---|---|
| | N (%) | N (%) | |
| **Age groups** | | | 0,671† |
| **65-69** | 12 (66,7) | 9 (81,8) | |
| **70-85** | 6 (33,3) | 2 (18,2) | |
| **Sex** | | | 0,534† |
| **Female** | 6 (33,3) | 3 (27,3) | |
| **Male** | 12 (66,7) | 8 (72,7) | |
| **Side** | | | 0,514† |
| **Right** | 7 (38,9) | 5 (45,5) | |
| **Left** | 11 (61,1) | 6 (54,5) | |
| **Type of injury** | | | 0,060†† |
| **Penetrating** | 11 (61,1) | 11 (100) | |
| **Ruptur** | 6 (33,3) | 0 | |
| **Perforating** | 1 (5,6) | 0 | |
| **Location** | | | 0,111†† |
| **Zone I** | 8 (44,4) | 9 (81,8) | |
| **Zone II** | 2 (11,1) | 1 (9,1) | |
| **Zone III** | 8 (44,4) | 1 (9,1) | |
| **Size of injury** | | | 0,237† |
| **≤5 mm** | 4 (22,2) | 5 (45,5) | |
| **>5 mm** | 14 (77,8) | 6 (54,5) | |
| **Ocular trauma score** | | | <0,001†† |
| **Grade I** | 3 (16,7) | 0 | |
| **Grade II** | 12 (66,7) | 0 | |
| **Grade III** | 2 (11,1) | 6 (54,5) | |
| **Grade IV** | 1 (5,6) | 5 (45,5) | |
| **Grade V** | 0 | 0 | |
| **Initial VA** | | | 0,001† |
| **≤20/200** | 18 (100) | 5 (45,5) | |
| **>20/200** | 0 | 6 (54,5) | |
| **Time to presentation** | | | 0,110† |
| **<12 hours** | 11 (61,1) | 10 (90,9) | |
| **>12 hours** | 7 (38,9) | 1 (9,1) | |

†: Fisher's Exact test, ††: Chi-square test, VA: Visual Acuity, N: Number

variables were analyzed between groups using Student's t-test, and abnormally distributed variables were analyzed using the Mann-Whitney U test. Categorical variables were compared using Fisher's exact and chi- square tests. Statistical significance was set at $p < 0.05$.

**Tablo 5.** Examination findings of the healthy eye

| Feature | Frequency N (%) |
|---|---|
| **Anterior segment** | |
| **Normal** | 5 (17,2) |
| **Cataract** | 23 (79,3) |
| **Pseudophakia** | 1 (3,4) |
| **Fundus** | |
| **Normal** | 23 (79,3) |
| **Diabetic Retinopathy** | 2 (6,9) |

N: Number

## DISCUSSION

Ocular trauma, particularly open-eye injury, is an important but largely preventable cause of unilateral blindness. According to the World Health Organization, an estimated 285 million people of all ages have visual impairment or blindness globally, and approximately 60 percent of these people are aged 50 years and above (12,13). In 2020, the leading cause of blindness in people aged 50 years and above was cataracts, followed by glaucoma, incompletely corrected refractive error, age-related macular degeneration, and diabetic retinopathy. The leading causes of visual impairment are incomplete correction of refractive errors and cataracts (13). Ocular trauma is the leading cause of monocular blindness worldwide. More than 55 million cases are reported each year, of which 1.6 million result in vision loss. Approximately 200,000 cases of ocular trauma involve open-globe injuries (14).

Age-related vision changes in geriatric patients are potential risk factors for serious eye injuries, and open-eye injuries are an important cause of blindness in the older population (15). In a study that analyzed 11,320 traumatized eyes, 51 percent of patients over the age of 60 years had a final visual acuity below 20/200 (legal level of blindness), and many of the traumas were preventable (16). In our study, the final visual acuity was 20/200 in 18 (62%) of the 29 patients who presented with open-globe injuries.

For all ages, men are more likely to be affected by eye trauma than women, which can be explained by the fact that men engage in more active work, sports, and dangerous activities. However, at 60 years and above, the ratio of affected women to men was almost equal. Studies have reported that women are more affected than men. This is because both sexes engage in similar activities after the age of 60 years (such as agricultural activities in the farm or garden) and are affected by factors such as retirement (5,17–19). In our study, the mean age was 68.8 ± 5.1 years and the men/women ratio was 2.2/1.

The main causes of ocular trauma in geriatric patients are falls, accidents in agricultural activities, and traffic accidents. Injuries mostly occur at home, on farms, and in gardens. (5,17,20,21). Some comorbidities (neurological, orthopedic, and psychiatric) in the geriatric population play an important role in the higher incidence of falls compared to young people.

When all age groups were included, open-eye injuries were mostly penetrating injuries. However, rupture-type injuries increased significantly in patients aged 60 years (9,11,20,22).

In our study, injuries were caused by accidents at home in 51.7% of patients. Penetrating injuries occurred in 22 of 29 patients. 24% of the patients stated that they were exposed to trauma because they were careless while doing housework, and 22% suffered trauma due to a fall caused by low vision. The majority of patients with outdoor trauma were injured by wood branch while cutting wood to light a stove or working in the garden.

To predict the anatomical and functional state of the affected eye in patients presenting with open-globe injury is important. Furthermore, to be able to talk to the patient in the above-mentioned direction, especially geriatric patients and those with low vision in the nonaffected eye is also significant. Certain parameters are used to predict prognosis. Factors such as wound location, wound size, affected area, ocular trauma score, and visual acuity at first admission can provide important clues for the prognosis and final visual outcome. Several studies have investigated these parameters.

Wounds larger than 5 mm, wounds involving zones II and III (sclera- retinal involvement, accompanying retinal detachment, optic nerve damage, and vitreous hemorrhage), low ocular trauma score, and low visual acuity at the first examination (hand motion, light perception, and no light perception) are associated with poor prognosis (23).

In this study, 23 of the 29 patients had a visual acuity of 20/200 or less at the time of first admission. Eighteen patients had a final visual acuity of 20/200 or less, and 11 had a final visual acuity greater than 20/200. The mean ocular trauma score of patients with a final visual acuity of 20/200 or less was lower than that of the other groups. Low visual acuity and ocular trauma scores were also important indicators for predicting prognosis, especially at first admission.

When previous studies are scanned, the average time for first application is between 0-6 hours. In this study 21(%72.4) of 29 patients were admitted to the emergency department or our ophthalmology clinic on the day of the trauma(between 0-12 hours after trauma). 7 patients were admitted between 12-24 hours and one of our patients was brought to us 28 hours after the trauma by a estranged relative who noticed that he was traumatized. Patients living alone and away from their families presented to the emergency department later than patients living with or close to their families.However, no findings such as infection or lower final visual acuity compared to other patients were detected related to late presentation.

Endophthalmitis is an important complication in patients presenting with open-globe injuries, and various studies have reported the prevalence of the condition (ranging from 1–10%). Additionally, endophthalmitis is a complication that may result in blindness and eye loss, hence the management



of the condition is important. Factors that increase the risk of developing endophthalmitis include intraocular foreign bodies, traumatic lens dislocation drop, intraocular tissue prolapse, and diabetes (24).

None of our patients had an intraocular foreign body, and 17 patients had accompanying uveal tissue prolapse, but no endophthalmitis was observed in any of our patients.

Evisceration was performed, and the prosthetic eye was used for aesthetic concerns, reducing the risk of sympathetic ophthalmia and increasing life expectancy in young patients with a final visual acuity of no light perception. However, geriatric patients have a shorter life expectancy and fewer aesthetic concerns compared to young patients, so the evisceration rate is lower. In our study, the final visual acuity was determined to be no light perception in seven patients, and evisceration was applied to two of these seven patients to prepare the ground for the prosthetic eye.

When we examined the eyes of patients in our study who were not affected by trauma, we observed pathologies such as cataracts, age-related macular degeneration, glaucoma, and diabetic retinopathy that reversibly and irreversibly reduced vision. Treatment and follow-up are extremely important in patients with diabetes mellitus, which may result in the paradox of falling and cause repetitive trauma due to low vision. Diabetes may also limit the patient's daily activities and independence. Low vision may also psychologically affect patients (25).

We believe that trauma in elderly patients may be caused by lower energy traumas unlike young patients. Simple home accidents may result in serious penetrating or perforating injuries. Most falls in the geriatric population occurred while walking (20). The rate of open-globe injuries because of falls in the geriatric population is extremely high at 65% compared with only 4% in persons younger than 65 years (20). Surgical incisions due to previous surgical history and age-related decreases in corneal and scleral collagen cross-links responsible for the integrity of the cornea and sclera are thought to be the reasons for this.

## CONCLUSION

Rehabilitation and follow-up processes, especially in individuals over 65 years of age, are needed to prevent eye trauma that reduces vision or results in legal blindness, to maintain the independence of participation in daily activities that may occur after trauma, and to overcome the psychological effects that result, especially due to low vision. Therefore, increasing public awareness is important.

**Conflicts of interest:** No conflict of interest.

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ORIGINAL ARTICLE

# ARE C-REACTIVE PROTEIN AND PROCALCITONIN EFFECTIVE BIOMARKERS FOR URINARY TRACT INFECTION IN ELDERLY PATIENTS? WHAT SHOULD BE ADMINISTERED FOR EMPIRICIAL TREATMENT?

## Abstract

**Introduction:** In the absence of typical overt symptoms, diagnosis of urinary tract infection is more difficult in elderly individuals. This study investigated the benefits of C-reactive protein, procalcitonin, and leukocyte levels in supporting the diagnosis of urinary tract infection in the elderly and causative factors.

**Materials and Method:** A retrospective examination of information from a hospital data system of patients > 65 years of age, who were diagnosed with urinary tract infection in a 4-year period, was performed. Bacterial identification and antibiotic susceptibility tests were performed.

**Results:** In the case group, procalcitonin and C-reactive protein levels were higher than those in the control group, and a moderately positive correlation with urinary tract infection was found ($p<0.001$, $r=0.454$). Although procalcitonin was a better predictor than C-reactive protein , the risk criteria for C-reactive protein were also very close to those of procalcitonin. The cut-off values for C-reactive protein and procalcitonin were 6.93 mg/L and 0.075 ng/ml, respectively, and C-reactive protein levels were normal in 20% of cases. The most frequently isolated microorganisms were Escherichia coli (56%) and Klebsiella pneumoniae (16%). The extended-spectrum beta-lactamase rate was 35% for E. coli and 43% for K. pneumoniae isolates. Fosfomycin and ertapenem were the most effective antibiotics.

**Conclusion:** Procalcitonin levels were high; however, the fact that C-reactive protein was found to be normal in one-fifth of cases should serve as a warning that urinary system infection can be missed in elderly patients in cases in which only C-reactive protein level is evaluated.

***Keywords:*** Aged; Drug Resistance; Urinary Tract Infections; C-Reactive Protein; Procalcitonin; Leukocytes.

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## INTRODUCTION

Aging of the immune system, comorbid chronic diseases, and the deterioration of organ function increase the frequency and severity of infections among elderly patients (1). Urinary system infections are the second most common infections in the elderly population (2). Urinary and fecal incontinence, dehydration, impaired consciousness, cystocele, rectocele, vaginal atrophy, estrogen deficiency, prostate diseases, and lack of physical activity are factors that increase susceptibility to these infections (2,3). Diagnosis is more difficult if typical symptoms, such as dysuria, pollakiuria, and urgency are absent, and atypical symptoms may further complicate diagnosis. Elderly patients with urinary system infections present with symptoms including confusion and general condition disorders. Clinician suspicion is of great importance in the diagnosis. It may not always be possible to obtain a urine sample due to consciousness problems among elderly patients; as such, it may be necessary to obtain a sample using a catheter. Therefore, there is a need for more practical biomarkers to be investigated in blood samples. For this purpose, we aimed to investigate the utility of C-reactive protein (CRP), procalcitonin, and blood leukocyte levels in the diagnosis of urinary system infection.

CRP is a protein secreted from the liver after stimulation of interleukin IL-1, IL-6 and TNF-alpha. It's main biological functions are to bind to bacteria, activate the classical complement pathway, and facilitate phagocytosis. The release of CRP from hepatocytes is elicited by infection, inflammation, and tissue damage, and becomes detectable within 6 h, and peaks at 36–50 h. Because of these properties, CRP is the most commonly used acute-phase reactant and the most widely used biomarker of inflammation (4,5).

Procalcitonin is a specific and sensitive parameter for the diagnosis and follow-up of systemic inflammation and bacterial infection. Bacterial endotoxins are the strongest stimulators of procalcitonin production. Procalcitonin measurements are used to differentiate nonbacterial diseases such as viral, autoimmune, and oncological diseases from bacterial infections. Procalcitonin synthesis occurs in nonthyroid tissues during the inflammatory response to bacterial infection, peaks rapidly then declines rapidly, providing useful information for decision-making regarding the initiation and reduction of antimicrobial therapy; however, it is costly (6,7,8).

Aging and fragility can lead to changes in the levels of serum inflammatory proteins; therefore, it is important to determine cut-off values for CRP and procalcitonin in the elderly.

Antibiotics are often empirically administered to treat urinary tract infections (UTIs). However, the problem of resistance that develops owing to the inappropriate use of antibiotics leads to failure of empirical treatment. Therefore, it is necessary to determine the resistance rates in our country, and even in our region, when choosing empirical antibiotics. The present study investigated how CRP, procalcitonin, and leukocyte levels are affected by UTIs in patients > 65 years of age and their contribution to diagnosis as well as urinary system infectious agents, and antibiotic susceptibility, and antibiotics that can be selected for empirical treatment.

## MATERIALS AND METHOD

This study was conducted by retrospectively examining the past four years of laboratory data and records housed in the hospital data system of patients > 65 years of age, who were treated at a 100-bed private hospital and diagnosed with UTI. Between March 2018 and March 2022, patients > 65 years of age, who presented with symptoms such as fever, dysuria, pollakiuria, and incontinence suggestive of urinary system infection, as well as with atypical symptoms such as clouding of consciousness, general condition disorder,



confusion, and pyuria (> 10 leukocytes in urine sediment) and significant growth in urine culture were included in the study. The demographic characteristics of the patients, leukocyte count (/mm3) , CRP and procalcitonin (PCT) levels, on the first day of admission and the identification and antibiogram results of bacteria isolated from urine as urinary infectious agents were recorded. This study was approved by the Clinical Research Ethics Committee of Demiroglu Bilim University (Approval date: 20.12.2022; decision number: 2022-25-03) in accordance with declaration of Helsinki. Due to the retrospective design of the study and the use of anonymized patient data, requirements for informed written consent were waived. Midstream urine samples were collected, if necessary, using a catheter, and inoculated onto 5% sheep blood agar and eosin methylene blue agar for microbiological analysis and culture. Plates were then incubated at 37°C for 18–24 h; growth of > 100,000 colonies/mL was considered to be significant. Samples from which > 1 microorganism was isolated were considered to be contaminated. Duplicate strains grown from the same patient were excluded from the evaluation. Bacteria isolated from growing specimens were identified using conventional methods (colony morphology and Gram staining) using an automated identification system (Vitek 2, bioMerieux, Marcy-l'Étoile, France). Antibiotic susceptibilities were determined using Vitek 2 Compact Cards in accordance with European Committee on Antimicrobial Susceptibility Testing ("EUCAST") standards. Intermediate-susceptible strains were considered to be resistant. ESBL resistance was determined according to the results obtained from the automated identification and antibiogram systems; however, confirmatory tests were not performed, which may be considered a limitation of the present study. After applying the exclusion criteria for patients diagnosed with urinary system infection (no other infection detected, no malignancy and immunosuppression, no operation, and no thyroid disease), 202 patients with available CRP, procalcitonin, and leukocyte data recorded simultaneously on the first day of admission were included. In addition, 200 patients who visited other outpatient clinics for other reasons, between the same years, were > 65 years of age, had no infection, malignancy, or immunosuppression, and no history of recent surgery, were included as the control group.

CRP levels were analyzed with a quantitative immunoturbidimetric method using a commercially available kit (Multigent CRP Vario) and a laboratory analyzer (Architect ci4000, Abbott Core Laboratory, Abbott Park, IL, USA). The measurement range of the test is 0.40–160 mg/L, and the normal value is ≤ 5 mg/L.

Procalcitonin levels were analyzed using an immunoassay method a commercially available kit and analyzer (Architect BRAHMS PCT, Abbott Core Laboratory, Abbott Park, IL, USA). The detection interval of the assay is 0.02–100 ng/mL, and the normal value is < 0.05 ng/mL.

## RESULTS

A total of 684 bacteria were isolated from the urine cultures of our patients aged 65-104 in a 4-year period as the causative agent of urinary system infection. The bacterial distribution is as follows: 381 E.coli (56% - 134 ESBL(+)35%), 107 Klebsiella pneumoniae (15.6%) - 46 ESBL(+) (43%), 59 Enterococcus spp. (8.6%), 54 Pseudomonas spp. (7.8%), 24 Proteus spp. (3.5%), 19 Enterobacter spp. (2.6%), 10 Acinetobacter spp (1.5%), 9 Morganella spp (1.3%), 8 Streptococcus agalactiae (1.2%), 6 MRSA (0.9%), 3 Salmonella spp (0.4%), 2 MRKNS (0.3%), 2 Citrobacter spp. (0.3%)

Antibiotic susceptibilities of E.coli isolates were as follows, 99% to fosfomycin, 98% to nitrofurantoin, 90% to amoxicillin - clavulanic acid, 90% to ceftriaxone, 89% to cefuroxime, 83% to ciprofloxacin, and 78% to trimethoprim sulfomethoxazole. Antibiotic susceptibilities

of ESBL (+) E.coli; 97% to fosfomycin, 95% to ertapenem, 85% to nitrofurantoin, 55% to amoxicillin- clavulanic acid, 32% to ciprofloxacin, and 36% to trimethoprim sulfomethoxazole; and antibiotic susceptibilities of Klebsiella pneumoniae isolates were, 85% to amoxicillin - clavulanic acid, 83% to ceftriaxone, 82% to cefuroxime, 70% to ciprofloxacin, 68% to trimethoprim sulfomethoxazole; for ESBL (+) Klebsiella susceptibility rates are as follows, ertapenem (92%), fosfomycin (82%), ciprofloxacin (58%), amoxicillin clavulanic acid (44%), trimethoprim sulfomethoxazole (34%). The most effective antibiotics against ESBL (+) bacteria were ertapenem and fosfomycin. Since nitrofurantoin is only recommended for E.coli strains in Enterobacteriaceae species, it was excluded from the evaluation in Klebsiella pneumoniae isolates. E.coli and Klebsiella pneumoniae are the two most frequently isolated microorganisms, with ESBL rates of 35% and 43%, respectively.

The mean age, CRP and procalcitonin levels of the patients and control group in the blood are given in table 1. There were no significance among gender (p=0.09)

There was no age difference between the case and control groups. (p=0.055)

Case frequency is higher in the 75-84 age group

Procalcitonin and CRP were higher in the case group than in the control group (p values <0.001 and <0.001, respectively)

**Table 1.** The mean age, CRP and Procalcitonin levels of the case and control groups

| Group Statistics | | | | | | |
|---|---|---|---|---|---|---|
| **casecont** | | **N** | **Median** | **Mean** | **Std. Deviation** | **Std, Error Mean** |
| **CRP** | Control | 200 | 2.2950 | 2.9790 | 2.00215 | .14157 |
| | Case | 202 | 18 | 40.0124 | 52.86034 | 3.71924 |
| **AGE** | Control | 200 | | 81.62 | 11.027 | .780 |
| | Case | 202 | | 79.64 | 9.499 | .668 |
| **PCT** | Control | 200 | 0,04 | . 0416 | .01636 | ,00116 |
| | Case | 202 | 0,4 | 1.9688 | 4.08896 | .28770 |

**Table 2.** Correlations between CRP, leukocytes and procalcitonin

| Correlations | | | | |
|---|---|---|---|---|
| | | **CRP** | **LOKOSIT** | **PCT** |
| **CRP** | Pearson Correlation | 1 | .280** | .454** |
| | Sig. (2-tailed) | | .000 | .000 |
| | N | 402 | 202 | 402 |
| **LEUKOCYTE** | Pearson Correlation | .280** | 1 | .236** |
| | Sig. (2-tailed) | .000 | | .001 |
| | N | 202 | 202 | 202 |
| **PCT** | Pearson Correlation | .454** | .236** | 1 |
| | Sig. (2-tailed) | .000 | .001 | |
| | N | 402 | 202 | 402 |

There was a positive moderate correlation between Procalcitonin and CRP ($p<0.001$, $r=0.454$).

Correlations between CRP, Leukocytes and procalcitonin are shown in table 2.

There was a significant difference between CRP measurements before and after treatment. ($p<0.001$)

Although the leukocyte correlations were significant, the correlation coefficients were low.

Although procalcitonin is a better predictor than CRP, risk measures of CRP were also found to be very close to procalcitonin. Cut off values and predictive values of CRP and procalcitonin are shown in table 3. Specificity and sensitivity values are visible on ROC curve (figure 1)

**Table 3.** Cut off values of CRP and Procalcitonin

| | Cut-off | AUC | Sensitivity | Specificity | Positive Predictive Value | Negative Predictive Value |
|---|---|---|---|---|---|---|
| **CRP** | 6.930 | 0.899 | 0.787 | 0.960 | 0.952 | 0.817 |
| **PCT** | 0.075 | 0.943 | 0.856 | 0.970 | 0.966 | 0.870 |

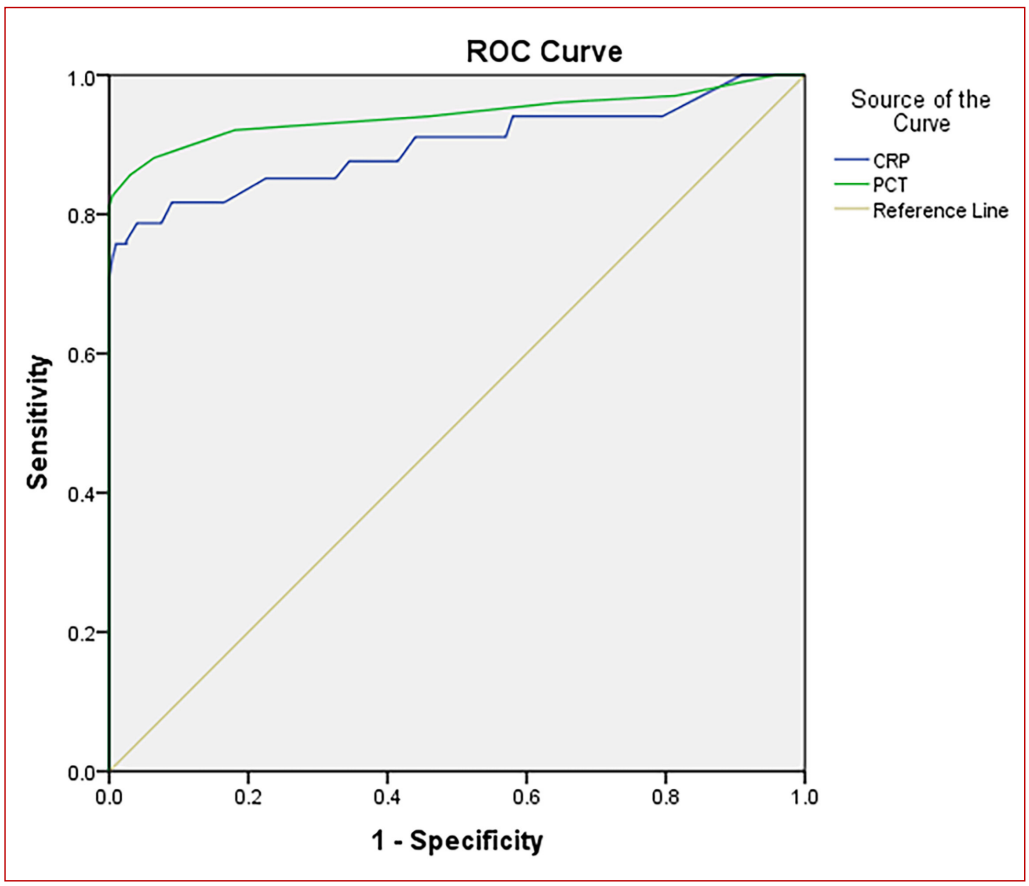



**Figure 1.** ROC curve

## DISCUSSION

Because urinary system infections can cause serious morbidity and mortality in elderly patients, early diagnosis and appropriate empirical treatment are important. Urine culture is the gold standard; however, obtaining results takes 48–72 h, and the difficulties in obtaining appropriate urine samples in elderly patients highlight the convenience of markers such as CRP, procalcitonin, and high blood leukocyte levels. In this study, we aimed to draw the attention of clinicians to the sensitivity of CRP as a biomarker, especially because it is a parameter that is frequently used in practice. In addition, a comparison of procalcitonin and CRP, which is a significantly more sensitive and specific indicator of infection but is not routinely used owing to its high cost, was also made. In our study, although procalcitonin was a better predictor than CRP, CRP risk measures were also found to be very similar to procalcitonin. The cut-off values were determined to be 6.93 mg/L for CRP and 0.075 ng/ml for procalcitonin. However, in our study, CRP level was found to be normal in 20% of the patients who were diagnosed with UTI with clinical complaints, pyuria, and significant growth in urine culture. This warns that normal CRP can sometimes be misleading and may be missed, even if the patient has a UTI. In our study, a moderate positive correlation was observed between procalcitonin and CRP levels.

In a study evaluating urinary system infections in elderly patients, the median CRP value was 7.5 mg/dL and >0.5 mg/dL in 93.7% of patients (9). The median CRP level in our study was 18 mg/L and > 5 mg/L in 80% of cases. This difference may be due to the fact that our cases were not differentiated as upper and lower UTIs. In a study by Xu et al., who evaluated renal involvement using technetium-99m dimercaptosuccinic acid (Tc-DMSA) scintigraphy in children, the diagnostic reference values for CRP, procalcitonin, and leukocytes in patients with acute pyelonephritis were 20 mg/L, 1 ng/ml, and 15,000/$mm^3$, repectively, which were higher than those obtained in our study (10). It is expected that CRP and, especially, procalcitonin values will be higher in cases with parenchymal involvement who are diagnosed with pyelonephritis, as in this study. A study by Kuil et al., which included 302 elderly nursing home patients, investigated CRP and procalcitonin at point of care and determined cut-off values of 6.5 mg/L and 0.025 ng/mL, respectively, with the diagnosis of both asymptomatic bacteriuria and UTIs (11). The authors concluded that CRP and procalcitonin were unsuitable biomarkers for differentiation. They attributed this to the fact that the patients had mild cases, with the majority experiencing lower UTIs without parenchymal involvement or systemic inflammation. The cut-off values in that study were lower than those in ours. Invasive bacterial infection was detected in 39 of 172 patients who attended the geriatric unit with acute complaints, and it was determined that a procalcitonin level <0.08 ng/ml ruled out infection in 97% of cases (12). This procalcitonin value is very close to our results. In a single-center, retrospective study involving adults with a mean age of 77 years and lower UTIs, Levine et al. found procalcitonin sensitivity to be 67% when the cut-off level of procalcitonin was 0.25 ng/mL (13). The reason why it was found to be higher than the value in our study may be due to the fact that the case group consisted of patients who presented to the emergency department with a more severe clinical conditions. This was a prospective study involving 61 hospitalized patients with a mean age of 82 years. The median procalcitonin level was 0.08 ng/ml, and the cut-off value was 0.18 ng/ml. (14).These inflammatory markers are expected to be higher because hospitalized patients have a more severe clinical condition, and most have pyelonephritis with parenchymal involvement. In our study, the cut-off values for CRP and procalcitonin were higher and lower than those in other studies. The reason why it was lower can be attributed to the fact that our control cases were selected from among those without signs of infection, fever, or malignancy, and



that most of our cases with UTIs were outpatients. In addition, pediatric patients and young adults have been evaluated in most studies, and changes in serum inflammatory proteins may occur in the elderly due to the aging of the immune system and decreased inflammatory response (15). In our study, the median CRP value in the patient group with UTI was 18 mg/L, the median value of procalcitonin was 0.400 ng/ml, and the mean and median CRP and procalcitonin levels were significantly higher in the urinary system infection patient group than in the control group.

In our study, the median leukocyte count in the patient group was 9470/mm3, with no significant difference from the control group. In other studies, it was reported that leukocytosis, which is an important indicator of bacterial infection, was detected in less than one-half of UTI cases. Our data and results from other studies suggest that the absence of leukocytosis in elderly patients is insufficient to exclude the diagnosis of UTI (9,16 ).

When the incidence of UTI in the cases was evaluated according to age group, it was observed that the frequency of the cases was higher in the 75–84 age group. Similar to our study, other studies reported that most cases were observed in the 75–84 age group (17 ).

In our study, *E. coli* (56%) and *K. pneumoniae* (16%) were the most frequently isolated pathogens, and were also the most common microorganisms in other studies (9,16,17 ). In a study involving an elderly patient group, Alpay et al. reported a prevalence of 66% and 15% for *E. coli* and *K. pneumoniae*, respectively, and ESBL rates of 49% for *E. coli* and 66% for *K pneumoniae (17 )*. In our study, ESBL rates were 35% for *E. coli* and 43% for *K pneumoniae* isolates, similar to other studies; the ESBL rate was higher in *K. pneumoniae*. Ayhan et al. reported the rate of ESBL in Gram-negative bacteria, which are the cause of urinary infection in geriatric patients, to be 56% for *E. coli* and 40% for *K. pneumoniae* (18 ).When other studies investigating urine cultures in our country were examined, the ESBL rates were between 17% and 56% for *E.coli* and 21% and 61% for *K. pneumoniae* (16,17,18,19,20,21,22). ESBL rates can vary not only according to country and region but also to different services at the same hospital.

Nitrofurantoin should be considered the first-line treatment, especially for simple cystitis. In our study, nitrofurantoin was one of the most effective antibiotics with a high sensitivity rate.

Fosfomycin is rapidly metabolized and excreted unchanged in the urine following oral ingestion, and single-dose convenience is also an important advantage. In various studies from our country, susceptibility rates for fosfomycin in Gram-negative bacteria were reported to be 91–100% and, in our study, susceptibility rates were found to be 99% in *E. coli* strains and 93% in ESBL-positive strains. Fosfomycin is one of the antibiotics of choice for the treatment of uncomplicated lower UTIs owing to its high sensitivity (19,20,21,22,23 ).

Ertapenem is a broad-spectrum, once-daily drug that is effective against ESBL-secreting bacteria. The susceptibility of urine isolates to ertapenem was high in both our study and others (18,19,20,22,23). It can be safely used as an empirical treatment, particularly in cases involving pyelonephritis.

In our study and others, fluoroquinolones were antibiotics with increased resistance rates owing to their frequent preference and unconscious use. It has been reported that amoxicillin-clavulanic acid resistance rates are gradually increasing in urinary isolates, and it has been reported that, in cases in which resistance to an antibiotic exceeds 20%, it would be more appropriate to not use this drug for empirical treatment (24).

The main limitations of our study were that UTIs were not classified as hospital- or community-acquired, nor were upper and lower UTIs distinguished. Because patient records and data were evaluated retrospectively using electronic

media, this information was not included in the study because reliable results could not be obtained in this regard.

It is important to emphasize that UTIs may be present in elderly patients presenting with faint symptoms even if CRP level is normal, and this should not be overlooked. Moreover, procalcitonin is a more useful marker for the diagnosis of UTI if there is difficulty in collecting urine samples. If the diagnosis is not pyelonephritis, the patient can be treated with empirically initiated fosfomycin or nitrofurantoin. Because pyelonephritis may cause bacteremia and urosepsis in the elderly, a more judicious approach would be to start with a broad-spectrum antibiotics and narrow the spectrum according to antibiogram results in empirical treatment; as such, ertapenem is a reliable option. When using cephalosporins in the empirical treatment of pyelonephritis, it is necessary to consider high ESBL rates; therefore, they should not be preferred in elderly individuals with risk factors.

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ORIGINAL ARTICLE

# SYSTEMIC IMMUNE INFLAMMATION INDEX AND NEUTROPHIL TO ALBUMIN RATIO CAN PREDICT LEFT VENTRICULAR HYPERTROPHY IN GERIATRIC HEMODIALYSIS PATIENTS

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## Abstract

**Introduction:** A link exists between inflammation and left ventricular hypertrophy, which is a risk factor for cardiovascular disease in patients with end-stage renal failure. Neutrophil, lymphocyte, and platelet counts are used to calculate the systemic immune inflammation index. To calculate the neutrophil to albumin ratio, we divided the total number of neutrophils by the albumin concentration. Some articles have illustrated the value of systemic immune inflammation index and neutrophil to albumin ratio for diagnosing disorders associated with inflammation. The purpose of this study was to investigate whether a connection exists between left ventricular hypertrophy and inflammation, as measured by systemic immune inflammation index and neutrophil to albumin ratio, in hemodialysis patients aged >65 years.

**Materials and Method:** This study included 51 patients who had been receiving HD for at least three months. Test results and echocardiography measurements were obtained from patient files.

**Results:** Average patient age was 72.88±5.12 years. Patients were divided into two groups based on left ventricular hypertrophy status. C reactive protein, systemic immune inflammation index and neutrophil to albumin ratio were considerably lower in the left ventricular hypertrophy (-) group, and multivariate logistic regression analysis revealed that high neutrophil to albumin ratio was an independent predictor of left ventricular hypertrophy (odds ratio [OR]:8.83, 95 percent confidence interval [CI]:1.32-28.83, P .0005), in conjunction with a high C reactive protein level (OR:3.45, 95 percent CI:1.905-6.645, P .005).

**Conclusion:** Neutrophil to albumin ratio correlates with C-reactive protein and left ventricular hypertrophy, thereby predicting the inflammation characteristic of left ventricular hypertrophy.

***Keywords:*** Inflammation; Hypertrophy, Left Ventricular; Renal Dialysis.

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## INTRODUCTION

At least 40 percent of deaths caused by end-stage renal illness can be attributed to cardiovascular causes. Left ventricular hypertrophy (LVH) is a significant health concern and risk factor for mortality (1). Inflammation is the body's first line of defense in response to excessive volume and pressure (2, 3).

Individuals with end-stage renal illness experience risk factors unique to uremia in addition to traditional cardiovascular risk factors. Increased production of endothelial adhesion molecules, chemokines, and cytokines has been observed in these tissues. The inflammatory marker C-reactive protein (CRP) has been linked to LVH and cardiovascular mortality (4, 5).

Neutrophils are known to participate in inflammatory processes (6). The recently established systemic immune inflammation index (SII) is computed by first multiplying platelet and neutrophil levels, then dividing this product by the number of lymphocytes. Studies have demonstrated SII's diagnostic utility for a number of malignancies and inflammatory disorders (7, 8).

Inflammation and cardiovascular mortality are known to correlate with blood albumin levels (9). Neutrophil numbers are also known to correlate with inflammation and cardiovascular mortality. To date, the predictive usefulness of integrating these two features is not completely clear. SII and NAR may both be easily approximated by utilizing the amounts of albumin, neutrophils, lymphocytes, and platelets obtained from routine blood testing. The use of these values as inflammatory indicators is not complicated and does not incur excessive costs. The purpose of this study was to determine whether there are connections between LVH, NAR, and inflammation detected by SII in hemodialysis patients.

## MATERIALS AND METHOD

Fifty-one ESRD patients undergoing hemodialysis treatment were recruited to participate in this study. Patients with ESRD who lacked any residual renal function and had been undergoing HD (three times per week for four hours per session with standard bicarbonate dialysate) for a minimum of three months were considered eligible for inclusion. Patients were not included in this study if they had a history of using statins, steroids, or immunosuppressant medications; heart failure; a recent acute coronary or cerebrovascular incident; an autoimmune illness; malignancy; liver cirrhosis; or a current infection at the time of HD. Patients with moderate-to-severe valve pathologies were also excluded from this study.

The study was approved by the regional ethics board and was carried out in compliance with the ethical principles outlined in the Helsinki Declaration. All patients provided consent after being fully informed. Patient files were reviewed to obtain demographic information such as age at the time of the research, length of time spent on dialysis, and the existence of diabetes mellitus in the background. Data from laboratory and echocardiography measurements were gathered and placed in the patient's dossier. Thirty minutes after finishing their weekly hemodialysis session, the patients' blood pressure was measured using either a shunt arm or non-arteriovenous fistula.

Echocardiography was performed two to twenty-four hours after hemodialysis. Echocardiography and computation of dimensions and various heart volumes were performed in accordance with the recommendations of the American Society and European Association of Echocardiography. Echocardiographic assessment comprised the endo-cavitary dimensions of the left ventricle and other cardiac chambers. The left ventricular mass was calculated using the Devereux formula 17:1.04 [(LVID + PWT + IVST)3 - LVID3] 0.8 + 0.6, where LVID represents the left ventricular internal diameter, PWT represents the thickness of the posterior wall, and IVST represents the thickness of the intraventricular septum. Men with a left ventricular

mass index (LVMI) > 115 g/m$^2$ and women with an LVMI of greater than 95 g/m$^2$ were diagnosed with left ventricular hypertrophy.

The systemic immune inflammation index (SII) was calculated by multiplying the platelet count by the neutrophil count and dividing the product by the number of lymphocytes. NAR was calculated by dividing the number of neutrophils by the concentration of albumin present in the sample.

For the purpose of statistical analysis, SPSS (Statistical Package for the Social Sciences, Chicago, Illinois) version 25.0, for Windows was used. Continuous variable data are typically presented using mean and standard deviation, unless a different format is specifically required. To compare groups, either the student's t-test (where the data had a normal distribution) or the Mann–Whitney U test (for data without normal distribution) was performed. The Chi-square test was used to compare categorical variables. Estimates of the effects of the different variables on mortality were obtained using univariate analysis. In univariate analysis, the model contained parameters with a P-value of 0.05, which enabled its use in multivariate regression analysis. Cutoff levels of SII and NAR for predicting LVH were accurately determined by analyzing receiver operating characteristic (ROC) curves. The value that corresponded to the highest sensitivity and specificity values in the ROC analysis was chosen as the optimum cutoff value. P.05 on both sides were considered statistically significant.

## RESULTS

Males comprised 29 (56.9%) of the 51 participants in the study. The average age was 72.88 ± 5.12 years. Nine patients were diagnosed with diabetes (21.4%), 24 with hypertension (59.5%). Five participants (11.9%) smoked. The average systolic blood pressure was 129.5 ± 11.7 mmHg, while the average diastolic blood pressure was 75.01 ± 6.6 mmHg. The mean CRP was 15.3 ± 9.5 mg/dl, and 68.6 percent of the patients had LVH. Table 1 shows the clinical results and laboratory data for the study cohort.

Dividing participants into two groups based

**Table 1.** Demographic, clinical and echocardiographic parameters in HD patients and control group

| Parameter | HD patients (n=51) |
|---|---|
| **Age (years)** | 72.88 ± 5.12 |
| **Gender (male, n, %)** | 29 (56.9%) |
| **Comorbidites** | |
| **Diabetes (n, %)** | 9 (21.4%) |
| **Hypertension (n, %)** | 24 (59.5%) |
| **SBP (mmHg)** | 129.5 ± 11.7 |
| **DBP (mmHg)** | 75.01 ± 6.6 |
| **Kt/V** | 1.48 ± 0.24 |
| **Hemoglobin (g/dL)** | 11.19 ± 1.12 |
| **Glucose (mg/dl)** | 145.46 ± 52.59 |
| **Albumin (g/dL)** | 4.2 ± 3.3 |
| **TC (mg/dl)** | 158.48 ± 41.71 |
| **TG (mg/dl)** | 161.59 ± 100.18 |
| **HDL-C (mg/dl)** | 37.34 ± 12.66 |
| **LDL-C (mg/dl)** | 91.16 ± 33.03 |
| **CRP (mg/L)** | 15.3±9.5 |
| **SII** | 788.69±601.6 |
| **LVMI** | 149.52±48.86 |
| **LVH (n, %)** | 35(67.9%) |
| **NAR** | 1.57±0.99 |

Abbreviations: HD, hemodialysis; CKD, chronic kidney disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; CRP, C-reactive protein; LVMI, left ventricular mass index; LVH, Left ventricular hypertrophy; SII, systemic immune inflammation index; NAR, neutrophil-to-albumin ratio.



on the presence or absence of LVH resulted in no difference between groups in sex or age.

Systolic and diastolic blood pressure and ultrafiltration volumes were comparable between groups. The LVH (+) group had a lower Kt/V (1.53 ± 0.2 versus 1.45 ± 0.25; p 0.05).

CRP and SII levels were considerably lower in the LVH group, although albumin levels were not significantly different. LVH (+) patients were found to have significantly higher NAR levels (Table 2).

Multivariate analysis was used to determine the significance of several LVH risk variables. These variables were age, sex, NLR, CRP, SII, albumin, NAR, SBP, DBP, and HT. Multivariate logistic regression analysis revealed that a high NAR score was an independent predictor of developing LVH (odds ratio [OR]:8.83, 95 percent confidence interval [CI]:1.32-28.83, P .0005), as was high CRP

**Table 2.** Demographic and clinical parameters in HD patients with and without LVH

| Parameter | LVH (-) (n=16) | LVH (+) (n=35) | P |
|---|---|---|---|
| **Age (years)** | 73.8 ± 5.1 | 72.5 ± 5.1 | >0.05 |
| **Gender (male, n, %)** | 9 (56%) | 20 (57%) | >0.05 |
| **Diabetes (n, %)** | 3 (19%) | 6 (17%) | >0.05 |
| **Hypertension (n, %)** | 7 (43%) | 17 (48%) | >0.05 |
| **Ultrafiltration(ml)** | 2980 ± 940 | 2850 ± 950 | >0.05 |
| **Hemoglobin (g/dL)** | 11.01 ± 1.22 | 11.27 ±1.08 | >0.05 |
| **Glucose (mg/dl)** | 144.39 ± 48.9 | 145.95 ± 54.88 | >0.05 |
| **Albumin (g/dL)** | 4.4 ± 0.3 | 4.1 ± 0.6 | >0.05 |
| **Cr (mg/dl)** | 8.02 ± 1.56 | 8.13 ± 1.94 | >0.05 |
| **Ferritin (ng/mL)** | 475.39±284.9 | 393.68±262.15 | >0.050 |
| **Kt/V** | 1.53 ± 0.2 | 1.45 ± 0.25 | 0.03 |
| **CRP (mg/L)** | 6.82 ± 5.77 | 9.18 ± 2.22 | 0.004 |
| **SII** | 610.33±431.68 | 870.22±422.11 | 0.003 |
| **NAR** | 0.96 ± 0.42 | 1.84 ± 1.05 | 0.002 |
| **PTH (pg/ml)** | 736.67±517.68 | 628.45±463.72 | >0.05 |
| **TG (mg/dl)** | 165.95±145.08 | 159.6±76.01 | >0.05 |
| **HDL-C (mg/dl)** | 40.35 ± 14.8 | 35.96 ± 11.52 | >0.05 |
| **LDL** | 88.51 ± 29.9 | 92.37 ± 34.68 | >0.05 |

Abbreviations: LVH, left ventricular hypertrophy; HD, hemodialysis; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; Cr, creatinine; PTH, parathyroid hormone; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; CRP, C-reactive protein; LVMI, left ventricular mass index; SII, systemic immune inflammation index; NAR, neutrophil-to-albumin ratio.

level (OR:3.45, 95 percent CI:1.905-6.645, P .005). SII and the presence of HT were not significant factors (OR:0.999 percent, 95 percent CI:0.994-1.004, P > 0.05; OR:1.001 percent, 95 percent CI:0.928-1.001, P > 0.05, respectively) (Table 3).

Analysis of the area under the receiver operating characteristic curve revealed an optimal cutoff value of 0.986 for use of NAR to predict the development of LVH, with 69 percent sensitivity and 72.5 percent specificity (area under the ROC curve:0.757 [95 percent confidence interval:0.627-0.887], P .005). An optimal CRP cutoff value of 4.65 predicted the development of LVH with a sensitivity of 56% and specificity of 44%, and the area under the curve was 0.695 (95 percent confidence interval:0.549-0.840; P .005; Figure 1).

**Table 3.** Binary logistic regression analysis

| | | | 95% C.I.for EXP(B) | |
|---|---|---|---|---|
| | **Sig.** | **Exp(B)** | **Lower** | **Upper** |
| **NAR** | ,0032 | 9,741 | 1,32 | 28,83 |
| **SII** | ,933 | 0,999 | ,994 | 1,004 |
| **CRP** | ,004 | 3,45 | 1,905 | 6,675 |
| **KTV** | ,500 | ,290 | ,008 | 10,555 |
| **ht(1)** | ,832 | ,830 | ,148 | 4,653 |

Abbreviations: NAR, neutrophil-to-albumin ratio; SII, systemic immune inflammation index; CRP, C-reactive protein; ht- presence of hypertension.

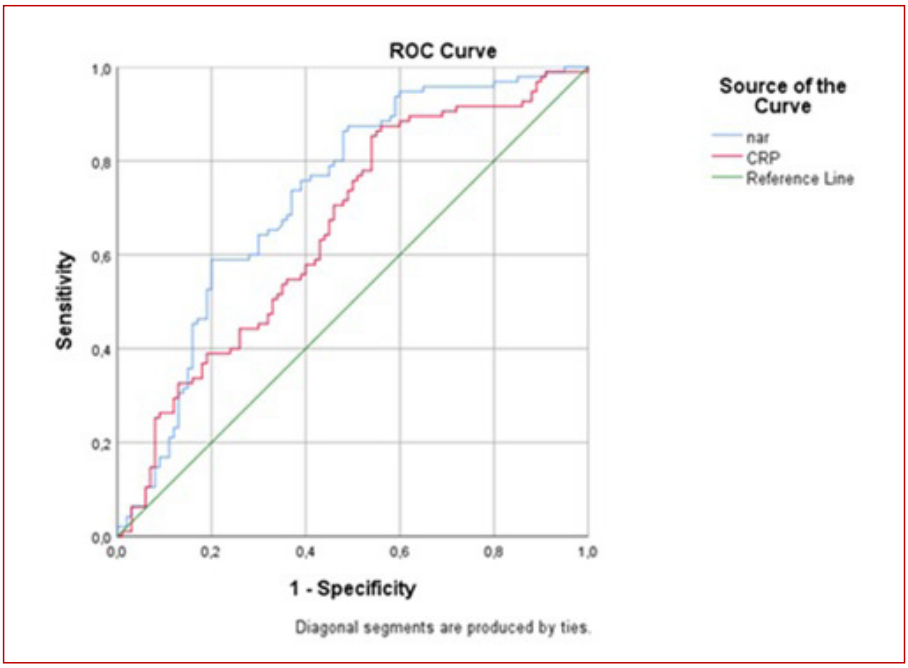



**Figure 1.** ROC curve

## DISCUSSION

The most significant finding of this study was that the NAR score, which is an innovative method for measuring inflammation, can independently predict LVH.

In addition to conventional risk factors, ESRD patients have risk factors uniquely associated with uremia. Risk factors include hypertension, anemia, volume load, phosphorus metabolism, uremic toxin accumulation, and inflammation. These factors all have the potential to play a role in left ventricular damage and hypertrophy (2, 3).

Among the patients who participated in our study, 68.6% were diagnosed with LVH. These findings are consistent with those obtained by Foley et al. (10) and London et al. (11), who discovered that approximately 75% of individuals diagnosed with end-stage renal illness had LVH.

Renal patients who suffer from anemia also tend to have left ventricular hypertrophy (11). Hemoglobin level is a good indicator of the degree of left ventricular hypertrophy (LVH), and each g/dl drop in HB level is associated with a 50% decrease in LV systolic performance (12). During our examination, we found that Hb levels were identical between groups. This may occur as a secondary effect of anemia therapy.

KT/V and URR ratios were used to evaluate the dialysis dose, which is related to the quality of hemodialysis. The measurement of urea before and after HD is at the core of both techniques (13). Urea levels are evaluated at least once per month, although frequency may vary from center to center. According to the findings of Manuel et al., CRP levels are much higher in people who are unable to achieve an ideal Kt/V ratio (14). We concluded that the LVH group had lower Kt/v. This may be due to inflammation caused by a uremic environment, or it may be because people in this demographic have a propensity to consume an excessive amount of water.

Inflammation, fibrosis, and oxidative stress are known to be involved in left ventricular remodeling (15). LVH has been linked to elevated CRP levels (15). The neutrophil-lymphocyte ratio, often known as the NLR, is a measurement of inflammation that has seen a significant increase in popularity over the past several years (16). The systemic immunological inflammation index (SII) is a recently developed measure generated by multiplying platelets with NLR. As a result, the number of platelets in the blood and NLR were combined to obtain an improved indicator of inflammation.

Activated neutrophils increase levels of myeloperoxidase, matrix metalloproteinases 2 and 9, and reactive oxygen metabolites (17). These compounds may accelerate the progression of early atherosclerosis and contribute to plaque instability by exerting effects on the endothelium (18-20). Throughout the course of this inflammatory process, chemokines, secreted proteins, and microRNAs work together to activate platelets (17). As a direct result, platelet counts increase (17). Because SII takes into account NLR and platelet count, it is thought that this value is more sensitive than others (18). However, in our study, no significant difference in SII was observed between groups with and without LVH. It is possible that this was due to the use of heparin, which resulted in fewer platelets being detected in the blood.

Approximately 60 percent of serum protein content is albumin, which has a half-life of 19 days (19,20). Low levels are linked to malnutrition, kidney and liver disorders, cancer, and inflammation (21). Recent studies have suggested that one indicator of chronic inflammation, rather than a dietary condition, is reduced blood albumin levels (21). It is possible that the longer half-life of albumin in comparison with other blood features enhances its usefulness for identifying chronic inflammation.

NAR is a relatively new measure of inflammation. NAR was calculated using albumin and neutrophil counts. Our study found it to be the most valuable

factor in identifying LVH. CRP level was also useful. The diagnostic value of NAR is greater than that of CRP. This may be because its computation incorporates many parameters.

The inflammatory aspect of LVH development may result in increased NAR. Although LVH is commonly associated with hypertension, HT was not identified as a predictor of LVH in our multivariate analysis.

Activation of the inflammatory response enhances cytokine production. Inflammatory cytokines and cells help to alter the cardiovascular system. Wu et al. revealed that neutrophil-produced S100a8/S100a9 proteins increase Ang II-induced cardiac inflammation and fibrosis regardless of the blood pressure response (21). HT was not a predictor of LVH, and LVH may be produced by enhanced inflammation of the angiotensin pathway.

There are some limitations to this investigation. Small sample size and a cross-sectional study approach necessitated the concurrent calculation of SII levels and NAR. Only one center was used for this study. Expanded follow-up studies with more patients at several centers are needed.

The inflammatory nature of LVH might be predicted by NAR owing to its association with CRP. However, our results need to be verified in other large-scale prospective studies.

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ORIGINAL ARTICLE

# EXAMINATION OF THE FACTORS AFFECTING THE COGNITIVE LEVELS AND RECOVERY STATUS OF GERIATRIC PATIENTS UNDERGOING SURGICAL INTERVENTION

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## Abstract

**Introduction:** The aim of this study was to examine the factors affecting the cognitive levels and recovery status of geriatric patients who undergo surgical intervention.

**Materials and Method:** This was a descriptive cross-sectional study that was conducted between December 30, 2021-August 30, 2022 with 250 geriatric patients who underwent major surgical intervention in the cardiovascular, orthopedics, and general surgery departments of a hospital in Turkey. The descriptive data form, postoperative recovery index, and mini-mental state examination were used as data collection forms. The data of the study were collected with geriatric patients who were in the 48–72-hour postoperative period. The data were analyzed using the Statistical Package for Social Sciences 24.0.

**Results:** The mean age, mini-mental test score and recovery index score of the patients are 69.70±4.81, 24.71±3.07, 2.29±0.33 respectively. It was found that the risk of cognitive impairment increased with increasing age. It was determined that the day of hospitalization before the operation, the application of general anesthesia, the duration of anesthesia, the first mobilization time, the malnutrition, the intensive care stay in the postoperative period made recovery difficult. A negative statistically significant relationship was found between the mini-mental state examination score and postoperative recovery index scores.

**Conclusion:** Approximately half of the patients were at risk of cognitive impairment, which negatively affected the postoperative recovery process. A comprehensive preoperative evaluation of geriatric patients, provision of optimal nutrition, and early mobilization during the postoperative period will positively affect the recovery process. In-service training on the care of geriatric patients is recommended for healthcare professionals.

***Keywords:*** Aged; Surgery; Postoperative Period; Dementia.

This study was conducted as a master's thesis (2022) in Kutahya Health Sciences University, Institute of Post-graduate Education, Department of Nursing

## INTRODUCTION

The need for surgical intervention is increasing due to the increasing health problems of geriatric individuals (1,2). As anesthesia becomes safer and surgical techniques improve, the rate of surgery performed on elderly patients is also increasing. However, elderly patients have higher morbidity and mortality rates in the postoperative period compared to younger patients (2,3). Deterioration in physical functions, comorbidities, and weakness in coping with stress in geriatric patients cause postoperative complications (4). Additionally, a delayed wound healing process due to nutritional deficiency, decrease in intestinal peristalsis, tendency of hemorrhagic shock, decrease in immune functions, sarcopenia, decline in cognitive functions, and impaired functional status can be observed (5).

Cognitive changes are also frequently observed in geriatric individuals undergoing surgical intervention (1). The cause of cognitive changes seen during the postoperative period may be due to the transmission of microemboli that formed during the surgical procedure to the brain, general anesthesia, and analgesia during the postoperative period. Patients with cognitive problems have nutrition, communication, sleep problems and self-care insufficiency (6). In addition, learning, attention and memory are affected in geriatric individuals due to cognitive changes (7,8). Postoperative recovery is a complex process with physiological, functional, and psychological dimensions. The determinants of the patient's recovery process during the postoperative period are cognitive functions, psychological well-being, ensuring physical functions, sleep quality, and pain control (9). Cognitive changes in elderly patients are directly related to the complications that may be encountered during the postoperative period and the patient's discharge time (1). Therefore, postoperative recovery may be difficult in geriatric patients with cognitive impairment.

In the literature, there is no study to date comparing the cognitive changes and recovery status of geriatric patients during the postoperative period. This study was conducted to examine the factors affecting the cognitive levels and recovery status of geriatric patients who undergo surgical intervention.

## MATERIALS AND METHOD

### Study Design

This descriptive and cross-sectional study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist for cross-sectional studies.

### Sample and Procedure

The study population consisted of patients who underwent surgical intervention in the cardiovascular, orthopedics, or general surgery clinics of a university hospital in Turkey from December 30, 2021, to August 30, 2022. The sample of the study consisted of 250 geriatric patients who met the inclusion criteria. These patients were selected by simple random sampling method. The inclusion criteria were; (1) undergoing major surgical intervention (more than 90 minutes) related to cardiovascular surgery, orthopedics or general surgery, (2) being 65 years of age or older, (3) being able to communicate verbally within 48-72 hours after the surgical intervention, (4) being literate and (5) volunteering to participate in the study. The exclusion criteria were (1) not being able to communicate, (2) having any disease (including psychological disorders and dementia) that may affect ability to make decisions, and (3) taking sedatives, antipsychotics, and medications that may affect cognitive state. The power of the study was found to be 95.3% for a sample size of 250 with a 5% margin of error. The G*Power 3.0.1 program was used to perform the power analysis based on the data obtained at the end of the study in order to determine the effect size.

The descriptive data form, postoperative recovery index (PORI), and mini-mental state examination (MMSE) were used as data collection forms. The descriptive data form was prepared by the researchers with the literature and consisted of 25 questions (age, sex, marital status, educational status, body mass index (BMI), smoking and alcohol use, clinical diagnosis, previous surgical intervention, systemic diseases, medications used continuously, preoperative hospital stay, postoperative day, intensive care unit stay, American Society of Anesthesiologists (ASA) score, duration of surgery, type and duration of anesthesia, time to first mobilization, nutritional deficiency, and analgesics used postoperatively). The MMSE was developed by Folstein et al. (1975) (10). The Turkish validity and reliability study was conducted by Güngen et al. (2002) (11). The MMSE consists of categories of recording memory, orientation, attention and calculation, recall, and language. Each question is worth 1 point, and the total score is 30 points. People with scores of 24 or higher are considered to be in normal health, while a score of 23 and below is considered an indicator of cognitive impairment (11). The kappa value of MMSE was determined as 0.92 in the study of Güngen et al. (11). PORI was developed by Butler et al. (2012) and consists of 25 items (12). Its Turkish validity and reliability was conducted by Cengiz and Aygin (2019) (13). It has 5 subdimensions: psychological symptoms, physical activities, general symptoms, bowel symptoms, and appetite symptoms. Scores of the items included in the subdimensions are summed, their averages are calculated, and their subdimension scores are determined. For the PORI total score, all of the items scores are summed and their average is calculated. High scores from the index indicate more difficulty in postoperative recovery, while low scores indicate that postoperative recovery is easier (13) (Figure 1). The Cronbach's alpha value of PORI was determined as 0.96 in the study of Cengiz and Aygin (13). In our study, Cronbach's alpha coefficient was found to be 0.817.

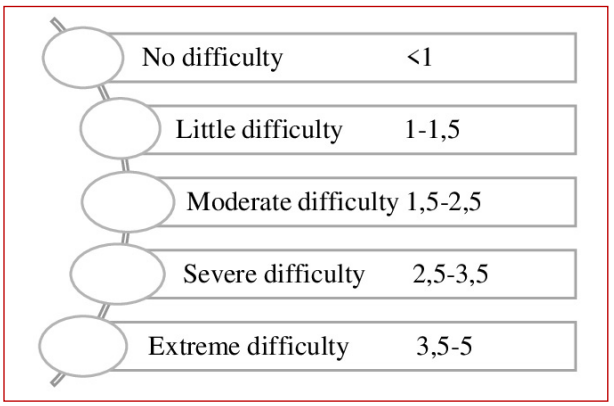



**Figure 1.** Scoring system for the PORI total score and subdimension scores.

### Data Collection

The data of the study were collected via face-to-face interviews with geriatric patients who underwent major surgical interventions for cardiovascular issues, orthopedics, and general surgery and who were in the 48–72-hour postoperative period. Intraoperative information (type and duration of anesthesia, duration of surgery, ASA score) was obtained from the patient file. The average data collection time was 20–25 minutes.

### Statistical Analysis

IBM SPSS Statistical Package for Social Sciences 24 (IBM SPSS, New York, USA) was used for statistical data analysis. Frequency tables and descriptive statistics were used to interpret the findings. In descriptive statistics, number (n) and percentage (%) were calculated for categorical data, and mean, standard deviation, median, and minimum and maximum values were calculated for continuous variables. The Kolmogorov-Smirnov test was performed to determine whether the data were suitable for normal distribution. The Mann-Whitney U and Kruskal-Wallis tests were used for two group comparisons. The chi-square test was used to determine the



difference between groups. It was established that there was no missing data among those obtained. In addition, Pearson correlation analysis was performed to examine the relationship between the variables. Statistical significance was accepted at $p< .05$ in all of the analyses performed in this study.

### Ethical considerations

Prior to data collection, ethics committee approval (decision dated 22.12.2021 and numbered 2021/17-17) was obtained from the Non-Interventional Clinical Research Ethics Committee of the university, and institutional permission (decision dated 29.11.2021 and numbered 2021/126) was obtained from the hospital. Written and verbal consent were obtained from the patients, and the study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

## RESULTS

The mean age of the patients participating in the study was 69.70±4.81 years, the mean duration of surgery was and the mean duration of anesthesia was. It was determined that 62.4% of the patients were female, 67.6% were married, and 72.8% had a first mobilization time of more than 24 hours.

The total PORI score of the patients was 2.29±0.33, and it was determined that they had moderate difficulty in recovery. The mean MMSE score was 24.71±3.07, and 40% of the patients were at risk of cognitive impairment (Table 1).

When the age groups of the patients and MMSE scores were compared, the MMSE scores of those in the 65–69-year age group were higher than those in the ≥75-year age group ($p< .05$). When the sex of the patients and MMSE scores were compared, the MMSE scores of men were higher than those of women ($p< .05$). When the educational attainment of the patients and MMSE scores were compared, the MMSE scores of those with high school and higher educational attainment were significantly higher than those with literate and primary education ($p< .05$) (Table 2).

**Table 1.** Distribution of Scale Scores (N=250)

| Scale | | Mean±S.S | Min | Max |
|---|---|---|---|---|
| **Postoperative Recovery Index** | Psychological Symptoms | 1.53±0.42 | 1.0 | 3.8 |
| | Physical Activities | 3.96±0.60 | 2.4 | 5.0 |
| | General Symptoms | 1.54±0.74 | 1.0 | 5.0 |
| | Bowel Symptoms | 1.22±0.52 | 1.0 | 4.0 |
| | Appetite Symptoms | 1.80±0.63 | 1.0 | 4.0 |
| | **PORI - Total** | 2.29±0.33 | 1.5 | 3.6 |
| **Mini-Mental State Examination** | | 24.71±3.07 | 15.0 | 30.0 |
| | | **Number** | **Percentage** | |
| Risk of cognitive impairment* | | 100 | 40 | |
| No risk of cognitive impairment | | 150 | 60 | |

* MMSE score less than 23

**Table 2.** Comparison of Sociodemographic Characteristics of Patients with Scale Scores

| | | | | MMSE | | PORI | |
|---|---|---|---|---|---|---|---|
| **Variable** | | **n** | **%** | **x̄ ± s.s** | **Median [IR]** | **x̄ ± s.s** | **Median[IR]** |
| **Age** | 65-69 (1) | 149 | 59.6 | 25.7 ± 3.04 | 25.0 [6.0] | 2.26 ± 0.32 | 2.2 [0.4] |
| | 70-74 (2) | 59 | 23.6 | 24.76 ± 2.86 | 24.0 [5.0] | 2.34 ± 0.36 | 2.3 [0.4] |
| | ≥75 (3) | 42 | 16.8 | 23.36 ± 3.15 | 23.0 [4.0] | 2.31 ± 0.33 | 2.3 [0.5] |
| | **Statistical analysis** | | | $\chi^2$ =8.253 **p=0.016 [1-3]** | | $\chi^2$ =2.102 p=0.350 | |
| **Sex** | Woman | 156 | 62.4 | 24.27 ± 2.87 | 24.0 [4.0] | 2.28 ± 0.33 | 2.3 [0.4] |
| | Male | 94 | 37.6 | 25.45 ± 3.28 | 26.0 [5.0] | 2.29 ± 0.35 | 2.2 [0.4] |
| | **Statistical analysis** | | | Z=-2.961 **p=0.003** | | Z=-0.093 p=0.926 | |
| **Martial Status** | Married | 169 | 67.6 | 24.78 ± 3.19 | 25.0 [6.0] | 2.29 ± 0.32 | 2.3 [0.4] |
| | Single | 81 | 32.4 | 24.57 ± 2.83 | 24.0 [4.0] | 2.28 ± 0.35 | 2.2 [0.4] |
| | **Statistical analysis** | | | Z=-0.396 p=0.692 | | Z=-0.591 p=0.554 | |
| **Education level** | Literate (1) | 211 | 84.4 | 24.41 ± 3.02 | 24.0 [5.0] | 2.28 ± 0.34 | 2.2 [0.4] |
| | Elementary (2) | 20 | 8.0 | 25.10 ± 2.71 | 25.5 [5.0] | 2.37 ± 0.32 | 2.2 [0.5] |
| | High school (3) | 19 | 7.6 | 27.63 ± 2.52 | 28.0 [3.0] | 2.26 ± 0.29 | 2.2 [0.3] |
| | **Statistical analysis** | | | $\chi^2$ =18.476 **p=0.001 [1.2-3]** | | $\chi^2$ =1.256 p=0.534 | |
| **BMI classes** | Normal | 48 | 19.2 | 24.15 ± 3.28 | 24.0 [6.0] | 2.29 ± 0.31 | 2.3 [0.5] |
| | Overweight | 83 | 33.2 | 24.61 ± 3.24 | 24.0 [5.0] | 2.29 ± 0.37 | 2.2 [0.4] |
| | Obese | 119 | 47.6 | 25.01 ± 2.85 | 25.0 [5.0] | 2.28 ± 0.32 | 2.3 [0.4] |
| | **Statistical analysis** | | | $\chi^2$ =0.678 p=0.410 | | $\chi^2$ =0.025 p=0.875 | |
| **Smoking** | Yes | 27 | 10.8 | 25.19 ± 3.31 | 24.0 [7.0] | 2.30 ± 0.41 | 2.2 [0.5] |
| | No | 223 | 89.2 | 24.65 ± 3.05 | 25.0 [5.0] | 2.29 ± 0.32 | 2.2 [0.4] |
| | **Statistical analysis** | | | Z=-0.811 p=0.417 | | Z=-0.203 p=0.839 | |
| **Alcohol** | Yes | 6 | 2.4 | 26.33 ± 2.42 | 27.0 [5.0] | 2.21 ± 03.6 | 2.2 [0.6] |
| | No | 244 | 97.6 | 24.67 ± 3.08 | 24.0 [5.0] | 2.29 ± 0.33 | 2.2 [0.4] |
| | **Statistical analysis** | | | Z=-1.352 p=0.176 | | Z=-0.489 p=0.647 | |

MMSE: Mini-Mental State Examination, PORI: Postoperative Recovery Index

When the PORI scores of the patients were compared with the clinics they were treated in, the PORI scores of the patients treated in CVS were higher than those of those treated in orthopedics and general surgery (p< .05). When the intensive care hospitalization status and PORI scores of the patients were compared, the scores of those with intensive care hospitalization were higher (p< .05). When the duration of initial mobilization and PORI scores of the patients were compared, the PORI scores of those who were mobilized after more than 24 hours were higher than other groups (p< .05). When the risk of malnutrition was compared with the PORI scores of the patients, the PORI scores of those with malnutrition risk were higher (p< .05). No statistically significant difference was found between the clinical and operative characteristics of the patients and the mean MMSE scores (p> .05) (Table 3).



**Table 3.** Comparison of Clinical Characteristics of Patients and Scale Scores

| | | | | MMSE | | PORI | |
|---|---|---|---|---|---|---|---|
| **Variable** | | **n** | **%** | **$\bar{x}$ ± s.s** | **Median [IR]** | **$\bar{x}$ ± s.s** | **Median[IR]** |
| **Clinic** | Orthopedics (1) | 185 | 74.0 | 24.65 ± 3.00 | 25.0 [5.0] | 2.27 ± 0.32 | 2.2 [0.4] |
| | General surgery (2) | 33 | 13.2 | 25.24 ± 3.29 | 25.0 [5.0] | 2.22 ± 0.33 | 2.2 [0.5] |
| | Cardiovascular sur(3) | 32 | 12.8 | 24.50 ± 3.32 | 24.0 [7.0] | 2.49 ± 0.33 | 2.5 [0.3] |
| | **Statistical analysis** | | | $\chi^2$ =1.236 p=0.539 | | $\chi^2$ =14.240 **p=0.001 [1.2-3]** | |
| **Systemic disease** | No | 44 | 17.6 | 25.45 ± 3.17 | 26.0 [5.0] | 2.23 ± 0.37 | 2.1 [0.4] |
| | Yes | 206 | 82.4 | 24.55 ± 3.04 | 24.0 [5.0] | 2.30 ± 0.33 | 2.3 [0.4] |
| | **Statistical analysis** | | | Z=-1.772 p=0.076 | | Z=-1.740 p=0.082 | |
| **History of surgery** | Yes | 205 | 82.0 | 24.63 ± 2.96 | 24.0 [5.0] | 2.29 ± 0.33 | 2.3 [0.4] |
| | No | 45 | 18.0 | 25.07 ± 3.58 | 25.0 [7.0] | 2.26 ± 0.33 | 2.2 [0.5] |
| | **Statistical analysis** | | | Z=-0.928 p=0.354 | | Z=-0.750 p=0.453 | |
| **Which day** | Postop 2nd day | 153 | 61.2 | 24.69 ± 2.98 | 24.0 [5.0] | 2.26 ± 0.34 | 2.2 [0.4] |
| | Postop 3rd day | 97 | 38.8 | 24.74 ± 3.23 | 25.0 [6.0] | 2.33 ± 0.33 | 2.4 [0.5] |
| | **Statistical analysis** | | | **Z=-0.143 p=0.886** | | Z=-2.321 **p=0.020** | |
| **Stay in ICU** | No | 109 | 43.6 | 24.61 ± 2.77 | 24.0 [5.0] | 2.18 ± 0.32 | 2.1 [0.4] |
| | Yes | 141 | 56.4 | 24.79 ± 3.30 | 25.0 [6.0] | 2.38 ± 0.32 | 2.4 [0.4] |
| | **Statistical analysis** | | | Z=-0.599 p=0.549 | | Z=-5.196 **p=0.001** | |
| **ASA** | II (1) | 107 | 42.8 | 24.96 ± 2.84 | 25.0 [4.0] | 2.19 ± 0.31 | 2.2 [0.4] |
| | III (2) | 143 | 57.2 | 24.42 ± 3.20 | 24.0 [5.0] | 2.35 ± 0.33 | 2.4 [0.4] |
| | **Statistical analysis** | | | Z=-1.774 p=0.074 | | Z=-3.184 **p=0.001** | |
| **Type of anesthesia** | General (1) | 80 | 32.0 | 25.01 ± 3.22 | 24.5 [6.0] | 2.35 ± 0.35 | 2.4 [0.4] |
| | spinal (2) | 126 | 50.4 | 24.76 ± 3.15 | 25.0 [5.0] | 2.23 ± 0.29 | 2.2 [0.4] |
| | Combined (3) | 44 | 17.6 | 24.02 ± 2.46 | 24.0 [4.0] | 2.34 ± 0.38 | 2.3 [0.5] |
| | **Statistical analysis** | | | $\chi^2$ =3.091 p=0.213 | | $\chi^2$ =6.956 **p=0.031 [1-2]** | |
| **First mobilization** | 12 hours and under(1) | 14 | 5.6 | 25.50 ± 3.59 | 26.5[7.0] | 2.01 ± 0.28 | 2,0 [0,4] |
| | 13-24 hours (2) | 54 | 21.6 | 24.63 ± 2.70 | 24.0[4.0] | 2.15 ± 0.31 | 2,1 [0,3] |
| | Over 24 hours (3) | 182 | 72.8 | 24.68 ± 3.14 | 24.5[6.0] | 2.35 ± 0.32 | 2,3 [0,4] |
| | **Statistical analysis** | | | $\chi^2$ =0.920 p=0.631 | | $\chi^2$ =28.577 **p=0.002 [1.2-3]** | |
| **Analgesic use** | Opioid | 39 | 15.6 | 25.13 ± 3.35 | 25.0[5.0] | 2.27 ± 0.44 | 2,3 [0,6] |
| | Non-Opioid | 105 | 42.0 | 24.79 ± 3.11 | 25.0[6.0] | 2.25 ± 0.36 | 2,2 [0,4] |
| | Both of them | 106 | 42.4 | 24.48 ± 2.94 | 24.0[4.0] | 2.33 ± 0.25 | 2,3 [0,4] |
| | **Statistical analysis** | | | $\chi^2$ =1.794 p=0.408 | | $\chi^2$ =5.786 p=0.055 | |
| **Risk of malnutrition** | Yes* | 61 | 24.4 | 24.84 ± 3.20 | 24.0[6.0] | 2.47 ± 0.41 | 2,5 [0,5] |
| | No | 189 | 75.6 | 24.67 ± 3.04 | 25.0[5.0] | 2.23 ± 0.28 | 2,2 [0,4] |
| | **Statistical analysis** | | | Z=-0.354 p=0.723 | | Z=-4.491 **p=0.001** | |

MMSE: Mini-Mental State Examination, PORI: Postoperative Recovery Index

**Table 4.** Examination of the Relationships between the Cognitive Level, Recovery State and the Factors Related to the Operation Characteristics

| Correlation (N=250) | | Mini-Mental State Examination | Postoperative Recovery Index |
|---|---|---|---|
| **Preoperative hospital stay** | *r* | -0.038 | 0.233 |
| | *p* | 0.550 | **0.001** |
| **Intensive care stay** | *r* | 0.052 | 0.334 |
| | *p* | 0.415 | **0.001** |
| **Duration of surgery** | *r* | 0.066 | 0.158 |
| | *p* | 0.299 | **0.012** |
| **Duration of anesthesia** | *r* | 0.022 | 0.175 |
| | *p* | 0.728 | **0.005** |
| **Age** | *r* | -0.201 | 0.131 |
| | *p* | **0.001** | **0.038** |

r: Spearman correlation

There was a negative, very weak, but statistically significant relationship between MMSE scores and age ($p< .05$). A positive, very weak/weak, and statistically significant correlation was found between the PORI scores of the patients and preoperative hospitalization day, intensive care stay, duration of surgery, duration of anesthesia, and age ($p< .05$) (Table 4).

A negative, very weak, but statistically significant correlation was found between MMSE and PORI scores ($p< .05$) (Table 5).

**Table 5.** Examination of the Relationship between the Cognitive Level and Recovery State

| Correlation (N=250) | | Postoperative Recovery Index |
|---|---|---|
| **Mini-Mental State Examination** | r | -0.124 |
| | p | **0.049** |

r: Spearman correlation

## DISCUSSION

The mean MMSE was 24.71±3.07, and 40% of the patients were at risk of cognitive impairment. In addition, it was determined that the risk of cognitive impairment increased as the age of the patients increased. Previous studies have also reported a decline in cognitive function-based abilities in geriatric individuals with advanced age (7,14). Cognitive changes have also been reported in patients undergoing surgical intervention (15,16). It has been reported that the incidence of cognitive changes in elderly patients undergoing major surgery varies between 20–90% (17,18,19). While these results can be explained as a physiological consequence of aging, surgery-related (neuro) inflammation has also been reported to play an important role in the development of cognitive decline (20). Conditions such as pain, lack of sleep, visual or physical impairment, dehydration, hypoxia, hypercapnia, hypotension, hyperglycemia, unbalanced nutrition, electrolyte imbalance, and blood loss may also cause changes



in cognitive function in geriatric individuals after surgery (15,17).

In this study, it was determined that the patients' postoperative recovery level was at medium difficulty. Although the studies conducted with geriatric individuals undergoing major surgical intervention in the literature are very limited, it is stated that patients in parallel with our study have difficulties in the recovery process during the postoperative period (2,9,13). The postoperative recovery process is complicated by changes in physiological and psychological status and the risk of side effects. It was determined this study that postoperative recovery became more difficult as the patient age increased. Similarly, it has been reported in the literature that recovery becomes more difficult with increasing age (9,21,22). It is thought that psychological-physiological problems and a lack of social support for geriatric patients negatively affect recovery. In this study, as the preoperative hospitalization days of the patients increased, their postoperative recovery was negatively affected. In the study of Ansari et al. (2019), reported that the risk of surgical site infection increased with the long duration of hospitalization during the preoperative period (23). It is thought that the possible flora in the hospital may cause opportunistic infections, especially in older fragile patients, and may negatively affect the postoperative process of these patients.

It was found that patients who underwent cardiovascular surgery and had postoperative intensive care hospitalization had a more difficult recovery process. Geriatric patients are mostly followed up in intensive care due to respiratory failure and cardiovascular diseases and these diseases make recovery difficult and increase mortality (6). Yolcu et al. (2015) also reported that patients who underwent cardiovascular surgery recovered with more difficulty (21). It is thought that the prolonged duration of cardiovascular surgery, use of a heart-lung machine, cross-clamping times, the presence of wounds on the leg and sternum where the saphenous vein was removed, and intensive care hospitalization make it difficult for cardiovascular surgery patients to recover. Additionally, these patients also have chronic diseases. The presence of chronic diseases in geriatric patients increases the ASA score. In the study, a high ASA score was found to more difficult the recovery process. Butler et al. (2012) reported that ASA score affects the patient's recovery process in the postoperative period (16). The presence of comorbidities in most geriatric patients causes high ASA scores and adversely affects their recovery process. This situation delays wound healing and mobilization of patients and increases the need for intensive care. It is also known that patients with high ASA scores are more affected by the negative effects of general anesthesia. In the study found that those with a longer duration of anesthesia and those who underwent general anesthesia recovered more difficulty. It has been reported in the literature that geriatric individuals are more sensitive to anesthetics and more susceptible to postoperative complications, making recovery difficult (6). Moreover it has been reported that the complication rate is higher in patients undergoing general anesthesia and that their duration of intensive care and hospital stay is longer (16). General anesthesia is thought to cause difficulty in the recovery process because it affects all systems and increases the risk of complications. Another factors that negatively affects the recovery process are late mobilization and nutritional deficiency. In total, 72.8% of our patients first mobilized after the first 24 hours during the postoperative period. In the study, it was determined that geriatric patients with a mean score of 3.96±0.60 in the PORI physical activities subscale had the most difficulty in performing physical activities. It was also determined that patients who first mobilized after more than 24 hours had a more difficult recovery than those who first mobilized within a shorter period. Ladurner et al. (2022) found that the earlier mobilization of 237 geriatric patients who underwent femoral neck fracture

surgery reduced postoperative complications (24). Aydın Çil and Yayla (2021) found that the risk of malnutrition in orthopedic surgery patients caused the development of postoperative complications (5). In addition Nogueira et al. (2022) reported that a protein-rich diet accelerated recovery in the postoperative period (25). Since early mobilization and nutrition are positively affects the healing process, patients' mobilization and nutrition should be supported.

In this study, the cognitive level of patients decreases, the postoperative recovery process becomes more difficult. Geriatric individuals in the postoperative period may experience difficulties during the recovery process due to physical limitations, pain, and inability to perform self-care. In addition, cognitive change also negatively affects the recovery process of geriatric individuals. During the aging process, the duration of physical and mental reactions increases and there is a change in cognitive processes (7). The learning process of geriatric individuals changes and they need additional time for learning (7). In addition, loss of concentration and memory is observed in geriatric individuals (8). All these situations may negatively affect the care of individuals who have undergone surgery and their ability to manage the postoperative recovery process. Therefore, the cognitive levels of geriatric patients undergoing surgical intervention should be evaluated with standard tests.

## CONCLUSION

In conclusion, in this study, approximately half of the patients were at risk of cognitive impairment, which negatively affected the postoperative recovery process. It was determined that the postoperative recovery process is difficult, and factors such as ASA score, type and duration of anesthesia, and modifiable risk factors, including nutrition and mobilization, affect this process. Nursing care should be planned in line with evidence-based practices by determining the factors that will negatively affect the recovery process after surgical intervention. A comprehensive preoperative evaluation of geriatric patients, provision of optimal nutrition, and early mobilization during the postoperative period will positively affect the recovery process. In-service training on the care of geriatric patients is recommended for healthcare professionals.

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ORIGINAL ARTICLE

# ASSESSING THE NUTRITIONAL STATUS OF COMMUNITY-DWELLING ELDERLY REGISTERED WITH FAMILY MEDICINE CENTERS

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## Abstract

**Introduction:** Malnutrition is a serious health problem that threatens the health of individuals, with a prevalence rate of 5–15% among community-dwelling elderly people. This study aimed to assess the prevalence of malnutrition among community-dwelling elderly people in primary care using the Mini Nutritional Assessment test and to analyse its relationship with sociodemographic characteristics and geriatric syndromes.

**Materials and Method:** Data of 248 out of 826 elderly patients registered at family medicine centers were analyzed. Malnutrition was assessed using the Mini Nutritional Assessment test, and sociodemographic characteristics and geriatric syndromes were assessed using an interviewer-administered questionnaire.

**Results:** This study included 248 participants aged 72.51±5.85 years, 50.4% (n=125) of whom were males. The Mini Nutritional Assessment results showed that 85.9% (n=213) had a normal nutritional status and 14.1% (n=35) were malnourished or at risk of malnutrition. Malnutrition was statistically significantly associated with income status (p =0.003), body mass index (p =0.002), hearing and vision loss (p =0.011; p ≤0.049, respectively), history of falls (p =0.001), oral health (p =0.001), and polypharmacy (p =0.010).

**Conclusion:** Malnutrition rates are low among community-based elderly individuals in family medicine centers. To prevent malnutrition and its related diseases, family medicine physicians play an important role in facilitating early screening, and thus minimizing the risk of increased malnutrition rates increase and irreversible damage. So Mini Nutritional Assessment should be applied at primary health care.

***Keywords:*** Malnutrition; Aged; Primary Health Care.

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## INTRODUCTION

Malnutrition in elderly is a nutritional concern; it is exacerbated by increasing obesity rates, leading to health decline, reduced quality of life, diminished functionality, increased health costs, and prolonged hospitalization. Significant improvements in cognitive and physical functions and health-related quality of life have been observed when malnutrition is identified early and effectively treated, underscoring the importance of addressing malnutrition and its risk in community-dwelling elderly (1). Malnutrition is a condition in which body structure and function are adversely affected by impaired nutrient utilization due to inadequate or excessive intake of energy and essential nutrients (e.g., proteins, carbohydrates, vitamins, minerals). Malnutrition is a serious health problem that threatens the health of individuals, and previous studies have reported a rate of 5–15% among community-dwelling elderly people, approximately 40% among hospitalized elderly, and an increase to 85% among those in nursing homes (2,3). Geriatric syndromes are in a vicious cycle of malnutrition, and malnutrition and its risk should be detected early to break this cycle (4). The European Society of Clinical Nutrition and Metabolism (ESPEN) recommends the Mini Nutritional Assessment (MNA) test to detect malnutrition and its risk. The MNA has been reported to detect prevalence rates of 2% and 24% for malnutrition and its risk, respectively (5). Moreover, Sarıkaya et al. showed that the MNA test could be used in Turkish older adults. In addition, the sensitivity and specificity have been reported as 92% and 86% for the MNA, respectively, and 94% and 81% for its short-form (MNA-SF), respectively (6). This study aimed to assess the prevalence of malnutrition among community-dwelling elderly people in primary care using the MNA and to analyse its relationship with sociodemographic characteristics and geriatric syndromes.

## MATERIALS AND METHOD

### Participants

This cross-sectional and descriptive study included 826 patients aged ≥65 years who registered at Family Health Center in two different districts and volunteered to participate in the study. Based on a power analysis with 95% reliability, 5% margin of error, and 15% prevalence, at least 159 patients were required for this study.

The patients were categorized into three age groups: young (65–74 years), old (75–84 years), and very old (≥85 years) elderly, and were evaluated by two physicians. Body mass index (BMI, kg/m$^2$) was calculated and categorized as normal (18.5–24 kg/m$^2$), overweight/pre-obesity (25–30 kg/m$^2$), class 1 obesity (30–34 kg/m$^2$), class 2 obesity (35–39 kg/m$^2$), and class 3 obesity/morbid obesity (> 40 kg/m$^2$) (7).

The MNA tests were applied to the participants, while a face-to-face interviews were was conducted using questionnaires comprising sociodemographic characteristics and geriatric syndromes. Patients who refused to participate or were diagnosed with severe psychiatric illnesses were excluded.

### Data collection

The MNA-SF, which comprises six items inquiring about appetite status, weight loss, mobility, psychological stress, acute disease, and BMI, was applied first. This form had a total score of 14 points, with a score >12 indicating the absence of malnutrition, 8–11 indicating malnutrition risk, and <7 indicating the presence of malnutrition. If the MNA-SF score is 11 and below, it indicates undernutrition status and the long form of test (MNA-LF) should be performed (8). The long form of the test, which comprises 12 items assessing bed dependency, polypharmacy, number of meals, pressure sores, independent living status, type of food consumed, amount of water consumed daily, and anthropometric measurements, was determined to participants with MNA-SF score

<12 points. The MNA-LF had a total score of 30 points, with a score ≥24 indicating the absence of malnutrition, 17–24 indicating malnutrition risk, and <17 indicating the presence of malnutrition.

Oral health examinations included oral cavity hygiene (e.g., tooth brushing and tooth stones), pain in the oral cavity, presence of mouth sores, and three or more missing or decayed teeth. Patients with prosthetic teeth and no complications were considered to have good oral health.

### Ethical approval statement

This study was approved by the Provincial Health Directorate and Clinical Research Ethics Committee (approval number: 23-KAEK-004). Written informed consent was obtained from all the participants.

### Statistical analysis

All statistical analyses were performed using the IBM SPSS Statistics 22. In addition to descriptive statistical methods (mean, standard deviation, and frequency), the chi-square, Fisher's Exact chi-square, and Fisher–Freeman–Halton Exact chi-square tests were used to compare qualitative data. Statistical significance was set at P <0.05.

## RESULTS

This study included 248 participants (125 males [50.4%] and 123 females [49.6%]). The mean age of the participants were 72.51±5.85 (65-95) years: 64.9% (young elderly), 31.5% (old elderly), and 3.6% (very old elderly). Regarding BMI, 21.4%, 45.2%, and 33.4% had normal weight, overweight, and obesity, respectively. Of those with obesity, 26.6%, 6%, and 0.8% had class 1, class 2, and class 3 (morbid) obesity. Most of the participants were married (77%), a majority (61.3%) had primary school education, and very few (8.9%) were active smokers. Out of total, 66.9% had a balanced income and expenses, while 14.9% had more expenses than income. Only a few of the participants (9.7%) were living alone, while approximately one-quarter (26.6%) with an extended family (e.g., son-daughter and grandchildren).

Hearing loss, vision loss, falls history, and fracture history were reported by 35.5%, 42.3%, 19%, and 2.6% of the participants, respectively. While 59.3% participants had good oral health, 40.7% had poor oral health, and dentures were used by 62.5% of the participants. Less than a quarter (24.6%) received help while eating and shopping, and only 4.8% of the participants had a history of hospitalization. The most common co-morbidity was hypertension (70.2%), followed by diabetes (34.3%), mental illness (22.6%), osteoporosis (10.1%), cerebrovascular disease (6%), and cancer (2.4%). Polypharmacy was present in more than half of the participants (52.8%).

Participants' responses to the MNA-SF are presented in Table 1. The MNA-SF scores ranged from 2 to 14 (mean 12.7±1.73 and median 13). The results showed that most of the participants (85.9%) had a normal nutritional status, 12.5% had a risk of malnutrition, and 1.6% had malnutrition. The MNA-LF was applied to 35 patients who scored <12 on the MNA-SF. The MNA-LF scores ranged from 10 to 25.5 (mean 20.63±3.73 and median 21.5). The results showed that most of the participants (74.3%) in the risk category of the MNA-SF were at risk of malnutrition, 14.3% had a normal nutritional status, and 11.4% were malnourished.

As shown in Table 2, no statistically significant differences were observed in nutritional status across the age group, gender, marital status, educational level, and smoking status categories (p >0.05). There was a statistically significant difference in income status and BMI classification according to nutritional status (p =0.003 and p =0.002, respectively). The rate of malnutrition in individuals with normal weight (7.5%) was significantly lower than that in those with overweight, obesity class 1, obesity class 2, and morbid obesity. Malnutrition risk rate was significantly higher in those whose



**Table 1.** Evaluation of MNA-SF test questions

| | | N (248) | % |
|---|---|---|---|
| **Food intake** | severe decrease | 3 | 1.2 |
| | moderate | 35 | 14.1 |
| | no decrease | 210 | 84.7 |
| **Weight loss** | > 3 kg | 4 | 1.6 |
| | unknown | 3 | 1.2 |
| | 1–3 kg | 29 | 11.7 |
| | none | 212 | 85.5 |
| **Mobility** | bed or chair bound | 1 | 0.4 |
| | able to get out of bed | 23 | 9.3 |
| | goes out | 224 | 90.3 |
| **Acute illness** | yes | 33 | 13.3 |
| | no | 215 | 86.7 |
| **Neuropsychological problems** | severe dementia | 9 | 3.6 |
| | mild dementia | 89 | 35.9 |
| | none | 150 | 60.5 |
| **Body mass index (kg/m$^2$)** | < 19 | 2 | 0.8 |
| | 19 ≤ BMI* < 21 | 2 | 0.8 |
| | 21 ≤ BMI* < 23 | 24 | 9.7 |
| | ≥ 23 | 220 | 88.7 |
| **MNA-SF**** | ≥ 12 | 213 | 85.9 |
| | 8≤ Risky ≤ 11 | 31 | 12.5 |
| | ≤ 7 | 4 | 1.6 |
| **MNA-LF*** (n=35)** | ≥ 24 | 5 | 14.3 |
| | 17 ≤ Risky < 24 | 26 | 74.3 |
| | < 17 | 4 | 11.4 |

*BMI: body mass index; **MNA-SF: short form of the mini nutritional assessment, ***MNA-LF: long form of the mini nutritional assessment

expenditures were higher than their income (18.9%) than those in those whose income was higher than their expenditures (4.4%).

Table 3 shows the nutritional status of the patients according to their health records. The rate of malnutrition risk was significantly higher in patients with hearing and vision loss (20.5% and 17.1%, respectively) than in those without hearing and vision loss (8.1% and 9.1%; respectively; p = 0.011 and p ≤0.049, respectively).

The rates of malnutrition risk and malnutrition were significantly higher in participants with a history of falls (29.8% and 6.4%, respectively) than in those without (8.5% and 0.5%, respectively; P = 0.001), with no statistically significant difference between patients with and without a history of fractures (p >0.05).

The proportion of participants with poor oral health (21.8%) was significantly higher than that of participants with good oral health (6.1%) (p =0.001).

**Table 2.** Evaluation of nutritional status according to demographic characteristics

| | | MNA-SF ≥12 | 8≤MNA-SF ≤11 | MNA-SF ≤7 | |
|---|---|---|---|---|---|
| | | n (%) | n (%) | n (%) | p |
| **Age groups** | Young elderly | 145 (90.1%) | 14 (8.7%) | 2 (1.2%) | |
| | Old elderly | 61 (78.2%) | 15 (19.2%) | 2 (2.6%) | 0.073* |
| | Very old elderly | 7 (77.8%) | 2 (22.2%) | 0 (0%) | |
| **BMI** | Normal | 38 (71.7%) | 11 (20.8%) | 4 (7.5%) | |
| | Pre-obesity | 99 (88.4%) | 13 (11.6%) | 0 (0%) | |
| | Obesity class 1 | 62 (93.9%) | 4 (6.1%) | 0 (0%) | **0.002**** |
| | Obesity class 2 | 13 (86.7%) | 2 (13.3%) | 0 (0%) | |
| | Morbidly obesity | 1 (50%) | 1 (50%) | 0 (0%) | |
| **Gender** | Male | 109 (87.2%) | 13 (10.4%) | 3 (2.4%) | 0.387*** |
| | Female | 104 (84.6%) | 18 (14.6%) | 1 (0.8%) | |
| **Marital status** | Married | 165 (86.4%) | 23 (12%) | 3 (1.6%) | |
| | Single | 3 (100%) | 0 (0%) | 0 (0%) | 0.863* |
| | Widow | 45 (83.3%) | 8 (14.8%) | 1 (1.9%) | |
| **Education** | İlliterate | 68 (84%) | 11 (13.6%) | 2 (2.5%) | |
| | Primary school | 130 (85.5%) | 20 (13.2%) | 2 (1.3%) | 0.798** |
| | High school | 7 (100%) | 0 (0%) | 0 (0%) | |
| | University | 8 (100%) | 0 (0%) | 0 (0%) | |
| **Smoking** | Yes | 20 (90.9%) | 1 (4.5%) | 1 (4.5%) | |
| | No | 143 (85.1%) | 22 (13.1%) | 3 (1.8%) | 0.459* |
| | Quit | 50 (86.2%) | 8 (13.8%) | 0 (0%) | |
| **Income status** | Income > exes | 42 (93.3%) | 2 (4.4%) | 1 (2.2%) | |
| | Income = exes | 144 (86.7%) | 22 (13.3%) | 0 (0%) | 0.003* |
| | Income < exes | 27 (73%) | 7 (18.9%) | 3 (8.1%) | |
| **Household** | Alone | 21 (87.5%) | 3 (12.5%) | 0 (0%) | |
| | Nuclear family | 140 (88.6%) | 15 (9.5%) | 3 (1.9%) | 0.280* |
| | Extended family | 52 (78.8%) | 13 (19.7%) | 1 (1.5%) | |

*Fisher's Exact test, **Chi-square test, ***Fisher–Freeman–Halton Exact test, MNA-SF: short form of mini nutritional assessment

**Table 3.** Assessment of nutritional status according to health records *

| | | MNA-SF ≥12 | 8≤MNA-SF≤11 | MNA-SF ≤7 | |
|---|---|---|---|---|---|
| | | n (%) | n (%) | n (%) | p |
| **Deafness** | Yes | 68 (77.3%) | 18 (20.5%) | 2 (2.3%) | **0.011** |
| | No | 145 (90.6%) | 13 (8.1%) | 2 (1.3%) | |
| **Vision loss** | Yes | 84 (80%) | 18 (17.1%) | 3 (2.9%) | **0.049** |
| | No | 129 (90.2%) | 13 (9.1%) | 1 (0.7%) | |
| **Falling history** | Yes | 30 (63.8%) | 14 (29.8%) | 3 (6.4%) | **0.001** |
| | No | 183 (91%) | 17 (8.5%) | 1 (0.5%) | |
| **Fracture history** | Yes | 7 (77.8%) | 2 (22.2%) | 0 (0%) | 0,414 |
| | No | 206 (86.2%) | 29 (12.1%) | 4 (1.7%) | |
| **Oral health** | Good | 137 (93.2%) | 9 (6.1%) | 1 (0.7%) | **0.001** |
| | Bad | 76 (75.2%) | 22 (21.8%) | 3 (3%) | |
| **Dentures** | Yes | 133 (85.8%) | 19 (12.3%) | 3 (1.9%) | 1.000 |
| | No | 80 (86%) | 12 (12.9%) | 1 (1.1%) | |
| **Assistance with meals and shopping** | Yes | 41 (67.2%) | 16 (26.2%) | 4 (6.6%) | **0.001** |
| | No | 172 (92%) | 15 (8%) | 0 (0%) | |
| **Hospitalization (in last 3 months)** | Yes | 3 (25%) | 6 (50%) | 3 (25%) | **0.001** |
| | No | 210 (89%) | 25 (10.6%) | 1 (0.4%) | |
| **Diabetes** | Yes | 70 (82.4%) | 14 (16.5%) | 1 (1.2%) | 0.375 |
| | No | 143 (87.7%) | 17 (10.4%) | 3 (1.8%) | |
| **Hypertension** | Yes | 149 (85.6%) | 23 (13.2%) | 2 (1.1%) | 0.623 |
| | No | 64 (86.5%) | 8 (10.8%) | 2 (2.7%) | |
| **Hyperlipidemia** | Yes | 59 (85.5%) | 9 (13%) | 1 (1.4%) | 0.930 |
| | No | 154 (86%) | 22 (12.3%) | 3 (1.7%) | |
| **Cerebrovascular diseases** | Yes | 11 (73.3%) | 3 (20%) | 1 (6.7%) | 0.122 |
| | No | 202 (86.7%) | 28 (12%) | 3 (1.3%) | |
| **Osteoporosis** | Yes | 23 (92%) | 2 (8%) | 0 (0%) | 0.837 |
| | No | 190 (85.2%) | 29 (13%) | 4 (1.8%) | |
| **Cancer** | Yes | 3 (50%) | 1 (16.7%) | 2 (33.3%) | **0.001** |
| | No | 210 (86.8%) | 30 (12.4%) | 2 (0.8%) | |
| **Polypharmacy** | Yes | 105 (80.2%) | 22 (16.8%) | 4 (3.1%) | **0.010** |
| | No | 108 (92.3%) | 9 (7.7%) | 0 (0%) | |

* Fisher–Freeman–Halton exact test, MNA-SF: Short form of Mini Nutritional Assessment

There was no statistically significant difference in nutritional status between those with and without dentures (p>0.05).

The rates of malnutrition risks (26.2%) and malnourishment (6.6%) were significantly higher (p = 0.001) among those who received assistance during eating and shopping than among those who did not receive assistance (8%, 0%).

The rates of malnutrition risks (50%) and malnourishment (25%) were significantly higher in those with a history of hospitalization than in those without (10.6% and 0.4%, respectively; (p =0.001). The rate of malnutrition (33.3%) was significantly higher in participants with a history of cancer than in those without (0.8%; p =0.001), with no significant differences between patients with and without other chronic diseases (p >0.05).

In addition, the malnutrition risk prevalence among the elderly with polypharmacy (16.8%) were significantly higher than those without polypharmacy (7.7%; p =0.010).

## DISCUSSION

Malnutrition rates in patients aged >65 years vary between 1.3% and 90% depending on the population studied (2,6,9,10). A study conducted among elderly individuals in Family Health Centers reported a malnutrition prevalence of 1.3% and a malnutrition risk prevalence of 24% (10). In our study, the prevalence of malnutrition according to the MNA-SF was 1.6%, and the rate of malnutrition risk was 12.5%. Meanwhile, the MNA-LF, which was administered to participants (n=35) who scored <12 points on the MNA-SF, showed a malnutrition rate of 11.4% and a malnutrition risk rate of 74.3%. We think that, our study included elderly individuals who were registered to our polyclinics, who did not apply due to any health problems, and who thought they were healthy, reduced the malnutrition rates.

As seen in many studies, malnutrition and malnutrition risk rates increase as studies move away from primary care (4,11,12). Moreover, these rates are high among individuals living in nursing homes or receiving home care services (9,13).

Previous studies have suggested that age is not associated with malnutrition or its risk in elderly patients (10,14). In our study, no significant difference was observed between age and nutritional status. This can be attributed to the fact that the participants comprised patients aged >65 years and that a different result may be obtained in studies wherein all age groups were evaluated together.

Bayrak et al. compared patients with normal nutritional status with those who were malnourished and at risk of malnutrition and found no significant differences in terms of income level, chronic diseases, educational level, and marital status (p >0.05) (2). In another recent study, a significant association was found between income status and malnutrition (p <0.038) (10). In our study, no significant differences were observed between nutritional status and gender as well as marital, educational, and smoking statuses among the participants (p >0.05). However, the rate of malnutrition risk in those with expenses exceeding their income (18.9%) was significantly higher than that in those with higher income than expenses (4.4%). We can say that this results are due to the fact that the elderly, who have limited purchasing power, cannot access the necessary foods for a balanced diet.

Polypharmacy may lead to decreased food consumption and malnutrition in elderly individuals (15). In our study, the rate of malnutrition risk was significantly higher in older adults with polypharmacy (16.8%) than in those without polypharmacy (7.7%; p =0.010), underscoring the necessity of addressing inappropriate drug use and implementing restrictions on drug categories that are repeatedly prescribed (16).

In addition, our findings revealed that the rate of malnutrition was significantly lower in participants with normal weight (7.5%) than in participants with overweight as well as those with obesity class



1, obesity class 2, and morbid obesity (p =0.002). However, those with obesity and low BMI have been considered to have malnutrition (17). Healthcare professionals should be aware of this issue. When assessing the nutritional status of elderly individuals, the MNA-SF and similar screening tests should be used in addition to BMI. In our study, 14.1% of elderly individuals were at risk of malnutrition, although none had a BMI <18.5 kg/m$^2$.

The risk of malnutrition was positively correlated with the number of geriatric syndromes. Functional dependence, multiple comorbidities, and malignancies have been associated with malnutrition (4). In our study, malnutrition risk was significantly higher in participants who required assistance with meals and shopping (p =0.001), elderly people with hearing and visual problems (p =0.011, p ≤0.049), those with a history of hospitalization in the last 3 months (p =0.001), and in those with malignancy (p =0.001).

Inadequate protein intake in malnutrition may increase the risk of falls and osteoporotic fractures due to decreased physical fitness and bone mineral density, muscle weakness, and impaired coordination (18). In another study, no significant association was found between malnutrition and fall risk and fracture occurrence (11). In our study, no significant association was observed between malnutrition and fracture occurrence; however, a significant association was observed between falls and malnutrition.

A study conducted in Japan reported that 74.1% of elderly individuals used dentures, and their nutritional status was negatively affected, as they consumed less meat and fish (19). In our study, denture use rate was 62.5%, which did not affect their nutritional status. The percentage of elderly people with dentures was lower because we categorized those who did not actively use dentures because of their dissatisfaction from poor oral hygiene when using dentures. In addition, the nutritional status of elderly people who were satisfied with their dentures may not have been affected because they had no food intake problems. However, the rate of malnutrition risk was significantly higher in individuals with poor oral health (21.8%) than in those with good oral health (6.1%; p = 0.001).

The strength of our study is that it comprehensively assessed the nutritional status of community-dwelling elderly individuals in primary care institutions. The inclusion of elderly participants who were registered at our family center, were not any symptoms were deemed healthy, rendered our study valuable. In addition, studies in the literature MNA-SF were generally used. In our study, we additionally applied the long form of the test to the patients required according to the MNA-SF results, this makes our work powerful. Nonetheless, our study has some limitations. We superficially used the calculations applied by dentists to assess the oral health of elderly individuals. There is a need for more comprehensive studies involving dentists on older adults, wherein these calculations can be assessed more professionally.

## CONCLUSION

Our findings show that, among community-based elderly individuals in family medicine centers, malnutrition rates were found to be low and malnutrition risk was higher in elderly who required assistance with meals and shopping, with hearing and visual problems, with a history of hospitalization and with polypharmacy. Considering the registered elderly population of each family physician working in primary care, nutritional status assessment for this population and interventions aimed at solving problems can be effective. Family medicine polyclinics, where elderly individuals visit every three months for their chronic diseases and medications, constitute a suitable ground for malnutrition screening. Malnutrition measurement and evaluation tests are requested by family physicians in the elderly individuals' follow-up section of the Disease Management Platform (20). To prevent malnutrition and its related diseases MNA should be applied in family medicine centers.

**Conflict of interest:** All authors declare that they have no conflicts of interest.

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ORIGINAL ARTICLE

# EVALUATING POTENTIALLY INAPPROPRIATE MEDICATIONS IN THE ELDERLY WITH SEVEN DIFFERENT SCREENING TOOLS

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## Abstract

**Introduction:** We aimed to determine the rates of potentially inappropriate medications using various screening tools and also the affecting factors in elderly patients.

**Materials and Method:** In this prospective cross-sectional study, we recorded in detail the concomitant chronic diseases, geriatric syndromes, and drugs used in elderly patients admitted to a university hospital and then assessed potentially inappropriate medications using seven different screening tools.

**Results:** The study included 315 patients (190 female; 125 male). We evaluated potentially inappropriate medication use with the PRISCUS, EU(7), Beers 2019, STOPP v2, and TIME-to-STOP criteria and evaluated potential prescription omissions with the START v2 and TIME-to-START criteria; the resulting identified rates of PIMs were 15.9%, 45.1%, 48.9%, 44.8%, 48.3%, 73.9%, and 97.5%, respectively. The lowest value was found with PRISCUS, as it uses fewer criteria than the others. The EU(7), Beers 2019, STOPP v2, and TIME-to-STOP results were similar to one another. START v2 and TIME-to-START yielded higher outcomes than the others due to the omission of vaccines in patients. The highest outcome was found with TIME-to-START due to the omission of the herpes zoster vaccine (97.5%), which appears only in that screening tool. Potentially inappropriate medication rates increased with the number of drugs used and with the number of concomitant chronic diseases.

**Conclusion:** This study detected potentially inappropriate medication use in approximately half of the patients with the EU(7), Beers 2019, STOPP v2, and TIME-to-STOP screening tools. There was a positive correlation between potentially inappropriate medications and polypharmacy and increased disease burden.

***Keywords:*** Potentially Inappropriate Medication List; Polypharmacy; Aged.

## INTRODUCTION

The number of drugs used and rates of polypharmacy have increased in the elderly due to an increase in concomitant chronic diseases and geriatric syndromes (1). Although diverse definitions are used, *polypharmacy* is most commonly accepted as the use of five or more drugs per day (2).

In the elderly, rates of medication use errors and potentially inappropriate medications (PIMs) as well as the risk of potential drug-drug interactions and adverse drug reactions increase with polypharmacy (3).

A PIM is a drug that should not be given because the risk of adverse effects outweighs the clinical benefit when there is evidence of safer, more effective alternative treatments for the same indication in the elderly (4–8). In addition, the omission of drugs or vaccines when there is a relevant indication, termed a potential prescribing omission (PPO), is accepted as inappropriateness (6,9).

Numerous screening tools have been developed for PIMs. The most commonly used include Beers criteria, the Screening Tool of Older Persons' potentially inappropriate Prescriptions/Screening Tool to Alert to Right Treatment (STOPP/START) criteria, the PRISCUS list, and the European Union (7)– Potentially Inappropriate Medications (EU[7]-PIM) list (5-8). Beers criteria were developed by Beers et al. in 1991 to evaluate drugs used by the elderly living in nursing homes; they were last updated by the American Geriatrics Society in 2019 (5). The STOPP/START criteria were developed by Gallagher et al. in 2008 as an alternative to Beers criteria that accounts for drugs used in Europe in evaluating medications used by the elderly. It was updated in 2015 as STOPP/START version 2 (v2) (6). The PRISCUS list was developed in Germany in 2010 and identified 83 drugs deemed potentially inappropriate for use in the elderly (7). The EU(7)-PIM was developed in 2015 by geriatricians from seven European countries (Germany, Estonia, France, Netherlands, Spain, Finland, and Sweden) and includes 282 drugs that are seen as PIMs in the elderly (8). In Turkey, the Academic Geriatrics Society developed the Turkish Inappropriate Medication use in the Elderly (TIME) criteria (TIME-to-STOP and TIME-to-START) in 2020 based on the STOPP/START criteria and the drugs used in our country (9).

This study employed seven different screening tools to evaluate the drugs used in elderly patients admitted to the hospital. We used five tools (Beers 2019, STOPP v2, PRISCUS, EU(7), and TIME-to-STOP) to identify PIM use and two (START v2 and TIME-to-START) for PPOs. We aimed to contribute to the literature by comparing different screening tools to determine PIM rates in the elderly and also by identifying factors affecting PIM use.

## MATERIALS AND METHOD

We obtained ethics committee approval for this prospective cross-sectional study. Patients were included who were aged 65 and over, had at least one chronic disease, used at least one drug per day for it, were admitted to general internal medicine outpatient clinics of Bursa Uludag University Hospital, Turkey, and agreed to participate in the study. Written consent was obtained from all patients. Patients who did not provide voluntary consent or could not answer the questionnaire were not included in the study.

Sociodemographic characteristics (such as age, gender, marital status, cohabitation, education level, concomitant chronic diseases, geriatric syndromes, and drugs used) were recorded by interviewing the patients in person using a pre-prepared questionnaire form. As part of the comprehensive geriatric assessment, we conducted some tests; the Mini Nutritional Assessment (MNA) for malnutrition, Yesavage Geriatric Depression Scale (GDS) for depression, Standardized Mini Mental Test (SMMT) for dementia, and 'Fatigue, Resistance, Ambulation,



Illnesses, Loss of weight' (FRAIL) scale for frailty. But we could not detect sarcopenia, which is a geriatric syndrome, because of no hand grip device in our unit at the time of study period.

The Charlson Comorbidity Index (CCI) was used to measure chronic disease burden (10). In this study, daily use of ≥ 5 drugs was accepted as polypharmacy, and the use of ≥ 10 drugs was accepted as hyperpolypharmacy (2). The rates of polypharmacy, urinary incontinence, chronic pain (pain lasting longer than three months), frailty, history of falling, insomnia, and malnutrition were investigated as geriatric syndromes.

The drugs used by the patients at the time of admission were evaluated in terms of PIMs and PPOs using the PRISCUS, EU(7), Beers 2019, STOPP/START v2, TIME-to-STOP and TIME-to-START screening tools. We investigated the relationship between PIMs and gender, age group (65-74 years and ≥ 75 years), presence of polypharmacy, and CCI score.

### Statistical Analysis

Statistical analyses of the study were performed with JASP 0.16.3 software. The categorical variables were presented as frequencies and percentages, and the quantitative variables were presented as the mean, standard deviation, and minimum and maximum values. The Shapiro-Wilk test was used to determine whether the quantitative variables fit the normal distribution. The Mann-Whitney U test was used for two-group comparisons of non-normally distributed quantitative variables.

The Fisher chi-square, Yates chi-square, and Pearson chi-square tests were used to compare groups of qualitative variables. For all tests, a p-value of $< .05$ was considered statistically significant.

## RESULTS

A total of 315 patients were included in the study during the one-year period between February 15, 2021 and February 15, 2022, of whom 190 were female and 125 male (female/male ratio: 1.52). The mean age was 70.6 ± 5.5 years. Table 1 shows their sociodemographic characteristics, and the most common concomitant chronic diseases and geriatric syndromes are shown in Table 2.

**Table 1.** Sociodemographic characteristics of the patients.

| | Number (%) |
|---|---|
| **Gender** | |
| Female | 190 (60.3%)* |
| Male | 125 (39.7%) |
| **Age groups** | |
| 65-74 | 261 (82.8%)* |
| ≥ 75 | 54 (17.1%) |
| **Marital status** | |
| Single | 2 (0.6%) |
| Married | 235 (74.6%)* |
| Divorced | 12 (3.8%) |
| Widoved | 66 (21%)* |
| **Household status** | |
| Alone | 42 (11.3%)* |
| With spouse | 235 (74.6%)* |
| With children | 35 (11.1%) |
| Others | 3 (0.95%) |
| **Education status** | |
| Illiterate | 22 (7%)* |
| Just literate | 38 (12%) |
| Primary school | 124 (39.4%) |
| Secondary school | 49 (15.6%) |
| High school | 46 (14.6%)** |
| University | 36 (11.4%)** |

*; p<0.01, **; p<0.001.

**Table 2.** Distribution of the most common concomitant chronic diseases and geriatric syndromes by gender.

| | Female | Male | Total |
|---|---|---|---|
| **Chronic diseases** | | | |
| Hypertension | 150 (77.3%) | 94 (77.7%) | 244 (77.4%) |
| Diabetes Mellitus | 88 (45.4%) | 60 (49.6%) | 144 (46.9%) |
| Dyslipidemia | 73 (37.6%) | 51 (42.1%) | 124 (39.3%) |
| Depression | 66 (34%)* | 26 (21.5%) | 92 (29.2%) |
| Chronic kidney disease (GFR < 60 ml/min) | 51 (26.3%) | 39 (32.2%) | 90 (28.6%) |
| Coronary artery disease | 30 (15.5%) | 43 (35.5%)** | 73 (23.2%) |
| Osteoporosis | 58 (29.9%)** | 9 (7.4%) | 67 (21.3%) |
| Hypothyroidism-Hyperthyroidism | 55 (28.4%)** | 10 (8.3%) | 65 (20.6%) |
| Peptic ulcer-Gastritis-Gastroesophageal reflux | 34 (17.9%) | 16 (12.8%) | 50 (15.9%) |
| Dementia | 41 (21.1%) | 8 (6.6%) | 49 (15.6%) |
| Asthma-COPD | 27 (14.2%) | 18 (14.4%) | 45 (14.3%) |
| Arthrosis- Arthritis | 29 (15.3%) | 15 (12.%) | 44 (14%) |
| Neuropathy | 28 (14.4%) | 16 (13.2%) | 44 (14%) |
| Benign prostatic hypertrophy | | 43 (34.4%)** | 43 (13.7%) |
| Arrhythmia | 16 (8.2%) | 10 (8.3%) | 26 (5.1%) |
| **Geriatric syndromes** | | | |
| Polypharmacy | 114 (60%) | 73 (58.4%) | 187 (59.4%) |
| Urinary incontinence | 45 (23.2%) | 34 (28.1%) | 79 (25.1%) |
| Chronic pain | 52 (27.4%)* | 16 (12.8%) | 68 (21.6%) |
| Frailty | 45 (23.2%) | 19 (15.7%) | 64 (20.3%) |
| Fall | 40 (20.6%) | 23 (19%) | 63 (20%) |
| Insomnia | 44 (22.7%)* | 14 (11.6%) | 58 (18.4%) |
| Malnutrition | 11 (5.7%) | 11 (9.1%) | 22 (7%) |

*; $p<0.05$, **; $p<0.001$.

Abbreviations: GFR; glomerular filtration rate, COPD; chronic obstructive pulmonary disease.

In this study, the number of female patients and patients aged 65-74 was significantly higher than the number of males and those ≥ 75 years, respectively. There was no difference between the age groups in terms of marital status, but the rate of being married was higher in men, and the rate of being widowed was higher in women. There was no difference between the age groups in terms of household status. The prevalence of living alone was higher in female patients, while living with a spouse was higher in male patients. The prevalence of being illiterate was higher in female patients, whereas high school and university graduation was more likely in male patients and in the 65-74 age group.



**Table 3.** Distribution of the number of drugs used daily by gender and age groups.

| Number of drugs used daily | Gender | | Total | Age groups | |
|---|---|---|---|---|---|
| | Female | Male | | 65-74 | ≥ 75 |
| 1-4 drugs | 76 (40%) | 52 (41.6%) | 128 (40.6%) | 107 (41%) | 21 (38.9%) |
| 5-9 drugs | 90 (47.4%) | 64 (51.2%) | 154 (48.9%) | 128 (49%) | 26 (48.1%) |
| ≥ 10 drugs | 24 (12.6%) | 9 (7.2%) | 33 (10.5%) | 26 (10%) | 7 (13%) |

**Table 4.** Most frequently used drugs by patients.

| Drugs used | Number (%) |
|---|---|
| ACEIs/ARBs | 179 (56.8%) |
| Diuretics | 120 (38.1%) |
| Beta blockers | 118 (37.5%) |
| Metformin | 113 (35.9%) |
| ASA | 109 (34.6%) |
| PPIs | 102 (32.4%) |
| CCBs | 97 (30.8%) |
| Statins | 84 (26.7%) |
| DPP-4 inhibitors | 57 (18.1%) |
| Levothyroxine | 54 (17.1%) |

Abbreviations: ACEIs; Angiotensin converting enzyme inhibitors, ARBs; Angiotensin receptor blockers, DPP-4; dipeptidyl peptidase-4, ASA; Acetylsalicylic acid, PPIs; Proton pump inhibitors, CCBs; Calcium channel blockers.

Hypertension, diabetes mellitus, dyslipidemia, depression, and chronic kidney disease were the most common concomitant diseases. The prevalence of hypothyroidism-hyperthyroidism (28.4% vs. 8.3%, p< .001), osteoporosis (29.9% vs. 7.4%, p< .001), depression (34% vs. 21.5%, p< .05), and dementia (21.1% vs. 6.6%, p<.001) was higher in female patients, while coronary artery disease (35.5% vs. 15.5%, p< .001) was higher in male patients. Moreover, approximately one-third of men (34.4% in men) had benign prostatic hypertrophy. The prevalence of chronic kidney disease (42.6% vs. 25.7%, p< .05), arrhythmias (18.5% vs. 6.1%, p< .01), and heart failure (14.8% vs 2.7%, p< .001) was higher in the ≥ 75 age group. There was no difference between the gender and age groups in terms of other concomitant chronic diseases. In addition to 59 patients diagnosed with depression and 8 patients with dementia at the time of admission, 33 patients were diagnosed with depression by the GDS, and 41 patients were diagnosed with dementia by the SMMT; appropriate recommendations and guidance were provided.

The most common geriatric syndromes were polypharmacy, urinary incontinence, and chronic pain. Chronic pain (27.4% vs. 12.8%, p< .05) and insomnia (22.7% vs. 11.6%, p< .05) were more common in women. Frailty (31.5% vs. 18%, p< .05) was higher in the ≥ 75 age group. There was no difference between the gender and age groups in terms of other geriatric syndromes.

Patients using at least one drug per day were included in the study, and the total number of drugs used by the patients at the time of admission was 1,873. Of these, 1,746 drugs that are used regularly every day (excluding 127 used for local effect, such as eye drops, nasal spray, and inhaler drugs) and used in weekly and monthly periods were evaluated. The mean number of drugs used daily by the patients was 5.5 ± 1.8. The rate of polypharmacy was 59.4%, and that of hyperpolypharmacy was 10.5% (Table 3). There was no difference between the gender and age groups in terms of polypharmacy and hyperpolypharmacy. The most frequently used drugs related to organs/systems were cardiovascular system (CVS) drugs in

**Table 5.** Distribution of potential inappropriate medications according to different screening tools by gender, age groups, number of drugs and disease burden.

| | PRISCUS | EU-7 | Beers 2019 | STOPP v2 | TIME-to-STOP | START v2 | TIME-to-START |
|---|---|---|---|---|---|---|---|
| **Total PIMs** | 50 (15.9%) | 142 (45.1%) | 154 (48.9%) | 141 (44.8%) | 152 (48.3%) | 233 (73.9%) | 307 (97.5%) |
| **Gender** | | | | | | | |
| **Female (n:190)** | 25 (12.9%) | 87 (44.8%) | 103 (53.1%) | 88 (45.4%) | 97 (50%) | 150 (77.3%) | 185 (97.4%) |
| **Male (n:125)** | 25 (20.7%) | 55 (45.5%) | 51 (42.1%) | 53 (43.8%) | 55 (45.5%) | 83 (68.6%) | 122 (97.6%) |
| **Age groups** | | | | | | | |
| **65-74 (n:261)** | 40 (15.3%) | 116 (44.4%) | 122 (46.7%) | 113 (43.3%) | 121 (45.4%) | 190 (72.8%) | 254 (97.3%) |
| **≥ 75 (n:54)** | 10 (18.5%) | 26 (48.1%) | 32 (59.3%) | 28 (51.9%) | 31 (57.4%) | 43 (79.6%) | 53 (98.1%) |
| **Number of drugs used** | | | | | | | |
| **1-4 drugs (n:128)** | 5 (3.9%) | 33 (25.8%) | 36 (28.1%) | 36 (28.1%) | 37 (28.9%) | 93 (72.7%) | 124 (96.9%) |
| **5-9 drugs (n:154)** | 33 (21.4%)* | 82 (53.2%)* | 89 (57.8%)* | 82 (53.2%)* | 87 (56.5%)* | 116 (75.3%) | 151 (98.1%) |
| **≥ 10 drugs (n:33)** | 12 (36.4%)** | 27 (81.8%)** | 29 (87.9%)** | 23 (69.7%)** | 28 (84.8%)** | 24 (72.7%) | 32 (97%) |
| **Disease burden (CCI score)** | | | | | | | |
| **0 point (n:52)** | 7 (13.5%) | 17 (32.7%) | 21 (40.4%) | 21 (40.4%) | 18 (34.6%) | 37 (71.2%) | 51 (98.1%) |
| **1-2 points (n:175)** | 25 (14.3%) | 71 (40.6%) | 82 (46.9%) | 69 (39.4%) | 77 (44%) | 127 (72.6%) | 170 (97.1%) |
| **3-4 points (n:69)** | 13 (18.8%)* | 41 (59.4%)* | 38 (55.1%)* | 38 (55.1%)* | 43 (62.3%)** | 54 (78.3%) | 67 (97.1%) |
| **≥ 5 points (n:19)** | 5 (26.3%)** | 13 (68.4%)** | 13 (68.4%)** | 13 (68.4%)** | 14 (73.7%)** | 15 (78.9%) | 19 (100%) |
| **Most frequently detected potentially inappropriate drugs/criteria** | **Drugs** → -NSAIDs (3.2%) -Piracetam (%3.2)-Alpha-1 blockers (2.5%) -Digoxin (1.3%) -Solifenacin (1.3%) | **Drugs** → -PPIs (9.5%) -NSAIDs (8.3%)-Trimetazidin (5.7%) -Glimepiride/ Sitagliptin (5.4%) -Diltiazem (3.8%) | **Drugs** → -PPIs (9.5%) -ASA (9.2%) -Antidepressant (8.9%) -NSAIDs (5.4%) -Anticholinergic (4.1%) | **Criteria** → -Indication of medicationcriteria (19.3%) -CVS criteria (12.3%) -GIS criteria (11.7%) -Antiplatelet/ Anticoagulant drugs (7.9%) -Musculoskeletal system criteria (7.6%) **Drugs** → -PPIs (9.5%) -ASA (7.6%) -NSAIDs (6%) | **Criteria** → -CVS criteria (20%) -GIS criteria (15.2%) -Musculoskeletal system criteria (9.8%) - Nervous system criteria(9.2%) -Antimuscarinic/ Anticholinergic drug burden criteria (2.5%) **Drugs** → -PPIs (9.5%) -ASA (7.6%) -NSAIDs (6%) | **Criteria** → -Vaccines criteria (57.5%) -CVS criteria (36.1%) -GIS criteria (15.6%), -Musculoskeletal system criteria (14.6%) -Analgesics criteria(1.6%) | **Criteria** → -Vaccines criteria (97.5%) -CVS criteria (20.6%) -GIS criteria (11.7) -Nervous system criteria (14.3%) -Musculoskeletal system criteria (10.2%) |

*; p<0.01, **; p<0.001.

Abbreviation: NSAIDs; Nonsteroidal anti-inflammatory drugs



260 (82.5%) patients, endocrine system drugs in 183 (58.1%) patients, and gastrointestinal system (GIS) drugs in 116 (36.8%) patients, respectively (Table 4). Table 5 shows the seven screening tools used to evaluate the patients' drugs for PIMs.

We separately evaluated the patients' drugs in terms of PIMs using five different screening tools (PRISCUS, EU[7], Beers 2019, STOPP v2, and TIME-to-STOP), finding no difference between the gender and age groups according to these tools. The rates of PIMs were significantly higher in patients with polypharmacy and in those with a greater chronic disease burden. When these screening tools were compared with one another, the rate of PIMs detected with PRISCUS was significantly lower than the others, while the rates of PIMs detected with EU(7), Beers 2019, STOPP v2, and TIME-to-STOP were similar. The most common drugs identified as PIMs were PPIs, ASA, and NSAIDs. PPOs, a type of PIM in which drugs/vaccines are omitted even though they are indicated, were evaluated with two screening tools (START v2 and TIME-to-START), and the rates of PIMs were higher than found by the other five screening tools. The most common reason for PPOs was omission of vaccines criteria. The vaccine omission rates were 45.7% for influenza vaccine, 45.1% for 13-valent pneumococcal vaccine, 76.8% for 23-valent pneumococcal vaccine, 84.8% for diphtheria-tetanus vaccine, and 97.5% for herpes zoster vaccine. The rate of PPO was higher with TIME-to-START, as it includes diphtheria-tetanus and herpes zoster vaccine criteria in addition to the influenza and pneumococcal vaccine criteria in START v2.

## DISCUSSION

Drug use and polypharmacy are common in the elderly, and different rates of polypharmacy have been reported according to study setting, such as in the general community, nursing homes, primary care institutions, outpatient clinics, and inpatient clinics. In a population-based survey conducted in the USA, the rates of polypharmacy and hyperpolypharmacy in the elderly are reported as 57% and 12% in women and 44% and 12% in men, respectively (11). A study examining the data of 466 patients in primary care in Germany reports that patients used an average of 3.7 prescription drugs and 1.4 over the counter drugs per day for a total of 5.1 drugs per day, and the rate of chronic polypharmacy was 26.7% (12). In a study of 1,332 elderly patients hospitalized in 38 internal medicine wards in Italy, polypharmacy rates are reported as 51.9% at admission and 67.0% at discharge (13). In a previous study with 721 elderly patients admitted to the General Internal Medicine outpatient clinic of our hospital, the mean number of drugs used daily was 4.6 ± 2.8, and the rates of polypharmacy and hyperpolypharmacy were 49.4% and 6.0%, respectively (14).

In the present study, the mean number of drugs used daily is 5.5 ± 1.8, and the rates of polypharmacy and hyperpolypharmacy are 59.4% and 10.5%, respectively. These values in the present study may be higher than in the previous study because, while all elderly patients were included in the previous study, the present study recruited only patients who had at least one chronic disease and used at least one drug per day.

The most common cause of polypharmacy is that chronic diseases and geriatric syndromes are common in the elderly. The most common chronic diseases in an Italian study were hypertension, diabetes mellitus, coronary heart diseases, atrial fibrillation, and chronic obstructive pulmonary disease (COPD) (13). In the previous study in our unit, hypertension, diabetes mellitus, dyslipidemia, and coronary artery disease were the most common chronic diseases (14). Similarly, the most common chronic diseases in the present study are hypertension, diabetes mellitus, dyslipidemia, depression, and chronic kidney disease.

An important consequence of polypharmacy is an increased risk of PIMs in patients. To identify PIMs, the present study employed the criteria of

PRISCUS, EU(7), Beers 2019, STOPP v2, and TIME-to-STOP to evaluate the drugs used by elderly patients; we used the START v2 and TIME-to-START criteria to identify PPOs .

In a study using PRISCUS to examine 335 different drugs in 2,363 prescriptions of 92 elderly patients in a geropsychiatry unit in Germany, 30.4% had at least one PIM, and the three most common PIMs were lorazepam, clonazepam, and olanzapine (15). In a study based on the health insurance database in Germany, the rate of PIMs with PRISCUS was 22%, and the three most common PIMs were antidepressants (6.5%), antihypertensives (3.8%), and antiarrhythmic drugs (3.5%) (16).

In a study using the EU(7)-PIM list in 428 elderly patients with cognitive impairment in Sweden, the rate of PIMs was 40.9%, and the three most common PIMs were zopiclone, digoxin, and sodium picosulfate (17). A study conducted with EU(7) in six European countries reports the rates of PIMs as 71.4% in Spain, 67.5% in Turkey, 67.1% in Portugal, 55.5% in Hungary, 50.2% in Czechia, and 42.8% in Serbia (18).

In a study using the Beers 2019 criteria to examine 8,477 drugs used by 1,874 patients in an outpatient clinic in China, the rate of PIMs was 35%, and the most common PIMs were alprazolam, estazolam, and pseudoephedrine compounds (19).

In a study conducted with the STOPP and START v2 criteria in a cohort of 102 patients in a geriatric psychiatry unit in Switzerland, the rates of PIMs are reported as 78% and 47%, respectively. According to the STOPP v2 criteria, the most common PIMs were benzodiazepines and neuroleptics in patients with a history of falls in the past three months. According to the START v2 criteria, the most prominent PPO was the omission of statin in independent patients with a history of coronary, cerebral, or peripheral vascular disease and more than five years of life expectancy (20).

Some studies have compared the scanning tools we used in the present study. In a study conducted with 3,189 patients in Germany, the rates of PIMs were 24.7% with PRISCUS and 70.1% with EU(7), and the most common PIMs identified by PRISCUS were amitriptyline, acetyldigoxin, nifedipine, and zopiclone, whereas the EU(7) most commonly identified omeprazole, diclofenac, ibuprofen, and ASA (21). In a study that evaluated the data of 400 patients in Brazil with different screening tools, the rates of PIMs were 46.2% with STOPP v2 and 59.5% with EU(7), and the most common PIMs were clonazepam, amiodarone, and glibenclamide with STOPP v2 and clonazepam, nifedipine, and amiodarone with EU(7) (22). In a study examining 4,386 prescriptions of 593 patients in Spain, the rates of PIMs were 57.4% with STOPP v2 and 68.8% with Beers 2019, and the most common PIM was prolonged use of benzodiazepines (36.6%) with STOPP v2 and prolonged use of PPIs (43.8%) with Beers 2019 (23).

In a study conducted with 90 patients in a nursing home in Portugal, the rates of PIMs were 64.4% with EU(7) and 85.5% with STOPP v2, and the most common PIMs were benzodiazepines with STOPP v2 and prolonged use of anxiolytics, sedatives, and hypnotics with EU(7) (24). A hospital study in Croatia evaluated the data of 276 patients and found rates of PIMs of 69% with STOPP v2 and 66.7% with EU(7); both screening tools identified the most common PIMs as benzodiazepines, PPIs, and tramadol (25).

The screening tools used in the present study yielded PIM rates of 15.9% with PRISCUS, 45.1% with EU(7), 48.9% with Beers 2019, 44.8% with STOPP v2, and 48.3% with TIME-to-STOP. The rate was significantly lower with PRISCUS than with the others because a total of 83 drugs were evaluated in the PRISCUS list, whereas > 250 drugs were evaluated in the EU(7), Beers 2019, STOPP v2, and TIME-to-STOP criteria. The PIM rates were similar among the latter screening tools. The most common PIMs were NSAIDs and piracetam with PRISCUS; PPIs and NSAIDs with EU(7); PPIs, ASA, and antidepressants with Beers 2019; PPIs, ASA, and



NSAIDs with STOPP v2; and PPIs, ASA, and NSAIDs with TIME-to-STOP. The most common cause of PIMs was the use of PPIs for longer than 8–12 weeks (except in special cases) and the use of PPIs due to polypharmacy. The PIM criteria for PPI were not included in the PRISCUS list; they are included in the EU(7) and TIME-to-STOP criteria, and they were added to the updated Beers 2015 and 2019 and the STOPP v2 criteria.

PPOs are accepted as a form of PIM, and the screening tools we used to examine PPO rates in our patients yielded rates of 73.9% (START v2) and 97.5% (TIME-to-START), which were higher than those found by the other screening tools. The most common PPO detected by both screening tools was omission of vaccines criteria. The rate of PPOs was higher with TIME-to-START than with START v2 because the latter includes only the omission of the pneumococcal vaccine and the annual influenza vaccine in the vaccine criteria, whereas TIME-to-START also includes the omission of the herpes zoster vaccine and the tetanus-diphtheria vaccine. The herpes zoster vaccine was not administered in 97.5% of the patients, probably because the vaccine was not available in the market for most of the study period.

The main limitation of our study is that it relied on single-center data, but we believe that our data reflect the patient profile in our country's tertiary university hospitals. Another limitation is that we identified the drugs used by our patients based on their own statements. To minimize this risk, however, the patients were asked to bring the drugs they used on their next visit, the use of drugs was questioned in detail, and the approval of the patient's relatives/caregivers was obtained.

In summary, the present study used five different screening tools to evaluate the drugs used by patients and found that the rates of PIMs were higher with the EU(7), Beers 2019, STOPP v2, and TIME-to-STOP than with PRISCUS. We also evaluated PPOs with two different screening tools and observed that the rates of PIMs found by START v2 and TIME-to-START were higher than found by PRISCUS, EU(7), Beers 2019, STOPP v2, and TIME-to-STOP. Moreover, we observed that PIM rates increase with the number of medications used and with the chronic disease burden score.

In conclusion, polypharmacy and its associated PIMs pose significant risks for the elderly. In our opinion, the PIM criteria is very important for rational drug use. These criteria can guide physicians in drug selection in the elderly. There may be differences in the drugs used in different countries. Therefore, it is important to identify and publish PIM criteria for drugs available in that country. However, it is also useful to know other country criteria and all these criteria should be updated periodically. As an example of the importance of updating, the PIM criterion related to PPIs was added to the updated criteria in 2015 and later. The most common drugs identified as PIMs were PPIs, ASA, and NSAIDs in this study. Determining and publishing PIM rates and the drugs that most commonly identified as PIM in different countries will increase physicians' awareness of the risks associated with the use of these drugs and contribute to rational drug use. Therefore, PIM lists are important educational tools and should be part of a comprehensive geriatric assessment. To reduce drug-related risks in the elderly, all patients should be evaluated with a comprehensive geriatric assessment, drugs with potential risks should be avoided, and indicated drugs and vaccines should not be omitted.

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ORIGINAL ARTICLE

# IMPACT OF ENRICHED DEMENTIA CARE PLANNING ON INDIVIDUALIZED CARE APPROACHES AND PSYCHOLOGICAL WELL-BEING OF RESIDENTS

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## Abstract

**Introduction:** The enriched dementia care-planning program seeks to enhance the quality of life for individuals with dementia by addressing their physical, emotional, social, and spiritual needs. This study aims to assess the impact of enriched dementia care planning on caregivers' individualized care approaches and the psychological well-being of residents.

**Materials and method:** A pretest and posttest cross-sectional one-group study including caregivers and persons with dementia. Formal caregivers (n=32) and individuals with dementia (n=17) were recruited from two nursing homes. Pretest and posttest measurements were conducted using distinct data collection tools for both caregivers and individuals with dementia. The caregivers were exposed to life story booklets, training modules, "about me" profiles, and individualized care tips and reminders over an eight-week period.

**Results:** Pre-test and post-test analysis indicated that staff perceptions of persons with dementia were more positive and communication between staff and residents improved at post-test (8.52±2.04) compared with the pre-test (7.10±1.71) ($p<0.05$). However, there was no significant change in residents' psychological well-being at the post-test ($p>0.05$).

**Conclusion:** The implementation of enriched care planning has the potential to empower caregivers to engage with residents and deliver individualized care with a more positive attitude. Enhancing communication between staff and residents is recognized as a pivotal factor with substantial potential for advancing individualized care initiatives in nursing homes.

***Keywords:*** Dementia; Nursing Homes; Person-Centered Care; Psychological Well-Being



## INTRODUCTION

Individualized care (IC) in long-term care is widely acknowledged as the optimal approach for enhancing both the quality of life and care provided (1, 2). The implementation of IC leads to improvements in well-being, health outcomes, individual functioning, autonomy, and patient satisfaction by tailoring care activities, preferences, and decisions to the unique characteristics of each individual (3). While this approach is recognized as crucial for enhancing the quality of nursing care delivery, there is a need for more effective strategies to further improve IC. Key priorities for providing and assessing individualized care in long-term care settings (LTC) have been identified as centered around 'relationships', understanding the individual, and identifying what matters most to them. One of the primary outcomes of individualized care is the well-being of the individual (4). Factors most closely associated with the quality of life and well-being of individuals with dementia include social interaction, effective communication, and the application of functional skills.

Enriched care planning is a person-centered approach that values individuals regardless of age or cognitive ability. It treats each person as a unique individual, seeks to understand the world from their perspective, listens to their voices, and acknowledges that all human lives are rooted in social relationships (5). This process involves creating a profile of the person's life, identifying, and documenting their needs, implementing the plan, and assessing health and well-being as an outcome (6). By considering all these factors, enriched care planning provides a framework for both the person with dementia and their caregiver(s) to determine and address their needs effectively. This area of study holds great importance due to the tendency to overlook the individuality and needs of people with dementia, often stemming from detrimental social psychology, including treating them like children, negative labeling, stereotyping, and adopting humiliating attitudes (7).

Various interventions have been implemented to enhance the person-centered care behavior of caregivers. Recent studies have identified influencing interventions such as improving communication through the use of memory books, regulating emotional responses of the staff, emphasizing residents' existing skills, increasing social contact, incorporating sensory stimuli, and providing training in communication techniques (8, 9). Additionally, sharing life stories in nursing homes has proven to be instrumental in developing individualized care plans, aiding in a deeper understanding of the individual, and explaining their current reactions (10).

Reported outcomes of individualized care include increased verbal or non-verbal communication by caregivers, more positive attitudes toward people with dementia, reduced restrictive staff behaviors and practices, and enhanced sensory stimuli and communication, achieved through a greater focus on caregiving behavior and the feelings of individuals (8, 11). The essential components of the enriched care-planning framework for dementia care were considered during the design of the study interventions. This framework encompasses five stages: gathering the person's life story, identifying necessary requirements for promoting good health and well-being, documenting these needs to create a care plan, implementing the plan, and conducting regular reviews to assess its effectiveness in maintaining health and well-being (6).

Consequently, life story booklets of individuals with dementia, communication training for caregivers, the use of 'About Me' profiles, and the sharing of person-centered care tips and reminders were implemented in two nursing homes. The eight-week program primarily aims to enable an individualized care approach for nursing home staff and, secondarily, to enhance the psychological well-being of the residents.

The research questions are as follows:

1. What is the impact of enriched care planning on the individualized care approaches (knowing the residents, autonomy and choice of the residents, staff-to-resident communication, and staff-to-staff communication) of nursing home staff?
2. What is the impact of enriched care planning on the psychological well-being of residents with dementia in nursing homes?

## MATERIALS AND METHOD

### Design

This study employed a pretest and posttest cross-sectional one-group study including caregivers and residents with dementia. The eight-week intervention program was applied in two nursing homes and this program consists of creating life story booklets of persons with dementia, training module for caregivers, the use of "About Me" profiles in residents rooms, and sharing of individualized care tips and reminders with caregivers in the nursing units. This study was carried out during Covid-19 pandemic between December 2020-February 2021.

### Sample

Two private nursing homes were selected using purposive sampling. The author informed the management team (head of nursing, chief doctor, and owner) of the two nursing homes regarding the study. After obtaining their consent, the author communicated with all the formal caregivers individually and invited them to participate in the study. The residents with dementia and their relatives were also informed individually, regarding the study and written consent was obtained. The two facilities had similar operating procedures (e.g., administrative structure, staffing structure) and were accepted to participate in the study (the bed capacities of these two nursing homes were 54 and 66, respectively).

Registered nurses with a 4-year bachelor degree, nursing associates with a 2-year education in care for older adults, and certified nursing assistants with a 3-months care certificate are responsible for the care of older adults in long-term care settings. The aforementioned roles are termed formal caregivers, in this study. All formal caregivers (n=32), residents (n=22), and their primary relatives were asked to participate in the study. Residents who have different types and stages of dementia were included in the study (n=17), registered nurses (n=15), nursing associates (n=11), and certified nursing assistants (n=6) consented to participate and formed the sample for this study (Figure 1).

### Procedures

Information for life story booklets was collected from family members of residents with dementia. The author contacted family members over telephone to inquire about the life stories of the residents. The open-ended interview questions for the life story booklet were designed in accordance with the content of the My Life Story booklet produced by Dementia UK. During the interview, information was obtained on the following topics: childhood memories, professional life, important relationships and places, past social activities and interests, significant life events, later life and retirement, and current interests and dislikes. Visual photographs or illustrations were included in the brochures to increase memorability. After the life story booklets were created, the stories of the residents were shared through face-to-face interviews with caregivers.

As part of the training module, the author created a presentation on communication and individualized dementia care. The contents of the training module were shared with three experts for feedback and revised accordingly. The training program lasted approximately 45 minutes per session. Caregivers were divided into four groups (5-10 staff in each group), and all the training sessions were completed in a week.

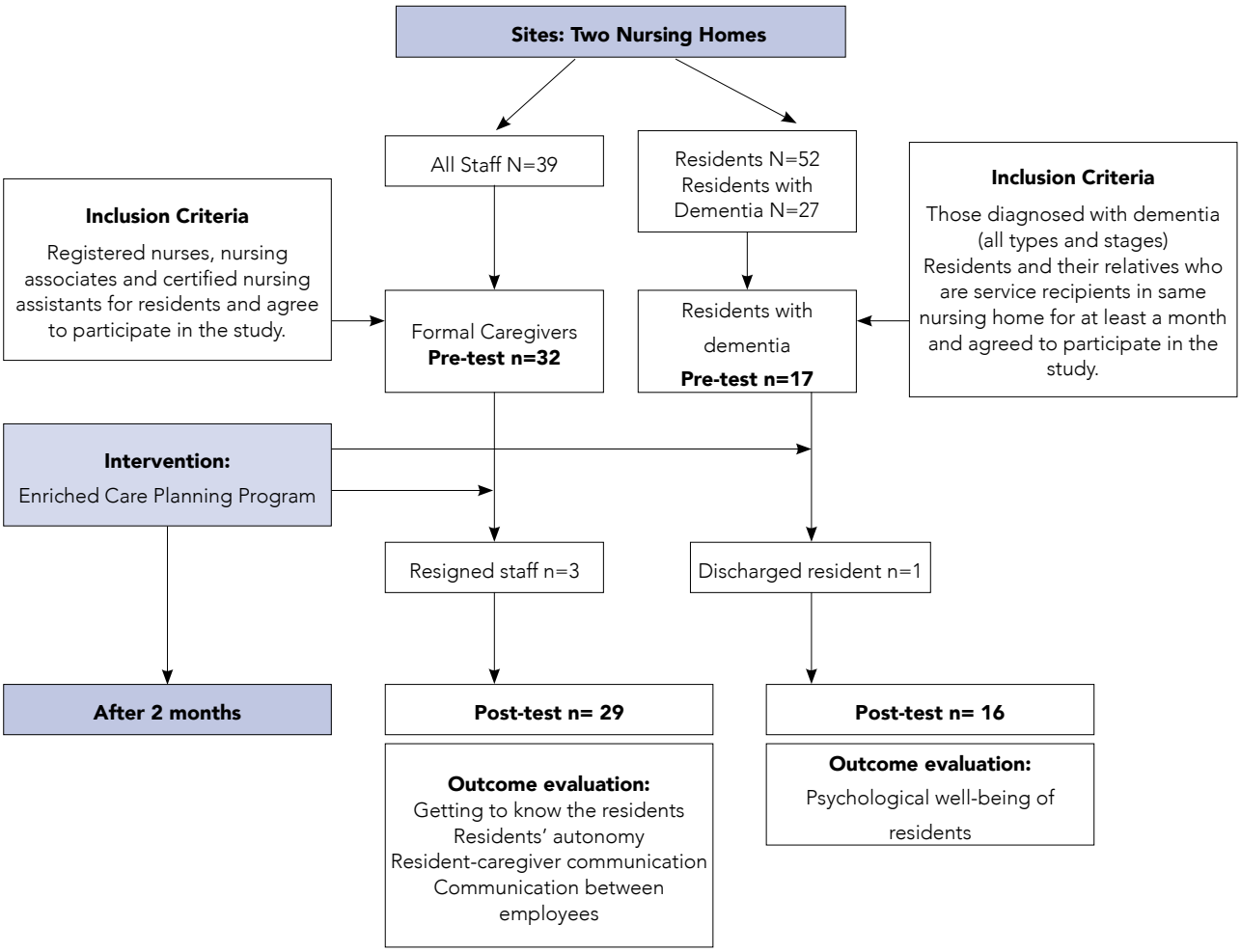



**Figure 1.** Study Sample

"About me" profiles comprise three parts. The first part of the profile presented the feedback from the caregivers regarding the measures required to improve the well-being of each resident according to their life stories. The second part of the profile comprised the resident's existing skills. The third part of the profile presented short notes regarding instances or articles that are of utmost importance to the residents. These profiles were displayed on a wall in the residents' rooms where it was easily visible to the nursing staff. Reminder tips for individualized care were posted once a week for four weeks, on the staff floors.

### Instruments

Questionnaire for descriptive characteristics of formal caregivers (i.e., age, gender, education level, marital status, certificate status, overall dementia care experience, dementia-related education) and individuals with dementia (i.e., age, gender, educational level, marital status, independence status) were used to collect the data. The outcomes for this study were measured using the Staff-based Individualized Care Inventory (ICI) (12) and Psychological Well-Being in Cognitively Impaired Persons (PWB-CIP) Scale (13). The Turkish short

**Table 1.** Characteristics of the Formal Caregivers (n=32)

| Variables | Mean±SD | Number | % |
|---|---|---|---|
| **Gender** | | | |
| Women | | 19 | 59.4 |
| Men | | 13 | 40.6 |
| **Age** | | | |
| 19-25 years | | 21 | 65.6 |
| 26-36 years | 25.9±8.23 | 8 | 25 |
| 37-56 years | | 3 | 9.4 |
| **Marital status** | | | |
| Single (never married and widowed) | | 27 | 84.4 |
| Married | | 5 | 15.6 |
| **Education** | | | |
| Primary School | | 1 | 3.1 |
| High School | | 8 | 25 |
| Vocational School | | 21 | 65.6 |
| University Degree | | 2 | 6.3 |
| **Positions** | | | |
| Nurse | | 15 | 46.9 |
| Elderly care assistants | | 11 | 34.4 |
| Personal care assistants | | 6 | 18.8 |
| **Experience Years** | | | |
| 0-1 years | | 13 | 40.6 |
| 1-3 years | | 6 | 18.8 |
| 3-6 years | | 12 | 37.5 |
| 6-12 years | | 1 | 3.1 |
| **Dementia Education** | | | |
| At school | | 6 | 18.8 |
| Seminars | | 3 | 9.4 |
| In service | | 6 | 18.8 |
| None | | 17 | 53.1 |

**Table 2.** Characteristics of Persons with Dementia (n=17)

| Variables | Mean±SD | Number | % |
|---|---|---|---|
| **Gender** | | | |
| Women | | 12 | 70.6 |
| Men | | 5 | 29.4 |
| **Age** | | | |
| 59-79 years | | 3 | 17.7 |
| 80-89 years | 84.59±11.9 | 7 | 41.1 |
| 90-104 years | | 7 | 41.1 |
| **Marital status** | | | |
| Married | | 4 | 23.5 |
| Single (never married and widowed) | | 13 | 76.5 |
| **Education** | | | |
| Primary School | | 5 | 29.4 |
| High School | | 5 | 17.6 |
| University | | 3 | 11.8 |
| Graduate school | | 2 | 11.8 |
| **Profession** | | | |
| Engineer | | 1 | 5.9 |
| Government officer | | 3 | 17.6 |
| House wife | | 7 | 41.2 |
| Self-employed | | 5 | 29.4 |
| Medical Doctor | | 1 | 5.9 |
| **Length of Stay in NH**** | | | |
| 5 months-2 years | | 11 | 64.7 |
| >2 years | | 6 | 35.3 |
| **Stages of Dementia** | | | |
| Early | | 4 | 23.5 |
| Mild | | 3 | 17.6 |
| Mild-to-Advanced | | 3 | 17.6 |
| Advanced | | 7 | 41.2 |
| **Social Activity** | | | |
| Able to Participate | | 6 | 35.3 |
| Not able to Participate | | 11 | 64.7 |
| **Independence** | | | |
| Independent | | 2 | 11.8 |
| Semi-independent | | 5 | 29.4 |
| Dependent | | 10 | 58.5 |

*There were 2 people who has no formal education in lifetime.

** NH: Nursing Homes

**Table 3.** Comparison of Individualized Care Approaches

| Subscale and/or Items | Pre-Test | Post-Test | Z* | P value |
|---|---|---|---|---|
| | $\bar{X}$±SD | $\bar{X}$±SD | | |
| **IC-Know (5 items)** | 17.10±2.38 | 17.41±1.80 | 0.641 | 0.521 |
| **IC-Autonomy and Choice (7 items)** | 28.52±2.86 | 26.24±3.36 | -2.691 | 0.007 |
| **IC- SR Communication ( 3 items)** | 7.10±1.71 | 8.52±2.04 | -3.771 | 0.000 |
| **IC- SS Communication (5 items)** | 16.24±2.64 | 16.76±2.84 | 0.883 | 0.377 |

IC-Know: Invidiualized Care-Knowing

IC-Autonomy and Choice: Invidiualized Care- Autonomy and Choice

IC-SR Communication: Invidiualized Care-Staff-to-Resident Communication

IC- SS Communication: Invidiualized Care-Staff-to-Staff Communication

P< 0.05

*Spearman Correlation Test

**Table 4.** Comparison for Psychological Well-being of Residents

| Subscale and/or Items | Pre-Test | Post-Test | Z* | P |
|---|---|---|---|---|
| | $\bar{X}$±SD | $\bar{X}$±SD | | |
| **PWB-CIP Scale (9 items)** | 30.44±3.79 | 29.69±3.00 | -0.948 | 0.343 |
| **Positive Affect (4 items)** | 11.50±2.55 | 11.25±3.35 | -0.147 | 0.883 |
| **Negative Affect (5 items)** | 17.44±2.96 | 16.88±2.63 | -0.907 | 0.365 |

PWB-CIP: Psychological well-being in cognitively ill persons

P<0.05

*Spearman Correlation Test

version of Likert-type ICI has 20 items and 4 sub-domains; (1) knowing the person or resident (IC-know), (2) providing opportunity for autonomy and choice (IC-autonomy), (3) communication staff to staff (IC-communication-SS) and (4) communication staff to resident (IC-communication-SR). The response format uses a four-point Likert-type scale for IC-Know, IC-communication-staff to staff, and staff to the resident (1. strongly disagree; 2. somewhat disagree; 3. somewhat agree; 4. strongly agree) and five-point Likert-type scale for IC-autonomy (1. very frequently; 2. frequently; 3. occasionally; 4. seldom; 5. never). Higher scores indicate better results in each domain. IC-know refers to the staff's own perceptions of how well they know the individuals they are caring for, and the six-item IC-know scale results in scores between 6 and 24. The eight-item IC-autonomy scale measures the general environment in which the staff work, and the possible scores fall between 8 and 40. The three-item IC-communication-SR scale focuses on how the staff communicates with the residents, with possible scores between 3 and 12. Finally, the five-item IC-communication-SS scale reflects the way the staff communicate with one another and with their supervisors, with possible scores lying between 5 and 20 (14).

The PWB-CIP scale consists of 9 items and is completed by the nursing staff's observation of the behavior of the person with cognitive impairment over the past 24 hours. The Likert type PWB-CIP scale (1-4 points) has two sub-dimensions which are positive affect/interaction and negative affect/interaction. The scale can be scored between 9 and 36 in total.

### Data Analysis

The Statistical Package for Social Science (SPSS Inc.) 26.0 for Windows was used for data analysis. This study used descriptive statistics to analyze participants' demographic data, and inferential statistics to compare the mean scores of pretests and posttests. The level of significance (p) was considered as (p) 0.05.

### Ethical Considerations

Permission to undertake the study was obtained from the Koç University Ethical Review Board. The author informed individuals with dementia, their families, and formal caregivers regarding the study. The researcher obtained written and verbal consent from all the participants.

## RESULTS

### Individualized Care Practices

Descriptive information of the participants is presented in Table 1 and 2. The mean ICI scores before and after the programs were compared. The posttest scores increased in all ICI subscales except the IC autonomy and choice subscale. The resident-caregiver communication resulted in a significant increase in posttest (pretest: 7.10±1.71 and posttest: 8.52± 2.04) ($p<0.05$), whereas the autonomy of the residents indicated a significant decrease (pretest: 28.52±2.86 and posttest: 26.24±3.36) ($p<0.05$) (Table 3).

### Psychological Well-Being of the Residents

The mean scores on the PWB-CIP Scale of individuals with dementia before and after the program were compared. There was a non-significant decrease between the pretest (30.44 ± 3.79) and posttest mean scores (29.69± 3.00) ($p>0.05$) (Table 4).

## DISCUSSION

The results of this study provide outcomes of an eight-week enriched dementia care planning intervention program related to individualized care approaches of caregivers and the psychological well-being of residents with dementia. The enriched care planning interventions mainly focused on sharing the life stories of the residents, existing skills of residents, and individualized care training of caregivers. Comparing the before and after the program results, a significant increase in communication between the staff and residents was observed. Conversely, there was a significant decrease in residents' autonomy; however, their psychological well-being remained essentially unchanged throughout the study.

Prior to this study, it was not routine practice to share residents' life stories with caregivers at participating facilities. Formal caregivers' perception of knowing the residents did not change significantly in posttest results. The life stories of the residents were shared by researchers in face-to-face meetings, however, afterward, it is a challenge to expect and motivate all formal caregivers who work with time pressure to read the life stories, as reported in another study (15). Additionally, the increased workload and finding adequate time during the pandemic may have led to insignificant outcomes, which is supported by the literature identifying the key determinants of individualized care delivery such as access to adequate resources (i.e., materials and sufficient time to perform their duties) (16). In a similar study conducted in the United States (US)



(17), exposure to life story collages did not change the caregivers' perception of knowing residents on posttest scores, and there was a significant increase in the level of knowledge of caregivers about the work history and family of the residents.

Resident autonomy and the choice sub-dimensions evaluate the institutional environment that supports resident autonomy (12). Supporting residents' autonomy, connecting with them, maintaining relationships, and maintaining existing skills play an important role in person-centered care (18). In this study significant decrease was found in the posttest for "residents' autonomy and choice" sub-dimension. A qualitative study conducted in focus interviews with caregivers and residents revealed that the freedom, autonomy, social life, and social activities of the older adults staying in care centers are restricted and their basic psychological needs could not be met owing to the COVID-19 pandemic (19). Understanding the preferences of the residents and providing activities of daily living aligned to their preferences is a necessity for the residents to feel that they have autonomy (20). During the current study, all activities with residents were restricted, which created an inability to perform daily participation and socialization during the COVID-19 period.

Strengthening communication with individuals with dementia is an initiative that supports person-centered care processes (9). In this study, in addition to sharing life stories with caregivers, "about me" profiles comprising brief information regarding individuals with dementia were posted in the residents' rooms. After these interventions, the communication scores between the residents and caregivers increased significantly in the post-test. Similarly, life stories and practices for becoming acquainted with the individual increased communication between staff and individuals with dementia (21-23). When caregivers know the residents' life stories, they feel empowered and become relationship-oriented rather than task-oriented (24).

In person-centered care, the quality of communication between formal caregivers is important, and therefore, insufficient communication can be an obstacle in the provision of person-centered care (24). Teamwork, having shared values, and value-based work improve the collaboration and dedication to care for residents in a person-centered manner, as expressed in qualitative studies in LTC facilities (25).

Another aspect of this study was to observe the changes in the psychological well-being of residents during the intervention. There was a significant positive change in nursing home staff attitudes, while there was no change in the well-being of the residents with dementia. Nursing home staff benefited more from the enriched care planning program and significant changes has been seen in their attitudes due to the possible positive effect of "investing in them at an educational level" (as an important human factor that increases team member productivity in working environments). The factors mostly associated with the quality of life and well-being of individuals with dementia were social interaction, communication, and the use of functional skills but there are also disease related factors effecting well-being of residents such as dementia stage progression and environmental conditions. It has been reported that with the decline in physical and mental health, well-being and quality of life also begin to decline. Further, as the dementia stage progresses, environmental factors and well-being are more related to one another (13). Accordingly, the number of people with advanced stage dementia participating in this study and the potential effects of the COVID-19 restrictions on resident autonomy may have had a negative impact on some indicators of well-being that are affected more by environmental conditions.

There are certain limitations to this study, such as the small sample size with one-group pre-test and post-test design. Since the research coincided with the COVID-19 pandemic, the restrictions and measures during this period caused certain changes

in the research process, and consequently, certain limitations were inevitable. During the COVID-19 pandemic factors such as restriction on visits to the long-term care environment, restricting residents to their rooms, interrupting social and daily activities, and longer working hours of the staff should be considered in the interpretation of the results of the study. The reason for the lack of impact on the well-being of persons with dementia from the implemented program could be an important limitation due to the fact that this patient group has different types and stages of dementia. Information about the types of dementia was not available, so this could be another limitation of the study.

## CONCLUSION

The results demonstrate that using enriched care planning has the potential to improve communication between caregivers and residents in long-term care environments. Easily accessible life story booklets that were enriched with visual images and original photographs helped to develop more positive attitudes toward individuals with dementia. Improvement in communication between staff and residents should be considered as useful initiatives for individualized care improvement. Additionally, eye-catching "about me" profiles displayed in residents' rooms were easily readable that reminded caregivers to initiate communication during the daily resident care activities. Other supportive interventions such as person-centered communication training, reminders about person-centered dementia care, and communication tips posted on the staff unit walls were effective in sustaining the intervention. Formal caregivers may have difficulty becoming acquainted with residents with dementia, who often have communication and social skill deficits. Introducing formal caregivers to residents' life stories and profiles and educating them about individualized care can improve relationships and commitment to individualized care. Strengthened relationships can have a positive impact on formal caregivers and can also lead to higher job satisfaction and reduced staff turnover. Enriched care planning should become routine practice in nursing homes, as currently it is not practiced to the expected extent in many countries. Recruitment of gerontological nurses in nursing homes with well-designed individualized care planning can improve nursing practice.

Future studies with larger samples and without the pandemic restrictions are recommended with additional measures such as the effect on quality of life, aggression, teamwork, and staff knowledge. The methodological strength of the same study would be enhanced by including a control group consisting of nursing home staff who did not receive the intervention program at all, providing only standard care, along with dementia patients residing in nursing homes receiving standard care in the future.

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ORIGINAL ARTICLE

# EVALUATION OF MORTALITY AND MORBIDITY ASSOCIATED WITH OSTEOPOROTIC HIP FRACTURE

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## Abstract

**Introduction:** Hip fractures in older adults are associated with significant morbidity, mortality, loss of independence, and financial burdens. In this study, we assessed how factors influenced these effects in elderly patients presenting with hip fractures.

**Materials and Method:** A prospective observational study was conducted over six months on all patients with fall and hip fractures above 50 years of age who presented to the orthopedics and traumatology clinic of our university hospital. Ambulation status, time until operation, vitamin D level, vertebral fractures, Charlson comorbidity index, and Fracture Risk Assessment Tool score were recorded. The patients' re-evaluated in the sixth month after the fracture. The relationship between death and risk factors was examined by regression analysis.

**Results:**105 patients were included in the study. The mortality rate was 23.8%. The immobility rate also increased from before the operation to after 1.9% to 31.4%. Univariate regression analysis showed that mortality is related to age, Charlson comorbidity index, smoking history, and Fracture Risk Assessment Tool hip score. At the same time, multivariate regression analysis revealed an association between body mass index, smoking history, and mortality.

**Conclusion :**Osteoporosis is a widespread disease that may remain hidden until complications, such as fractures, present themselves. Functional loss and mortality risk are high in patients with fractures. Age, Charlson comorbidity index, body mass index, smoking, Fracture Risk Assessment Tool hip score, and pre-fracture ambulation status affect mortality. A decrease in mortality can be achieved by monitoring risky individuals in fracture liaison services.

***Keywords:*** Risk factors; Mortality; Osteoporosis; Hip fractures.

## INTRODUCTION

One of the most critical complications of osteoporosis is hip fracture. Low trauma is the leading cause of osteoporotic hip fracture for more than half of the patients, with the rate increasing with age. It has been reported that between 8.4% and 36% of patients die within the first year after the development of the fracture (1). In addition, the ambulation of patients deteriorates after fracture and some even become in need of care. After 1 year, 40% of the patients could not walk independently. Despite increased economic costs and morbidity due to osteoporotic fracture, only 20% of patients receive antiresorptive therapy (2). Therefore, fracture liaison services (FLS) have been used worldwide to treat individuals with osteoporotic fractures, determine fracture risks in patients, and promote the pharmacological and non-pharmacological treatment of osteoporosis. FLS are structures created to include individuals with osteoporotic fractures in a secondary fracture protection program after surgery. They are generally created in tertiary care hospitals and enable many healthcare professionals to follow up and treat patients in a coordinated manner. Thus, the number of patients treated and compliance with treatment increases, and the risk of re-fractures and mortality decreases. Clinical, medical, and laboratory evaluation is indicated in all adults with osteoporotic fractures.

The primary acute treatment for osteoporotic hip fracture is surgery, recommended in the early period of the incident. Although early surgery after the fracture seems to lower mortality, there are still conflicts about delayed surgery time. Apart from mortality, functional outcomes are better in patients who undergo early surgery (3). In addition, gender, age, pre-fracture ambulation status, and comorbidities also affect mortality. The Charlson comorbidity index (CCI) is a validated index that calculates the comorbidities and predicts the risk of death. The index consists of 19 items corresponding to different medical comorbid conditions. A CCI score above 0 was associated with an increased risk of severe disease and death when controlled for age and sex.

Active vitamin D plays an essential role in calcium absorption and bone health. It is also crucial in balance, fall prevention, and muscle strength. If the vitamin D level is 20 ng/ml and below, it indicates deficiency, and if it is between 20 and 30 ng/ml, it indicates insufficiency. It has been shown that there is a significant relationship between low vitamin D levels and hip fractures. Vitamin D levels were found to be low in 96% of individuals who had hip fractures, and it was found to be below 9 ng/ml in 38% (4).

The most common fracture in osteoporosis is vertebral fracture. Even if the bone mineral density (BMD) measurement is standard, having a vertebral fracture is a high-risk indicator for other fractures. Since vertebral fractures may be clinically silent, they may not be detected unless spinal imaging is performed. Former or follow-up shortening may be an indication of vertebral fracture. It is recommended that patients be screened by performing vertebral fracture assessment (VFA) with lateral spinal view direct X-ray or DXA (5).

Fracture Risk Assessment Tool (FRAX) determines fracture risk in patients and includes many risk factors independent of BMD. It determines the 10-year risk of hip and major osteoporotic fractures (i.e., clinical vertebra, hip, forearm, and humerus) and guides the treatment decision. FRAX may be associated with mortality because it contains many risk factors and may indicate osteoporosis and vascular calcification (6). Smoking causes osteoporosis by directly affecting the bone metabolism of cadmium and indirectly by affecting the endogenous estrogen metabolism. Active smokers are at higher risk than those who quit. Smoking cessation for more than 10 years reduces the risk of hip fracture. In addition, a significant correlation was found between smoking and mortality in individuals with osteoporotic hip



fractures (2, 7).

Our study aimed to examine hip fractures and their outcomes in elderly patients in a tertiary care hospital in Turkey. Although risk factors for fracture are well defined, outcomes of patients with hip fractures are still a subject that merits further research.

## PATIENTS AND METHOD

A prospective observational study was conducted between June 2019 and December 2019 on all patients who presented to the orthopedics and traumatology clinic with osteoporotic hip fractures above the age of 50. The subjects were followed up for up to 6 months. Patient data were obtained from the patient file and by contacting the patient by phone. All patients over 50 who had a hip fracture because of low trauma and agreed to participate were included in the study.

The study was approved by the Faculty of Medicine Ethics Committee (18-11.1T/10) and was conducted following the Declaration of Helsinki. All participants in the study provided written informed consent to this work and agreed to the scientific use of their data.

### Demographic data and clinical assessment

The patients were evaluated at hospitalization and 6 months after hip fracture. Age, gender, height, weight, education level, patient's pre-fracture ambulation status, length of hospital stay, FRAX hip, and FRAX total values, time until the operation, type of operation, vitamin D level, vertebral fractures, smoking, and CCI score were noted at the time of hospitalization for osteoporotic hip fracture. Six months after the hip fracture, the patients were reassessed for mortality, ambulation status, and newly developed osteoporotic fracture. We assessed mobility limitations, which is the most common morbidity after hip fractures. Patients were questioned regarding their need for assistive devices. Ambulation statuses were classified as immobile, needs ambulatory support indoors, needs ambulatory support outdoors, and independently mobile.

For vitamin D levels, the 25-OH vitamin D measurement was evaluated; those patients with below 20 ng/ml were considered vitamin D deficient, and those with between 20 and 30 ng/ml were considered vitamin D insufficient. The radiologist evaluated the lateral spinal view according to the presence of fracture in terms of vertebral fracture, and patients with fractures were classified according to semiquantitative staging. FRAX score calculation was evaluated according to risk factors without bone mineral density. The CCI is a simple, easy-to-perform, and valid method to estimate the risk of death related to comorbid diseases. Classical CCI includes 19 medical conditions weighted 1–6 with total scores ranging from 0 to 33.

### Statistical Analysis

IBM SPSS Statistics performed statistical analyses for the Windows 25.0 (IBM Corp., Armonk, NY) package program. The level of significance was determined as $\alpha$=0.05 in all analyses. Numerical data were summarized as mean, standard deviation, median, and minimum and maximum values, and categorical data were summarized by frequency and percentage.

The primary outcome variable was mortality at the 6-month follow-up. Age, gender, body mass index (BMI), length of hospital stays, time until the operation, type of operation, FRAX hip and FRAX total values, smoking, vitamin D level, fracture presence in lateral vertebral view and CCI were first evaluated using univariate logistic regression analysis. Variables with significance below 0.25 in univariate logistic regression analyses were determined to be candidate variables for the multivariate model. Logistic regression results were given with odds ratios and 95% confidence intervals for these ratios.

The change in pre-fracture and post-fracture 6-month ambulation status were examined using the Wilcoxon signed-rank test. The effect of preoperative ambulation status on mortality was determined with the help of Fisher's exact test.

## RESULTS

The study included 105 patients: 79 females and 26 males. The mean age was 77.85. Twenty-five (23.8%) patients were found deceased within 6 months; 4% of deaths occurred during hospitalization, 24% in the first month after discharge, and 72% between 2 and 6 months.

The demographic findings of the patients are summarized in Table 1, and the clinical features of the patients are summarized in Table 2.

Forty-nine percent of patients were already using assistive devices before the fracture, but the requirement for use increased to 92%. Moreover, the immobility rate increased from 1.9% to 31.4%. Thirty-six percent of the patients were mobile independently before the fracture, and only 15% were independently ambulatory in the sixth month after the fracture. The ambulation status of the patients and the use of assistive devices are shown in Table 3. When the change in ambulation status between pre-fracture and post-fracture at 6 months was examined, worsening was observed in 58.1% of the patients ($p<0.001$).

In the univariate regression analysis, age, FRAX hip score, smoking, and CCI showed a statistically significant relationship with mortality ($p < 0.05$; Table 4). Variables with $p < 0.25$ in the univariate logistic regression analysis were analyzed with a multivariate model. In multivariate regression analysis, the relationship between elevated BMI, smoking, and mortality was statistically significant ($p < 0.05$; Table 5). Vertebral fracture distribution could not be analyzed because it was irregular.

The relationship between patients' pre-fracture ambulation status and mortality was examined;

**Table 1.** Demographic findings

| | |
|---|---|
| **Age (yr), mean ± *SD*** | 77.85 ± 9.94 |
| **Gender, *n* (%)** | **Female:** 79 (75.3%)<br>**Male:** 26 (24.7%) |
| **Educational status, *n* (%)** | **Illiterate:** 22 (21.2%)<br>**Literate:** 3 (2.9%)<br>**Primary education:** 63 (60.6%)<br>**High school:** 7 (6.7%)<br>**University:** 9 (8.7%) |
| **BMI (kg/m$^2$), *n* (%)** | **Underweight (<18.5):** 3 (2.9%)<br>**Normal (18.5–24.9):** 35 (33.3%)<br>**Overweight (25–29.9):** 39 (37.1%)<br>**Obese (>30):** 28 (26.7%) |
| **Smoking, *n* (%)** | **Never smoked:** 70 (66.7%)<br>**Quit:** 28 (26.7%)<br>**Active smoker:** 7 (6.7%) |
| **Alcohol consumption, *n* (%)** | **Never drank:** 100 (95.2%)<br>**Quit:** 4 (3.8%)<br>**Active alcohol drinker:** 1 (1%) |
| **Osteoporotic fractures before hip fracture, *n* (%)** | **No:** 73 (69.5%)<br>**Yes:** 32 (30.5%)<br>**Clinical vertebral fracture:** 5 (13%)<br>**Hips:** 11 (29%)<br>**Forearm:** 8 (21%)<br>**Proximal humerus:** 8 (21%)<br>**Others:** 6 (16%) |
| **Pre-fracture osteoporosis treatment, *n* (%)** | **Bisphosphonate:** 9 (8.5%)<br>**Denosumab:** 2 (1.9%)<br>**Teriparatide:** 0 |
| **Use of vitamin D, *n* (%)** | **None:** 100 (95.3%)<br>**Yes:** 5 (4.7%) |
| **Use of calcium supplements, *n* (%)** | **None:** 96 (91.5%)<br>**Yes:** 9 (8.5%) |

Note. BMI, body mass index; n, number; SD, standard deviation.

**Table 2.** Clinical features

| | |
|---|---|
| **Survival at 6 months,** *n* **(%)** | **Alive:** 80 (76.2%)<br>**Dead:** 25 (23.8%)<br>- **Men:** 7 (30% of men)<br>- **Women:** 18 (22.8% of women) |
| **Time of death,** *n* **(%)** | **During hospitalization:** 1 (4%)<br>**1 month:** 6 (24%)<br>**2–6 months:** 18 (72%) |
| **Type of operation,** *n* **(%)** | **Total hip replacement:** 3(2.8%)<br>**Endoprosthesis:** 38(36.2%)<br>**Proximal femoral nail:** 58(55.2%)<br>**Others:** 6(5.8%) |
| **Time until operation (days), median (min–max)** | 4 (1–25) |
| **Length of hospital stay (days), mean ± *SD*** | 7.73 ± 3.21 |
| **New fracture development after fracture,** *n* **(%)** | **None:** 98 (93.4%)<br>**Yes:** 7 (6.6%) |
| **Control vertebral radiographs,** *n* **(%)** | **None:** 56 (53.3%)<br>**Yes:** 49 (46.7%) |
| **Osteoporotic fracture on vertebral radiographs,** *n* **(%)** | **None:** 5 (10.2%)<br>**Yes:** 44 (89.8%) |
| **Fracture stage (semiquantitative classification),** *n* **(%)** | **Stage 1:** 32 (72.7%)<br>**Stage 2:** 4 (9.1%)<br>**Stage 3:** 8 (18.2%) |
| **Vitamin D level (ng/ml),** *n* **(%)** | **<10 ng/ml:** 33 (35.9%)<br>**10–19 ng/ml:**23 (25%)<br>**20–29 ng/ml:** 14 (15.2%)<br>**≥30 ng/ml:** 22 (23.9%) |
| **Vitamin D level (ng/ml), Median (Min–Max)** | 16 (3–77) |
| **CCI, median (min–max)** | 5 (1–12) |

Note. CCI, Charlson comorbidity index; n, number; SD, standard deviation.

**Table 3.** Ambulation status and assistive device use

| | **Pre-fracture** | **6-month control** |
|---|---|---|
| **Use of assistive devices** | **None:** 50.5%<br>**Yes:** 49.5% | **None:** 8%<br>**Yes:** 92% |
| **Ambulatory status** | **Immobile:** 1.9%<br>**Needs ambulatory support indoors:** 39%<br>**Needs ambulatory support outdoors:** 22.9%<br>**Independent ambulation**: 36.2% | **Immobile:** 31.4%<br>**Needs ambulatory support indoors:** 42.9%<br>**Needs ambulatory support outdoors:** 10.5%<br>**Independent ambulation** 15.2% |

**Table 4.** Univariate regression analysis of mortality

| Variable | OR | 95% confidence interval | | p |
|---|---|---|---|---|
| | | Lower | Upper | |
| Age | 1.091 | 1.020 | 1.166 | 0.011 |
| Gender (male) | 1.167 | 0.425 | 3.200 | 0.765 |
| BMİ | 1.079 | 0.994 | 1.172 | 0.070 |
| Time of operation | 1.001 | 0.964 | 1.039 | 0.971 |
| Length of hospital stay | 1.081 | 0.946 | 1.235 | 0.251 |
| FRAX major osteoporotic fracture | 1.041 | 0.999 | 1.085 | 0.055 |
| FRAX hip fracture | 1.062 | 1.003 | 1.125 | 0.038 |
| Smoking history | 2,856 | 1,132 | 7,206 | 0,026 |
| Vitamin D level | 1,011 | 0,982 | 1,041 | 0,457 |
| Vitamin D <10 ng/ml | 1,024 | 0,284 | 3,688 | 0,971 |
| Vitamin D 11–19 ng/ml | 0,889 | 0,217 | 3,643 | 0,870 |
| Vitamin D 20–29 ng/ml | 0,533 | 0,088 | 3,235 | 0,494 |
| CCI | 1.507 | 1.120 | 2.028 | 0.007 |

Note. BMI, body mass index; CCI, Charlson comorbidity index; FRAX, Fracture Risk Assessment Tool; OR, odds ratio.

**Table 5.** Multivariate regression analysis of mortality

| Variable | OR | 95% confidence interval | | p |
|---|---|---|---|---|
| | | Lower | Upper | |
| Age | 1.074 | 0.979 | 1.179 | 0.130 |
| BMI | 1.125 | 1.007 | 1.256 | 0.037 |
| FRAX major osteoporotic fracture | 0.997 | 0.853 | 1.165 | 0.969 |
| FRAX hip fracture | 1.080 | 0.882 | 1.323 | 0.456 |
| Smoking | 7,686 | 1,760 | 33,562 | 0,007 |
| CCI | 1.386 | 0.975 | 1.971 | 0.069 |

Note. BMI, body mass index; CCI, Charlson comorbidity index; FRAX, Fracture Risk Assessment Tool; OR, odds ratio.

50% of pre-fracture immobile patients died. This rate was found to be 34% in patients who needed ambulatory support indoors before the fracture, 25% in patients who needed ambulatory support outdoors, and 10.5% in those who ambulated independently. The better pre-fracture ambulation status is related to a lower post-fracture mortality risk with a low correlation (0.256).

## DISCUSSION

In this prospective, single-center cohort study, patients operated on for osteoporotic hip fracture were followed up for 6 months, and mortality, changes in ambulation status, and factors affecting mortality were investigated. Even in the first months after osteoporotic hip fractures, mortality rates



were high. In this study, 25 patients died in the first 6 months. Deceased patients constituted 23.8% of all participants. In a study conducted in Spain, the 6-month mortality was 23%, whereas a study from Italy showed a relatively low rate of 14.1% (8, 9). The cause of the low outcomes may be related to including patients who underwent surgery and those who followed conservatively. The mean hospital stay of the patients is 7.7 days. Mortality increases in hospitalizations lasting less than 10 days (10). In patients who are discharged in a short time after the operation, rehabilitation, osteoporosis treatment, and management of postoperative complications may be lacking, which may have led to an increase in mortality. In addition, since the study was conducted in a tertiary hospital, patients referred from secondary hospitals due to the high risk of surgery constitute some of our patients. Surgery on individuals with multiple risk factors may have been another reason for the increase in mortality.

Age is a possible risk factor for mortality in osteoporotic hip fractures. Elderly patients may suffer higher mortality rates. According to the results of this study, each 1-year increase in age raises the risk of death by 9.1%. However, age was not significant when included in the multivariate regression analysis. Although older age was a possible risk factor for death after a hip fracture, we could not find any strong evidence for older age as a risk factor for death after a hip fracture. The higher number of comorbidities in elderly patients affects mortality. It has been reported that heart failure, family history of hip fracture, and pre-fracture ambulation status interact with age and may affect mortality rates (8, 9). Male gender is a risk factor for mortality (8). Twenty-four percent of our patients were men, and 30% of the male and 22% of the female patients died in the first 6 months. Although mortality was higher in male patients, it was not statistically significant. In addition to the male gender, many factors, such as the patient's clinical condition, age, comorbidities, fracture type, type of surgery, length of hospitalization, and complications, can affect mortality (11).

Another affecting factor for osteoporotic hip fracture related to mortality is BMI. In the current literature, hip fracture seems less familiar in obese individuals than in standard and low weights. Some studies have shown that the risk of osteoporotic fractures increases with an increase in BMI. This association is partially explained by worse physical function in obese men (12). Modig et al. found that a BMI below 22 kg/m$^2$ is associated with higher mortality, called the obesity paradox (13). The study consisted of 8% obese and 26.9% overweight patients. Although complications are higher in obese or overweight patients, mortality rates are lower (14). In this study, in contrast to the literature, mortality was higher in patients with higher BMI. Each unit increase in BMI increases the risk of death by 12.5%. Compared with Modig et al., obese and overweight patients constituted a higher rate (26.7% were obese, and 37% were overweight). Metabolic syndrome and related complications seem more common in people with high-level BMI. Due to the high patient burden, the patients stayed in the hospital for a shorter period, so the complications that developed in the patients may not have been well managed. As a result, an increase in mortality may have been observed in people with high BMI.

The median time until the operation of our patients is 4 (1–25) days. No significant interaction was found when looking at its relationship with mortality. Surgery is recommended in the early period after osteoporotic hip fracture. Mortality is lower in patients who undergo surgery within the first 24 to 48 hours. Some studies found no increase in mortality due to a delayed operation (3, 15). Current guidelines recommend early surgery for patients with hip fractures (16). If the patient has an additional condition that requires treatment before surgery, there may be an increase in mortality by performing surgery without treating the problem

(17). Delaying the operation due to the treatment of comorbid medical conditions of our patients may have prevented an increase in mortality. The mean hospital stay of our patients was 7.73 ± 3.21 days. No significant interaction was found when looking at its relationship with mortality. Patient discharge in fewer than 10 days is associate with mortality (10). Since most of our patients were discharged in fewer than 10 days, the relationship between the length of hospital stay and mortality may not have been observed.

FRAX indicates fracture risk. Because the mortality rate increases in individuals with fractures, we aimed to evaluate the relationship between mortality and FRAX score. This study calculated that the probability of death increased as the FRAX hip fracture probability increased, and each unit increase in the FRAX hip score increased the risk of death by 6.2%. No significant relationship was found when the FRAX hip score was included in the multivariate regression analysis. Although the FRAX hip score was a possible risk factor for death after a hip fracture, we did not find any strong evidence for the FRAX hip score as a risk factor for death after a hip fracture. In a study conducted on patients with end-stage renal disease, FRAX major osteoporotic fracture risk was associated with mortality. FRAX may also be associated with mortality because it contains many risk factors and may indicate osteoporosis and vascular calcification (6).

Control vertebral radiographs of 46.7% of our patients could be taken. Vertebral collapse fracture was found in 89.8% of the patients who had radiographs; 73% of the fractures are Stage 1, 9% are Stage 2, and 18% are Stage 3 fractures. A retrospective study conducted in Japan found a compression fracture in the vertebrae in 78% of individuals with a history of hip fracture, like our study. Mortality was higher in patients with vertebral compression fractures (18). In a study conducted in Ireland, vertebral fractures were detected in 40% of osteoporotic hip fracture patients who underwent vertebral imaging. There was no significant relationship between mortality and the presence of vertebral fractures (19). In our study, however, a relationship between vertebral fracture and mortality could not be examined due to data distribution. Vertebral imaging could not be performed in all patients due to patient density and additional health problems. Since all our patients could not be evaluated, a significant relationship between mortality and vertebral fracture may not have been evaluated.

The mean vitamin D level of the patients was found to be 16 ng/ml. While 24% of the patients have normal vitamin D levels, 15.2% have vitamin D insufficiency, and 60.9% have a vitamin D deficiency. Considering the effect on mortality, no significant interaction was observed in the regression analysis. A study conducted in South Korea reported that 76.5% of individuals who had osteoporotic hip fractures had low vitamin D levels and that there was a relationship between low vitamin D and mortality. However, there was no independent risk factor (20). Vitamin D levels were low in 96% of individuals with osteoporotic hip fractures in the USA and 47% in Norway (21). This difference may have been observed in the patient population for many reasons, such as the study's season of the year, geographical location, diet, and use of food supplements.

In this study, 33.4% of the patients had a smoking history. Cigarette consumption causes a decrease in BMD. Although the mechanism is unclear, it causes a decrease in BMD, since calcium absorption from the intestines decreases by affecting serum estradiol, vitamin D, and PTH levels with cigarette consumption (22). Solbakken et al. found that 24.6% of patients with hip fractures had a smoking history, and there was a significant relationship between smoking and mortality (23). In the study of Bliuc et al., in which the factors affecting mortality due to osteoporotic hip fracture were examined, smoking was associated with mortality (2). Our study found



a significant relationship between smoking history and mortality. If the patient with a hip fracture smoked, the probability of death was 2.9 times higher. When other variables are kept constant, if a patient has a smoking history, the mortality risk increases 7.770 times compared to individuals without a smoking history.

CCI was used to calculate the morbidity risk in patients. This index estimates mortality according to comorbid conditions in patients. Each unit increase in CCI increases the risk of death by 50.7%. In a retrospective cohort study, the authors stated that CCI is the primary determinant of early and long-term mortality. In patients with a score below 5 who underwent early surgery, mortality was significantly lower. We found no relationship between CCI score and mortality after hip fracture, although we observed a significant association with mortality in the univariate analysis (24).

A significant correlation was found between the pre-fracture ambulation status of the patients and mortality, which was similar to previous studies (8, 9). Our subjects' limited ambulatory status before fracture may have resulted in higher mortality. While the ambulation status of 41.9% of the patients remained the same, the ambulation status of 58.1% worsened. Thirty-eight patients ambulated independently before the fracture, decreasing to 16 after the fracture. In a study conducted in Italy, 50.5% of the patients had a worsening ambulation status, and 4.3% showed improvement. Because the ambulation status of the patients was worse before the fracture in our study, it is expected that the ambulation status would be worse at the 6-month follow-up (8, 25).

The strengths of our study are that it is a prospective cohort study, the same person evaluated the patients at the time of and in the sixth month after the fracture, and hospitalization of patients in a center.

The limitations of our study are the absence of a control group, failure to assess patients' mental states, no rehabilitation data, vertebral fracture evaluation not performed in all patients, and 6 months of follow-up.

Osteoporosis is a widespread disease with ambiguous findings that may remain hidden until complications such as fractures are presented. Functional loss and mortality risk are high in patients with fractures. In addition, the cost to the healthcare system is relatively high. Age, CCI, FRAX hip fracture, smoking, BMI, and pre-fracture ambulation status affect mortality. Therefore, patients should be identified and treated before fractures develop. As FLS become more widespread, we expect lower mortality and morbidity in this vulnerable patient population.

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ORIGINAL ARTICLE

# MORTALITY PREDICTORS IN ELDERLY INTENSIVE CARE UNIT PATIENTS WITH ACUTE KIDNEY INJURY REQUIRING HEMODIALYSIS

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## Abstract

**Introduction:** The incidence of acute kidney injury is increasing in the elderly. This condition is especially serious during the course of critical illness, and the rate of mortality rises with the condition's increasing severity. We aimed to identify the risk factors for in-hospital, 28-day, and 90-day mortality among elderly patients admitted to the intensive care unit with acute kidney injury requiring dialysis.

**Materials and Method:** We conducted a retrospective study between January 2011 and December 2019 of patients 65 years of age and older who were hospitalized with acute kidney injury requiring dialysis in the intensive care unit of an internal medicine department.

**Results:** A total of 144 patients were evaluated, 63 male (43.75%) and 81 female (56.25%). The in-hospital, 28-day, and 90-day mortality rates were 40.9%, 47.2%, and 56.2%, respectively. Sepsis etiology was associated with poor prognosis. In univariate Cox regression analysis, we identified use of inotropes, final C-reactive protein, neutrophil to lymphocyte ratio as mortality predictors at all three time points. Use of inotropes, final C-reactive protein continued to be predictors of mortality in multivariate analysis. Age was not found to be a factor affecting mortality.

**Conclusions:** Data are limited on the outcomes of elderly patients with acute kidney injury requiring dialysis, but routinely evaluated laboratory parameters in intensive care practice may be predictive of mortality. Our results provide deeper understanding of how these variables interact and contribute to the risk of mortality. Chronological age alone should not be a consideration for hemodialysis.

***Keywords:*** Aged; Critical Care; Hemodialysis; Acute Kidney Injury; Mortality.

## INTRODUCTION

Acute kidney injury (AKI) is a serious condition that is observed especially in the course of critical illnesses. A multinational, multicenter prospective study reports septic shock as the condition's most common contributing factor (1). The causes of death in hospitalized patients with AKI have been identified as sepsis, cardiovascular disease (CVD), and malignancy, with pneumonia being reported as the main sequela of sepsis (2). AKI cases requiring hemodialysis are associated with increased mortality and morbidity both in hospital and after discharge (3). In recent years, the incidence of AKI requiring dialysis has increased 10% annually (4). Aging is strongly associated with AKI risk and incidence (4-7), although some contend that the risk of AKI requiring dialysis in the elderly is similar to that of young people. However, the incidence of AKI is increasing faster in young people (8).

Mortality in AKI has been reported at rates ranging from 31%–80%, and the highest mortality has been observed in AKI cases requiring dialysis (9). In the BEST kidney study, advanced age was found to be independently associated with in-hospital mortality in patients with AKI (1), which develops due to the co-occurrence of chronic diseases, structural and functional deterioration of the kidneys, and exposure to nephrotoxic agents (5, 6). The outcomes of patients with AKI requiring dialysis in the elderly population are not entirely clear, and the growing incidence of AKI requiring dialysis in that population makes it critical to identify the risk factors for mortality to support early intervention to improve outcomes. This study aimed to determine the mortality rate and the factors predicting mortality in elderly patients who develop AKI requiring hemodialysis.

## MATERIALS AND METHOD

This study was conducted retrospectively on patients followed up from 2011–2019 in the intensive care unit (ICU) of the Department of Internal Medicine of Ege University Faculty of Medicine. The study was approved by Ege University's ethics committee (No. 19-5.2T/69) and adhered to the principles of the Declaration of Helsinki. Elderly patients with AKI requiring dialysis upon admission to ICU or who developed AKI requiring dialysis during hospitalization were included, and all patients or their relatives provided written informed consent. Figure 1

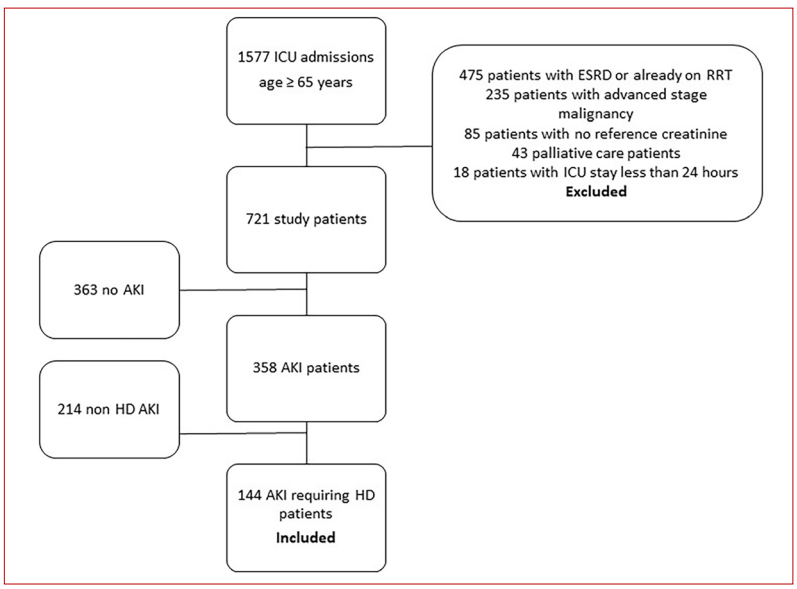



**Figure 1.** Flow chart of patient inclusion and exclusion



shows a flow chart of patient inclusion and exclusion. *Elderly patients* were defined as those aged 65 years or above (10). Patients were excluded who had a history of end-stage renal disease, were already on renal replacement therapy, were in palliative care, were at an advanced stage of malignancy, died in a period shorter than 24 hours, or had no reference creatinine in the past three months.

Demographic characteristics, comorbidities, AKI etiology, and laboratory data at admission and discharge/death were collected from electronic medical records. The previous diagnosis on clinical records sufficed for the confirmation of comorbidities, including CVD, hypertension (HT), diabetes mellitus (DM), chronic kidney disease (CKD), and heart failure (HF). The Sepsis-3 criterion was used to define sepsis (11), and the Acute Dialysis Quality Initiative consensus report was used to define cardiorenal syndrome (12). We compared survivors and non-survivors to identify the factors associated with mortality. The primary outcome was in-hospital mortality, and the secondary outcomes were mortality at 28 and 90 days after discharge. Deaths were categorized according to the time of occurrence as "in-hospital mortality" if they occurred during intensive care hospitalization, "28-day mortality" if they occurred within the first 28 days after ICU discharge, and "90-day mortality" if they occurred ≥29-90 days after ICU discharge.

### Statistical Analysis

The study analyzed various biomarkers, including albumin levels (baseline: 2.76%, follow-up: 5.52%), C-reactive protein levels (baseline and follow-up: 4.83%), neutrophil count (baseline: 0.69%, follow-up: 2.07%), lymphocyte count (baseline: 0.69%, follow-up: 2.07%), urea level (baseline and follow-up: 0.69%), creatinine level (baseline and follow-up: 0.69%), and the neutrophil/lymphocyte ratio (baseline: 0.69%, follow-up: 2.07%). Considering the low variability in these rates (predominantly below 5%) and the likelihood of a near-normal distribution of the data, the mean imputation method was employed for handling missing data. This approach aimed to enhance the credibility of the analytical results by maintaining the integrity of the data set. Mean imputation is particularly beneficial for consistency and validity of analyses when missing data is minimal and under the presumption of negligible inter-variable correlations.

The data presented in Tables 1, 2, and 3 underwent comprehensive analysis, segmented by patient demographic features and clinical conditions. For continuous variables, the analysis employed the mean ± standard deviation for normally distributed data, or the median with minimum and maximum values for non-normally distributed data, contingent upon the data's distribution. Categorical variables were summarized using frequencies and percentages. The normality of numerical variables was ascertained using Shapiro-Wilk, Kolmogorov-Smirnov, and Anderson-Darling tests. The selection of appropriate statistical tests was based on the outcomes of these normality assessments.

For categorical variables, the study utilized Pearson Chi-Square, Fisher's Exact, or Fisher Freeman Halton tests, depending on the number of expected observations, to determine the differences between groups.

In our study, the comparison of numerical variables between two independent groups was conducted using the Independent Samples T-test for variables with normal distribution. Conversely, the Mann-Whitney U test was employed for variables lacking normal distribution.

For the assessment of clinical variables such as NT-proBNP, troponin, mean platelet volume, systolic and diastolic blood pressure, mean arterial pressure, pulse pressure, and heart rate, we utilized the Wilcoxon signed rank test. This approach was specifically chosen for evaluating changes over time in the same patients, comparing measurements at admission (1) and at discharge or death (2). The test's focus was on discerning variations in repeated

measures within individual patients, rather than comparing median values across two independent samples. The application of this test enabled us to statistically analyze the evolution of clinical variables throughout each patient's treatment journey.

In our study, we extensively examined the relationship between mortality rates, including hospital, 28-day, and 90-day mortality, and various clinical variables such as albumin, C-reactive protein (CRP), neutrophils, lymphocytes, urea, creatinine, and the neutrophil/lymphocyte ratio (NLR). This analysis was facilitated by the use of the Nonparametric Analysis of Longitudinal Data in Factorial Experiments (NparLD) package within the R library. The NparLD package is particularly adept at handling non-normally distributed data, which is a characteristic trait of our clinical dataset. This capability is vital for ensuring robust analysis despite the non-normal distribution of our data. Additionally, the package efficiently addresses the complexities associated with longitudinal data, making it an ideal tool for analyzing time-based interactions in our research.

The NparLD package also supports advanced analytical methods, such as F2-LD-F1 and F1-LD-F1 analyses. The F2-LD-F1 analysis is crucial for investigating factorial designs with two factors at two levels, enabling thorough exploration of variable interactions over time. The F1-LD-F1 analysis, on the other hand, is designed for single-factor designs with repeated measures, allowing for detailed assessment of a variable's impact over multiple time points.

Furthermore, we employed key functions of the NparLD package like the Wald-Type Statistic (WTS), ANOVA-Type Statistic (ATS), and Modified ANOVA-Type Statistic in our analysis. These methodologies were instrumental in evaluating the influence of independent variables on the dependent variable, identifying differences between treatment groups, and tracking changes over time. The Modified ANOVA-Type Statistic, in particular, played a critical role in uncovering more complex interactions, with p-values serving as the preferred metric for these outcomes. These capabilities make the NparLD package an invaluable resource for accurately interpreting the intricate relationships among various clinical variables and mortality rates across different time intervals.

In the analysis of the data presented in Tables 5, 6, and 7, it was determined that the Nonparametric Analysis of Longitudinal Data in Factorial Experiments (NparLD) package could not be appropriately applied. The primary limitation stemmed from the extensive amount of missing data within these specific datasets. The NparLD package, while robust in handling complex and non-normally distributed data, requires a relatively complete dataset to effectively analyze longitudinal interactions and factorial designs. Given the significant gaps in the data, particularly in these tables, an alternative approach was deemed more suitable to ensure the accuracy and reliability of our findings. Consequently, we employed other statistical methods that are better equipped to handle such instances of missing data, ensuring that our analysis remained both rigorous and valid despite these data limitations.

In our study, we quantified the temporal impact on mortality using Cox regression analysis. This method involved incorporating variables like etiology, inotrope usage, and biomarkers such as CRP, Mean Platelet Volume (MPV), Creatinine, and Neutrophil counts. These were measured at two key points: baseline (t0) and follow-up (t1). The rationale for selecting these variables was based on theoretical considerations and initial univariate statistical analyses. To bolster the robustness of our model, we evaluated the correlations between these variables at both t0 and t1. This step was crucial to ensure the reliability of our findings and to make the interpretation of each variable's coefficients within the model more clear



and understandable. This approach was carefully chosen to provide a coherent and insightful understanding of how each variable influences mortality over time.

In summary, the NparLD package emerged as a vital tool, meeting the specific demands of our research and yielding results apt for our data structure. The statistical analyses were conducted using Jamovi (version 2.3.28), JASP (version 0.17.3), and R-project (version 4.3.2 for Windows), with a set significance level of 0.05 (p-value) for all statistical tests.

## RESULTS

### Demographic and Clinical Variable Analysis

In our analysis of demographic and clinical variables, no significant differences were observed between patients who survived hospitalization and those who did not in terms of age, sex, length of hospital stay, rates of discharge on permanent dialysis, and comorbidity rates ($p>0.05$ for each).

### Analysis of AKI Etiology and Inotrope Use on Mortality

Regarding the etiologies of Acute Kidney Injury (AKI), sepsis and malignancy-related etiologies were more prevalent in the mortality group, whereas cardiorenal syndrome, exposure to nephrotoxic drugs, and other causes were predominant in the survivors ($p<0.001$). Notably, the use of inotropes was significantly higher in patients who did not survive ($p<0.001$) (referenced in Table 1).

### 28-Day Mortality Analysis

Focusing on 28-day mortality, our study found no significant variances between the groups in terms of age, sex, hospital stay duration, discharge on permanent dialysis, and comorbidity rates ($p>0.05$ for each). In the comparison of AKI causes, patients who died within 28 days exhibited a higher incidence of sepsis and malignancy-related AKI, while those surviving within this period showed a higher occurrence of cardiorenal syndrome, nephrotoxic drugs, and other causes ($p<0.001$). Again, inotrope usage was significantly more frequent in the mortality group within 28 days ($p<0.001$) (as indicated in Table 2).

### 90-Day Mortality Analysis

Regarding 90-day mortality, there were no significant differences between the groups concerning age, sex, length of hospital stay, discharge rates with permanent dialysis, and comorbidity rates ($p>0.05$ for each). In contrasting AKI causes, cardiorenal syndrome, sepsis, and malignancy were more frequent in patients who died within 90 days, while nephrotoxic drugs and other causes were more common in the survivors of this period ($p<0.001$). Inotrope use continued to be significantly higher in the mortality group within 90 days ($p<0.001$) (as shown in Table 3).

### The Nonparametric Analysis of Longitudinal Data in Factorial Experiments

In terms of hospital mortality, the effects of time interaction with CRP, creatinine, and N/L ratio levels were significant ($p<0.05$ for each), while interactions with albumin, lymphocyte, neutrophil, and urea levels were not significant ($p>0.05$ for each). When analyzing 28-day mortality, we observed no significant time interaction effects with albumin, CRP, and lymphocyte levels ($p>0.05$ for each). However, interactions with neutrophil, urea, creatinine, and N/L levels were significant ($p<0.05$ for each). Similarly, in the 90-day mortality analysis, time interaction effects with albumin, CRP, and lymphocyte levels remained non-significant ($p>0.05$ for each), whereas significant effects were noted with neutrophil, urea, creatinine, and N/L levels ($p<0.05$ for each) (Table 4). (Figure 2, Figure 3 and Figure 4).

**Table 1.** Hospital Mortality Statistics: Detailed Patient Profile and Clinical Factors

| | Hospital Mortality | | p |
|---|---|---|---|
| | **Alive** (n=85) | **Mortality** (n=59) | |
| **Age †** | 75.3 ± 7.1 | 74.8 ± 7.3 | 0.709*** |
| **Gender ‡** | | | |
| Male | 35 (41.2) | 28 (47.5) | 0.564* |
| Woman | 50 (58.8) | 31 (52.5) | |
| **Length of Stay §** | 7.0 [3.0 – 36.0] | 8.0 [3.0 – 44.0] | 0.747** |
| **Discharge with Permanent Dialysis, yes ‡** | 14 (16.5) | 0 (NaN) | 0.999* |
| **Comorbidity ‡** | | | |
| Diabetes Mellitus, yes | 39 (45.9) | 24 (40.7) | 0.654* |
| Hypertension, yes | 72 (84.7) | 44 (74.6) | 0.195* |
| Coronary Artery Disease, yes | 34 (40.0) | 18 (30.5) | 0.322* |
| Chronic Renal Failure, yes | 15 (17.6) | 6 (10.2) | 0.312* |
| Chronic Heart Failure, yes | 33 (38.8) | 25 (42.4) | 0.799* |
| **ACI Etiology ‡** | | | |
| Cardiorenal Syndrome | 26 (30.6) | 12 (20.3) | **<0.001*** |
| Sepsis | 20 (23.5) | 31 (52.5) | |
| Malignancy | 11 (12.9) | 11 (18.6) | |
| Nephrotoxic Drugs | 15 (17.6) | 0 (0.0) | |
| Other | 13 (15.3) | 5 (8.5) | |
| **Use of inotropic support, yes ‡** | 16 (18.8) | 38 (64.4) | **<0.001*** |

Footnote: Table 3 presents data on hospital mortality using various statistical techniques and measurement indicators. The † symbol represents the value as Mean ± Standard Deviation. The ‡ symbol indicates that data are shown in number and percentage format (n (%)). The § symbol signifies that values are presented as median and range [Minimum-Maximum]. The symbols for statistical tests are defined as follows: *. Pearson Chi-Square, Fisher's Exact, or Fisher Freeman Halton test, these tests are used to assess the significance of differences in categorical data across groups. **. Mann-Whitney U test is employed for comparing median values between two independent samples. ***. Independent Samples T-Test is used to compare mean differences between two independent groups. The 'NaN' (Not a Number) value in the table indicates that the data is not available or cannot be calculated.



**Table 2.** Outcomes: Demographics and Clinical Characteristics

| | **Overall** (n=144) | **28-Day Mortality** | | **p** |
|---|---|---|---|---|
| | | **Alive** (n=76) | **Mortality** (n=68) | |
| **Age †** | 75.1 ± 7.2 | 74.8 ± 7.0 | 75.4 ± 7.4 | 0.638*** |
| **Gender ‡** | | | | |
| Male | 63 (43.8) | 30 (39.5) | 33 (48.5) | 0.355* |
| Woman | 81 (56.2) | 46 (60.5) | 35 (51.5) | |
| **Length of Stay §** | 7.0 [3.0 – 44.0] | 7.0 [3.0 – 44.0] | 8.0 [3.0 – 26.0] | 0.949** |
| **Discharge with Permanent Dialysis, yes ‡** | 14 (16.5) | 13 (17.6) | 1 (9.1) | 0.682* |
| **Comorbidity ‡** | | | | |
| Diabetes Mellitus, yes | 63 (43.8) | 36 (47.4) | 27 (39.7) | 0.449* |
| Hypertension, yes | 116 (80.6) | 64 (84.2) | 52 (76.5) | 0.337* |
| Coronary Artery Disease, yes | 52 (36.1) | 30 (39.5) | 22 (32.4) | 0.475* |
| Chronic Renal Failure, yes | 21 (14.6) | 11 (14.5) | 10 (14.7) | 0.999* |
| Chronic Heart Failure, yes | 58 (40.3) | 28 (36.8) | 30 (44.1) | 0.472* |
| **ACI Etiology ‡** | | | | |
| Cardiorenal Syndrome | 38 (26.4) | 22 (28.9) | 16 (23.5) | |
| Sepsis | 51 (35.4) | 18 (23.7) | 33 (48.5) | |
| Malignancy | 22 (15.3) | 10 (13.2) | 12 (17.6) | **0.001*** |
| Nephrotoxic Drugs | 15 (10.4) | 14 (18.4) | 1 (1.5) | |
| Other | 18 (12.5) | 12 (15.8) | 6 (8.8) | |
| **Use of inotropic support, yes ‡** | 54 (37.5) | 14 (18.4) | 40 (58.8) | **<0.001*** |

Footnote: In Table 1, various statistical analysis methods and measurement indicators are employed. The † symbol indicates that the provided value represents Mean ± Standard Deviation. The ‡ symbol signifies that the data are presented as number and percentage (n (%)). The § symbol denotes that values are presented as median and range [Minimum-Maximum]. Symbols and their corresponding statistical tests are as follows: *. Pearson Chi-Square, Fisher's Exact, or Fisher Freeman Halton test, these tests are used to determine if there is a significant difference between categorical data across two or more groups. **. Mann-Whitney U test is used to test for differences in median values between two independent samples. ***. Independent Samples T-Test is employed to compare mean differences between two independent groups.

**Table 3.** 90-Day Mortality Rates: Patient Demographics and Clinical Data Analysis

| | 90-Day Mortality | | p |
|---|---|---|---|
| | **Alive** (n=63) | **Mortality** (n=81) | |
| **Age †** | 74.2 ± 6.4 | 75.8 ± 7.6 | 0.186*** |
| **Gender ‡** | | | |
| Male | 25 (39.7) | 38 (46.9) | 0.485* |
| Woman | 38 (60.3) | 43 (53.1) | |
| **Length of Stay §** | 7.0 [3.0 – 35.0] | 8.0 [3.0 – 44.0] | 0.501** |
| **Discharge with Permanent Dialysis, yes ‡** | 9 (14.3) | 5 (22.7) | 0.504* |
| **Comorbidity ‡** | | | |
| Diabetes Mellitus, yes | 31 (49.2) | 32 (39.5) | 0.320* |
| Hypertension, yes | 53 (84.1) | 63 (77.8) | 0.458* |
| Coronary Artery Disease, yes | 22 (34.9) | 30 (37.0) | 0.930* |
| Chronic Renal Failure, yes | 6 (9.5) | 15 (18.5) | 0.201* |
| Chronic Heart Failure, yes | 20 (31.7) | 38 (46.9) | 0.095* |
| **ACI Etiology ‡** | | | |
| Cardiorenal Syndrome | 14 (22.2) | 24 (29.6) | |
| Sepsis | 15 (23.8) | 36 (44.4) | |
| Malignancy | 8 (12.7) | 14 (17.3) | **<0.001*** |
| Nephrotoxic Drugs | 14 (22.2) | 1 (1.2) | |
| Other | 12 (19.0) | 6 (7.4) | |
| **Use of inotropic support, yes ‡** | 10 (15.9) | 44 (54.3) | **<0.001*** |

Footnote: Table 2 employs various statistical methods and measurement indicators for analyzing data on 90-day mortality. The † symbol indicates the value is presented as Mean ± Standard Deviation. The ‡ symbol signifies that the data are shown as number and percentage (n (%)). The § symbol denotes values presented as median and range [Minimum-Maximum]. The symbols used for statistical tests and their meanings are: *. Pearson Chi-Square, Fisher's Exact, or Fisher Freeman Halton test, utilized to determine if there is a significant difference in categorical data across different groups. **. Mann-Whitney U test is used for testing differences in median values between two independent samples. ***. Independent Samples T-Test is employed to compare mean differences between two independent groups.



**Table 4.** Impact of Temporal Changes in Biochemical and Hematological Variables on hospital, 28-Day and 90-Day Mortality

| | **Hospital Mortality** | | **Mortality 28** | | **Mortality 90** | |
|---|---|---|---|---|---|---|
| | **Alive** (n=85) | **Mortality** (n=59) | **Alive** (n=76) | **Mortality** (n=68) | **Alive** (n=63) | **Mortality** (n=81) |
| **Albumin 1 §** | 3.3 [2.0 – 5.2] | 3.0 [1.4 – 4.2] | 3.3 [1.9 – 5.2] | 3.0 [1.4 – 4.2] | 3.4 [2.0 – 5.2] | 3.0 [1.4 – 4.2] |
| **Albumin 2 §** | 3.0 [0.3 – 4.5] | 2.6 [1.4 – 4.6] | 3.1 [0.3 – 4.5] | 2.6 [1.4 – 4.6] | 3.1 [0.3 – 4.5] | 2.6 [1.4 – 4.6] |
| **p** (NparLD)** | 0.546 | | 0.641 | | 0.549 | |
| **C-reactive protein 1 §** | 7.4 [0.1 – 39.5] | 14.1 [1.9 – 39.1] | 6.7 [0.1 – 39.5] | 13.3 [1.9 – 39.1] | 6.7 [0.1 – 37.8] | 13.1 [0.3 – 39.5] |
| **C-reactive protein 2 §** | 4.9 [0.0 – 44.0] | 12.4 [0.9 – 69.0] | 4.8 [0.0 – 44.0] | 12.2 [0.9 – 69.0] | 4.7 [0.0 – 44.0] | 11.0 [0.9 – 69.0] |
| **p** (NparLD)** | **0.040** | | 0.062 | | 0.089 | |
| **Neutrophil 1 §** | 9990.0 [3.8 – 36050.0] | 9620.0 [4.8 – 48290.0] | 9695.0 [3.8 – 36050.0] | 9690.0 [4.8 – 48290.0] | 9330.0 [3.8 – 36050.0] | 9880.0 [4.8 – 48290.0] |
| **Neutrophil 2 §** | 6400.0 [2.1 – 49850.0] | 10780.0 [6.2 – 48490.0] | 6155.0 [2.1 – 16180.0] | 10305.0 [6.2 – 49850.0] | 6160.0 [2.1 – 16180.0] | 9410.0 [6.2 – 49850.0] |
| **p** (NparLD)** | 0.035 | | **0.023** | | **0.001** | |
| **Lymphocyte 1 §** | 980.0 [0.1 – 14100.0] | 890.0 [0.3 – 12040.0] | 975.0 [0.1 – 14100.0] | 945.0 [0.3 – 12040.0] | 1170.0 [0.1 – 14100.0] | 860.0 [0.3 – 12040.0] |
| **Lymphocyte 2 §** | 1260.0 [0.3 – 3440.0] | 950.0 [0.6 – 3800.0] | 1265.0 [0.3 – 3440.0] | 960.0 [0.6 – 3800.0] | 1300.0 [0.3 – 3440.0] | 960.0 [0.6 – 3800.0] |
| **p** (NparLD)** | 0.432 | | 0.613 | | 0.866 | |
| **Urea 1 §** | 138.0 [17.0 – 429.0] | 151.0 [24.0 – 381.0] | 128.0 [17.0 – 371.0] | 153.0 [24.0 – 429.0] | 127.0 [17.0 – 371.0] | 153.0 [24.0 – 429.0] |
| **Urea 2 §** | 99.0 [23.0 – 253.0] | 162.0 [46.0 – 436.0] | 98.0 [23.0 – 253.0] | 149.5 [46.0 – 436.0] | 92.0 [23.0 – 253.0] | 140.0 [46.0 – 436.0] |
| **p** (NparLD)** | 0.079 | | **0.003** | | **0.004** | |
| **Creatinine 1 §** | 4.7 [1.0 – 15.0] | 3.7 [0.7 – 10.4] | 4.3 [0.7 – 12.3] | 4.3 [0.8 – 15.0] | 4.7 [1.0 – 12.3] | 4.2 [0.7 – 15.0] |
| **Creatinine 2 §** | 3.1 [0.5 – 9.9] | 4.2 [0.6 – 11.9] | 2.8 [0.5 – 9.9] | 3.8 [0.8 – 11.9] | 2.6 [0.5 – 9.9] | 3.7 [0.6 – 11.9] |
| **p** (NparLD)** | **<0.001** | | **0.002** | | **<0.001** | |
| **Neutrophil/ Lymphocyte Ratio 1 §** | 10.1 [0.4 – 97.2] | 8.8 [0.1 – 111.3] | 9.2 [0.4 – 97.2] | 9.6 [0.1 – 111.3] | 9.1 [0.4 – 74.8] | 10.4 [0.1 – 111.3] |
| **Neutrophil/ Lymphocyte Ratio 2 §** | 5.9 [0.8 – 28.0] | 9.0 [0.5 – 166.8] | 5.3 [0.8 – 28.0] | 9.3 [0.5 – 166.8] | 4.9 [0.8 – 28.0] | 8.9 [0.5 – 166.8] |
| **p** (NparLD)** | <0.001 | | <0.001 | | 0.004 | |

Footnote: In Table 4, the statistical analysis of hospital mortality and mortality at 28 and 90 days is presented. The § symbol indicates that values are represented as median with their respective (§) minimum and maximum range [Min.-Max.]. Data comparisons for albumin, C-reactive protein, neutrophil, lymphocyte, urea, creatinine, and neutrophil/lymphocyte ratio are made between groups 'Alive' and 'Mortality' at different time points (hospital, 28 days, 90 days). The '1' and '2' labels indicate values at admission and at discharge or death, respectively. For statistical comparison, the nonparametric analysis of longitudinal data is conducted using the R software package npaRLD (Nonparametric Analysis of Longitudinal Data in Factorial Experiments). The p** symbol denotes the significance levels determined by the nonparametric longitudinal data analysis (NparLD), providing a robust method for comparing medians across groups and time points.

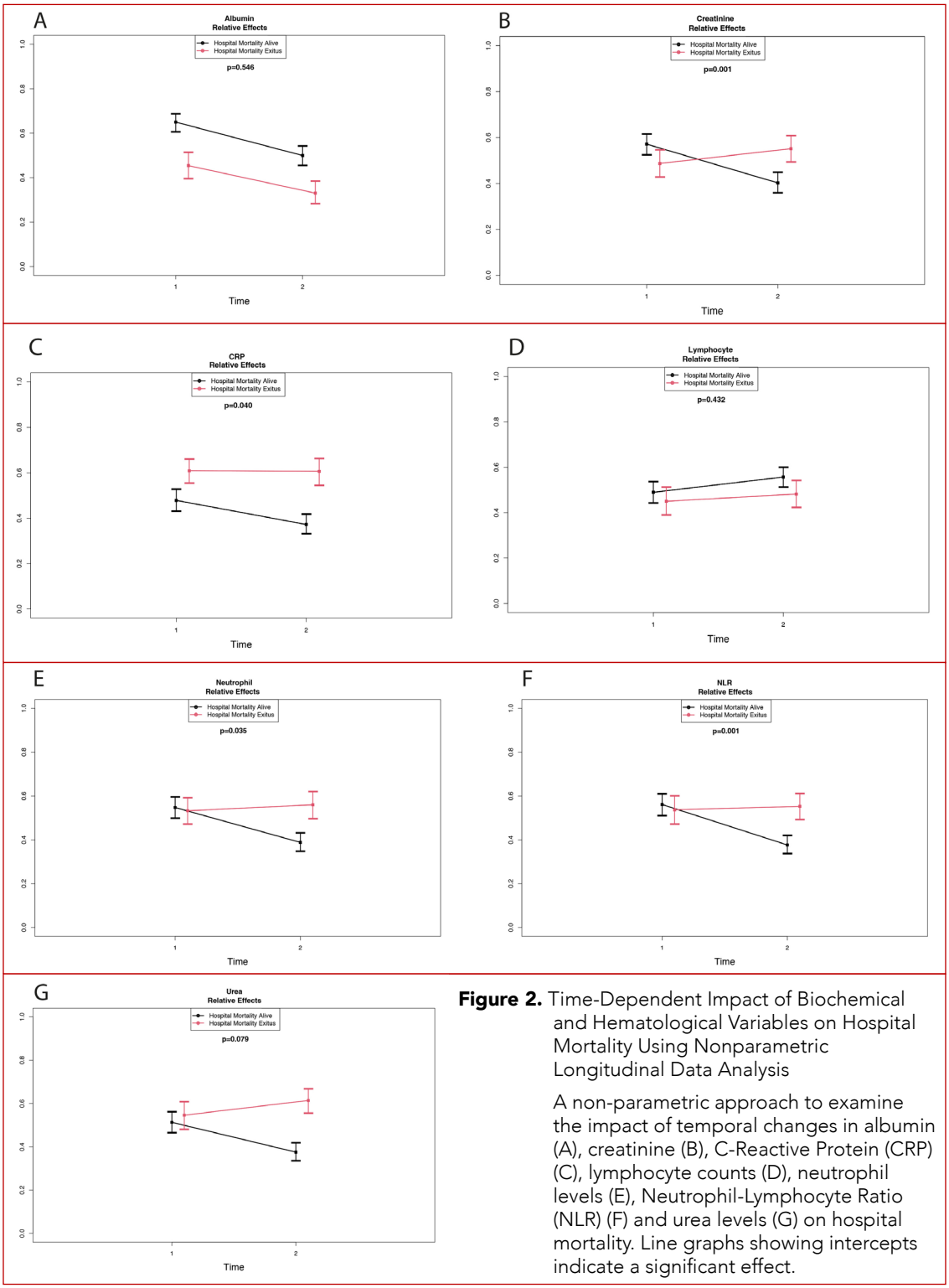



**Figure 2.** Time-Dependent Impact of Biochemical and Hematological Variables on Hospital Mortality Using Nonparametric Longitudinal Data Analysis

A non-parametric approach to examine the impact of temporal changes in albumin (A), creatinine (B), C-Reactive Protein (CRP) (C), lymphocyte counts (D), neutrophil levels (E), Neutrophil-Lymphocyte Ratio (NLR) (F) and urea levels (G) on hospital mortality. Line graphs showing intercepts indicate a significant effect.

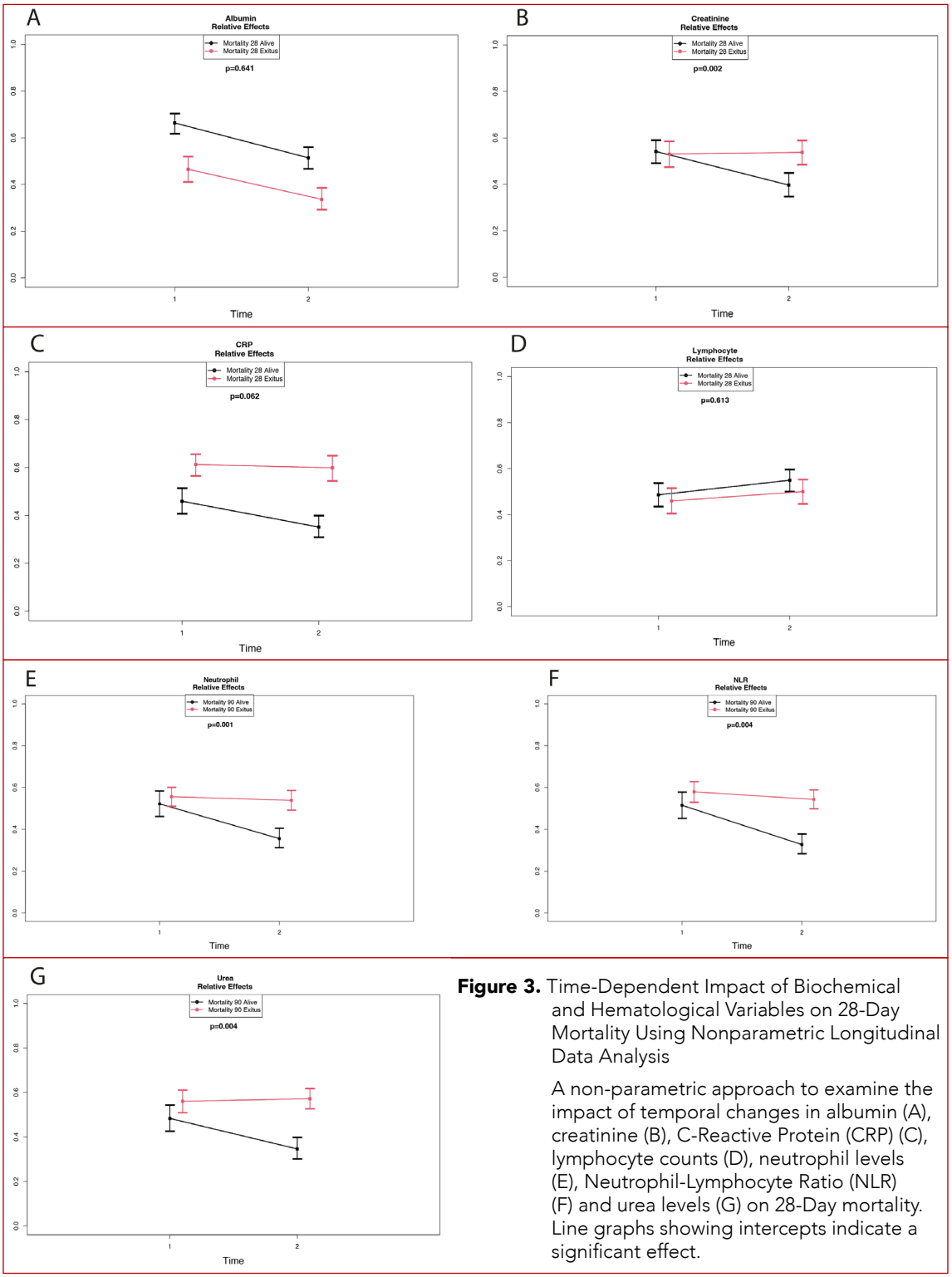



**Figure 3.** Time-Dependent Impact of Biochemical and Hematological Variables on 28-Day Mortality Using Nonparametric Longitudinal Data Analysis

A non-parametric approach to examine the impact of temporal changes in albumin (A), creatinine (B), C-Reactive Protein (CRP) (C), lymphocyte counts (D), neutrophil levels (E), Neutrophil-Lymphocyte Ratio (NLR) (F) and urea levels (G) on 28-Day mortality. Line graphs showing intercepts indicate a significant effect.

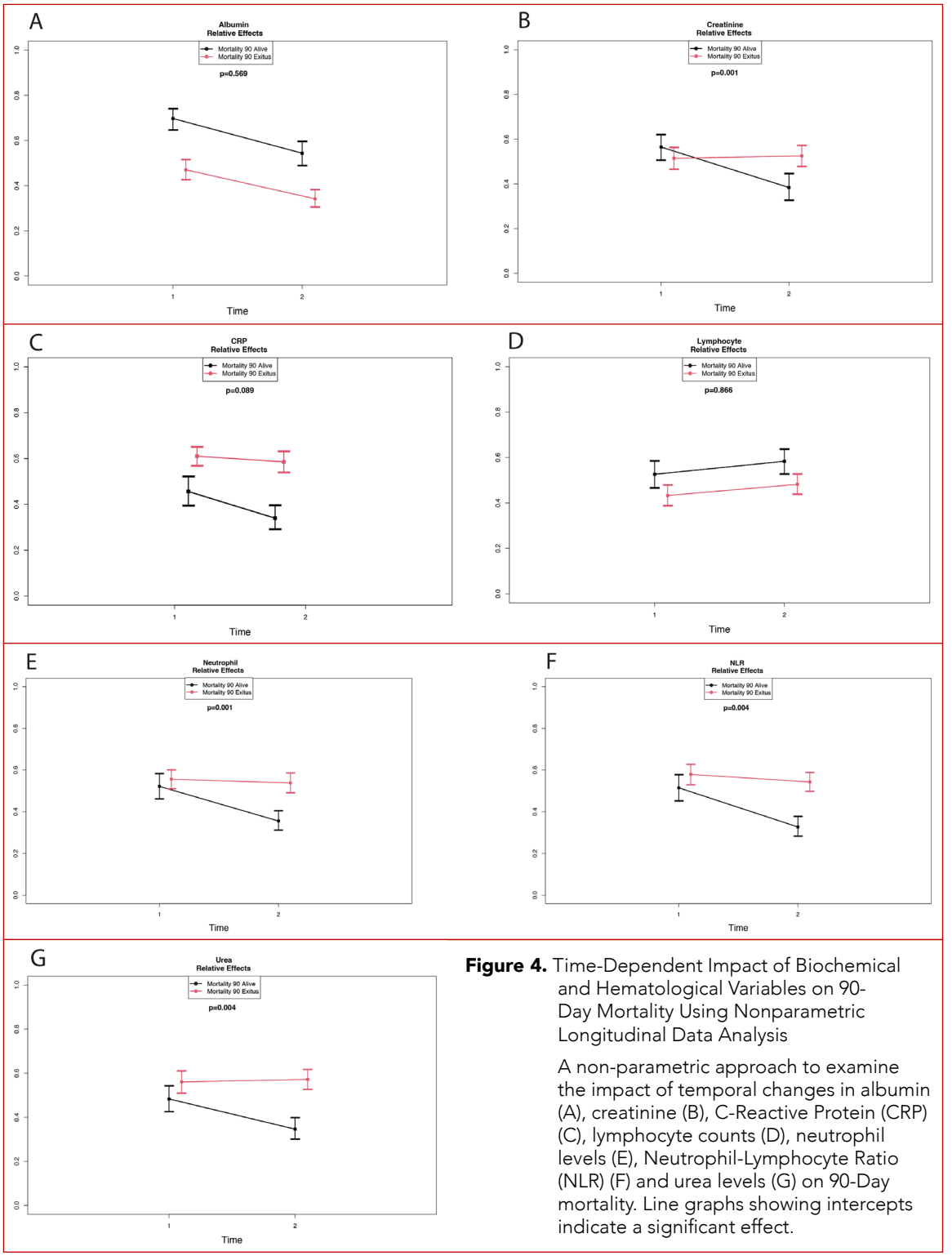



**Figure 4.** Time-Dependent Impact of Biochemical and Hematological Variables on 90-Day Mortality Using Nonparametric Longitudinal Data Analysis

A non-parametric approach to examine the impact of temporal changes in albumin (A), creatinine (B), C-Reactive Protein (CRP) (C), lymphocyte counts (D), neutrophil levels (E), Neutrophil-Lymphocyte Ratio (NLR) (F) and urea levels (G) on 90-Day mortality. Line graphs showing intercepts indicate a significant effect.



### Trends in NT-proBNP, Mean Platelet Volume, and Systolic Blood Pressure Across Different Time Points

During hospitalization, NT-proBNP levels significantly decreased in survivors (p=0.017), while remaining stable in patients with mortality (p=0.683). These levels were notably higher in patients with mortality at the second measurement (p=0.024). Mean platelet volume showed a significant increase in patients who died (p=0.027). Systolic blood pressure significantly decreased in patients with mortality (p=0.009) and was notably lower at the second measurement compared to survivors (p=0.001) (Table 5).

At the 28-day mark, NT-proBNP levels again decreased significantly in survivors (p=0.013) but did not change in patients with mortality (p=0.625). At the second measurement, these levels were significantly higher in patients with mortality (p=0.005). Systolic blood pressure showed a significant decrease over time in patients who died (p=0.038), with lower levels at the second measurement compared to survivors (p=0.010) (Table 6).

At the 90-day follow-up, a significant decrease in NT-proBNP levels was observed in survivors (p=0.013), with no change in patients with mortality (p=0.616). At the second measurement, NT-proBNP levels were significantly higher in patients with mortality (p=0.006). Systolic blood pressure did not show a significant change in survivors but was significantly lower in patients with mortality at the second measurement (p=0.005) (Table 7).

### Cox Regression Findings

Hospital Mortality: The univariate analysis revealed significant effects of AKI etiology, inotrope use, and levels of CRP (2) and NLR (2) on hospital mortality (p<0.05 for each). Specifically, sepsis was associated with a 2.4-fold increase in hospital mortality compared to cardiorenal syndrome, and inotrope use was linked to a 3.42-fold increase. A one-unit increase in CRP (2) and NLR (2) was found to elevate the risk of death by 3% and 1%, respectively. Multivariate analysis echoed these findings, showing that AKI etiology, inotrope use, and CRP (2) levels significantly influenced hospital mortality (p<0.05 for each), with sepsis raising mortality risk 2.59-fold compared to cardiorenal syndrome, and inotrope use increasing it by 1.96-fold. Additionally, each unit increase in CRP (2) upped hospital mortality risk by 4% (Table 8).

28-Day Mortality: In the univariate Cox model, AKI etiology, inotrope use, and levels of CRP (2), NLR (2), and creatinine (2) significantly affected 28-day mortality (p<0.05 for each). Sepsis resulted in a 2.8-fold increase in 28-day mortality compared to cardiorenal syndrome, and inotrope use led to a 3.01-fold increase. Increments of one unit in CRP (2), NLR (2), and creatinine (2) heightened the 28-day mortality risk by 3%, 1%, and 13%, respectively. The multivariate analysis indicated significant effects of AKI etiology, inotrope use, CRP (2), and creatinine (2) on 28-day mortality (p<0.05 for each). Sepsis increased the 28-day mortality risk by 1.99 times compared to cardiorenal syndrome, and inotrope use by 2.37 times. Moreover, each unit rise in CRP (2) and creatinine (2) increased the 28-day mortality risk by 4% and 1%, respectively (Table 9).

90-Day Mortality: The univariate analysis demonstrated significant impacts of AKI etiology, inotrope use, CRP (2), and NLR (2) levels on 90-day mortality (p<0.05 for each). Sepsis led to a 1.94-fold increase in 90-day mortality compared to cardiorenal syndrome, while nephrotoxic drug use showed a 90% reduction. Inotrope use was associated with a 2.64-fold increase in mortality. Increases of one unit in CRP (2) and NLR (2) raised the 90-day mortality risk by 3% and 1%, respectively. The multivariate analysis, including creatinine (2), revealed significant effects of AKI etiology, inotrope use, CRP (2), NLR (2), and creatinine(2) on 90-day mortality (p<0.05 for each). There was a 91% reduction in 90-day mortality in patients with nephrotoxic drug use compared to those with cardiorenal syndrome and

**Table 5.** Impact of Temporal Changes in Biochemical and Clinical Variables on in-hospital Mortality

| | Hospital Mortality | | p* |
|---|---|---|---|
| | **Alive** (n=85) | **Mortality** (n=59) | |
| **NT-proBNP 1 §** | 16514.0 [347.9 – 70000.0] | 9019.5 [924.0 – 95656.0] | 0.873 |
| **NT-proBNP 2 §** | 3681.0 [704.0 – 70000.0] | 18229.0 [330.0 – 70000.0] | **0.024** |
| **p**** | **0.017** | 0.683 | |
| **Troponin 1 §** | 71.0 [0.0 – 4413.0] | 110.5 [13.0 – 7590.0] | 0.236 |
| **Troponin 2 §** | 59.5 [16.0 – 145.0] | 161.0 [161.0 – 161.0] | 0.286 |
| **p**** | 0.313 | NaN | |
| **Mean Platelet Volume 1 §** | 10.9 [7.9 – 13.7] | 11.0 [7.9 – 13.1] | 0.632 |
| **Mean Platelet Volume 2 §** | 11.0 [7.3 – 14.0] | 11.4 [8.5 – 13.7] | 0.164 |
| **p**** | 0.441 | **0.027** | |
| **Systolic Blood Pressure 1 §** | 110.0 [80.0 – 215.0] | 113.0 [87.0 – 170.0] | 0.818 |
| **Systolic blood pressure 2 §** | 128.0 [100.0 – 145.0] | 86.0 [72.0 – 130.0] | **0.001** |
| **p**** | 0.332 | **0.009** | |
| **Diastolic Blood Pressure 1 §** | 66.0 [43.0 – 95.0] | 61.0 [48.0 – 95.0] | 0.818 |
| **Diastolic Blood Pressure 2 §** | 69.0 [60.0 – 89.0] | 53.0 [41.0 – 62.0] | **<0.001** |
| **p**** | 0.187 | **0.014** | |
| **Mean Arterial Pressure 1 §** | 88.5 [60.0 – 125.0] | 79.0 [61.0 – 116.0] | 0.455 |
| **Mean Arterial Pressure 2 §** | 96.3 [76.0 – 111.0] | 66.2 [51.0 – 73.0] | **<0.001** |
| **p**** | 0.330 | **0.014** | |
| **Pulse Pressure 1 §** | 42.5 [30.0 – 148.0] | 48.5 [32.0 – 120.0] | 0.643 |
| **Pulse Pressure 2 §** | 51.0 [33.0 – 70.0] | 32.0 [20.0 – 52.0] | **0.004** |
| **p**** | 0.451 | **0.050** | |
| **Heart Rate 1 §** | 102.0 [72.0 – 143.0] | 85.0 [61.0 – 110.0] | 0.188 |
| **Heart Rate 2 §** | 92.0 [77.0 – 107.0] | 95.5 [68.0 – 112.0] | 0.949 |
| **p**** | 0.221 | 0.625 | |

Footnote: In Table 5, hospital mortality data are analyzed with a focus on various physiological and laboratory parameters. The § symbol indicates that values are presented as median with the range [Minimum-Maximum]. The table compares parameters between 'Alive' and 'Mortality' groups at two different time points: 1 represents values at admission, and 2 represents values at discharge or death. The statistical tests applied are signified as follows: The * symbol denotes the use of the Mann-Whitney U test, which is employed to assess differences in median values between two independent samples. The ** symbol indicates the use of the Wilcoxon test, which is utilized for paired comparisons to evaluate differences in repeated measurements or matched samples within the same group. These tests help in understanding the statistical significance of differences observed in clinical measures such as NT-proBNP, troponin, mean platelet volume, systolic and diastolic blood pressure, mean arterial pressure, pulse pressure, and heart rate across the two groups and at different time points in the study. The 'NaN' (Not a Number) value in the table under hospital mortality for Troponin 2 indicates that the data is not available or cannot be calculated.



**Table 6.** Impact of Temporal Changes in Biochemical and Clinical Variables on 28-Day Mortality

| | Mortality 28 | | p* |
|---|---|---|---|
| | **Alive** (n=76) | **Mortality** (n=68) | |
| **NT-proBNP 1 §** | 10479.0 [347.9 – 70000.0] | 15223.0 [924.0 – 95656.0] | 0.232 |
| **NT-proBNP 2 §** | 3302.5 [704.0 – 62515.0] | 23869.0 [330.0 – 70000.0] | **0.005** |
| **p**** | 0.**013** | 0.625 | |
| **Troponin 1 §** | 62.0 [0.0 – 4413.0] | 110.0 [13.0 – 7590.0] | 0.093 |
| **Troponin 2 §** | 59.5 [16.0 – 145.0] | 161.0 [161.0 – 161.0] | 0.286 |
| **p**** | 0.313 | NaN | |
| **Mean Platelet Volume 1 §** | 11.0 [7.9 – 13.7] | 10.9 [7.9 – 13.1] | 0.891 |
| **Mean Platelet Volume 2 §** | 11.0 [7.3 – 14.0] | 11.4 [8.5 – 13.7] | 0.102 |
| **p**** | 0.753 | **0.010** | |
| **Systolic Blood Pressure 1 §** | 125.5 [80.0 – 215.0] | 106.5 [87.0 – 170.0] | 0.512 |
| **Systolic Blood pressure 2 §** | 125.0 [80.0 – 145.0] | 93.0 [72.0 – 130.0] | **0.010** |
| **p**** | 0.758 | **0.038** | |
| **Diastolic Blood Pressure 1 §** | 68.0 [43.0 – 95.0] | 60.0 [48.0 – 90.0] | 0.319 |
| **Diastolic Blood Pressure 2 §** | 68.0 [60.0 – 89.0] | 53.0 [41.0 – 86.0] | **0.005** |
| **p**** | 0.452 | 0.141 | |
| **Mean Arterial Pressure 1 §** | 90.0 [60.0 – 125.0] | 77.7 [61.0 – 100.0] | 0.161 |
| **Mean Arterial Pressure 2 §** | 93.5 [66.0 – 111.0] | 66.3 [51.0 – 100.0] | **0.006** |
| **p**** | 0.706 | **0.041** | |
| **Pulse Pressure 1 §** | 50.0 [30.0 – 148.0] | 43.0 [32.0 – 120.0] | 0.483 |
| **Pulse Pressure 2 §** | 51.0 [20.0 – 70.0] | 36.5 [24.0 – 52.0] | **0.024** |
| **p**** | 0.851 | 0.092 | |
| **Heart Rate 1 §** | 96.0 [61.0 – 143.0] | 96.0 [81.0 – 110.0] | 0.999 |
| **Heart Rate 2 §** | 90.0 [68.0 – 107.0] | 96.0 [95.0 – 112.0] | 0.295 |
| **p**** | 0.307 | 0.750 | |

Footnote: Table 6 focuses on the analysis of various clinical parameters and their association with 28-day mortality. The § symbol in the table represents that the values are given as median and range [Minimum-Maximum]. This table compares clinical measurements between the 'Alive' and 'Mortality' groups, specifically looking at changes from admission (1) to discharge or death (2). The * symbol indicates the use of the Mann-Whitney U test, which assesses differences in median values between two independent groups. The ** symbol denotes the application of the Wilcoxon test, used for paired comparisons to analyze differences in these parameters over time within the same group. Parameters such as NT-proBNP, troponin, mean platelet volume, systolic and diastolic blood pressure, mean arterial pressure, pulse pressure, and heart rate are evaluated to determine their significance in relation to mortality outcomes. The 'NaN' (Not a Number) value in the table under hospital mortality for Troponin 2 indicates that the data is not available or cannot be calculated.

**Table 7.** Impact of Temporal Changes in Biochemical and Clinical Variables on 90-Day Mortality

| | Mortality 90 | | p* |
|---|---|---|---|
| | **Alive** (n=63) | **Mortality** (n=81) | |
| **NT-proBNP 1 §** | 16514.0 [347.9 – 70000.0] | 9710.0 [924.0 – 95656.0] | 0.351 |
| **NT-proBNP 2 §** | 2589.0 [704.0 – 62515.0] | 11367.0 [330.0 – 70000.0] | **0.006** |
| **p**** | **0.013** | 0.616 | |
| **Troponin 1 §** | 56.5 [0.0 – 4413.0] | 110.5 [13.0 – 7590.0] | **0.010** |
| **Troponin 2 §** | 59.5 [16.0 – 145.0] | 161.0 [161.0 – 161.0] | 0.286 |
| **p**** | 0.313 | NaN | |
| **Mean Platelet Volume 1 §** | 10.9 [7.9 – 13.7] | 11.0 [7.9 – 13.1] | 0.745 |
| **Mean Platelet Volume 2 §** | 10.9 [7.3 – 14.0] | 11.4 [8.5 – 13.7] | **0.010** |
| **p**** | 0.805 | **0.003** | |
| **Systolic Blood Pressure 1 §** | 122.0 [83.0 – 215.0] | 110.0 [80.0 – 170.0] | 0.738 |
| **Systolic Blood pressure 2 §** | 128.0 [109.0 – 145.0] | 100.0 [72.0 – 140.0] | **0.005** |
| **p**** | 0.624 | 0.093 | |
| **Diastolic Blood Pressure 1 §** | 64.0 [43.0 – 95.0] | 65.0 [48.0 – 95.0] | 0.983 |
| **Diastolic Blood Pressure 2 §** | 68.0 [60.0 – 89.0] | 60.0 [41.0 – 86.0] | **0.019** |
| **p**** | 0.326 | 0.182 | |
| **Mean Arterial Pressure 1 §** | 88.0 [60.0 – 125.0] | 80.3 [60.0 – 116.0] | 0.363 |
| **Mean Arterial Pressure 2 §** | 96.0 [76.0 – 111.0] | 66.3 [51.0 – 100.0] | **0.009** |
| **p**** | 0.688 | 0.130 | |
| **Pulse Pressure 1 §** | 45.0 [34.0 – 148.0] | 48.0 [30.0 – 120.0] | 0.716 |
| **Pulse Pressure 2 §** | 51.0 [33.0 – 70.0] | 33.0 [20.0 – 63.0] | **0.008** |
| **p**** | 0.656 | 0.109 | |
| **Heart Rate 1 §** | 103.0 [72.0 – 143.0] | 86.5 [61.0 – 110.0] | 0.130 |
| **Heart Rate 2 §** | 94.5 [77.0 – 107.0] | 95.0 [68.0 – 112.0] | 0.953 |
| **p**** | 0.232 | 0.584 | |

Footnote: Table 7 presents data on 90-day mortality outcomes and their correlation with various clinical parameters. The § symbol indicates that the data are expressed as median values accompanied by their respective range [Minimum-Maximum]. This table compares clinical measurements, such as NT-proBNP and troponin levels, mean platelet volume, systolic and diastolic blood pressure, mean arterial pressure, pulse pressure, and heart rate, between the 'Alive' and 'Mortality' groups at two time points: '1' for values at admission and '2' for values at discharge or death. The statistical analysis is conducted using the * symbol, representing the Mann-Whitney U test, which is applied for assessing differences in median values between two independent groups. The ** symbol indicates the Wilcoxon test, which is used for paired comparisons, analyzing changes in these parameters over the course of the hospital stay within the same group. These analyses help in understanding the impact of these clinical parameters on mortality outcomes over a 90-day period. The 'NaN' (Not a Number) value in the table under hospital mortality for Troponin 2 indicates that the data is not available or cannot be calculated.



**Table 8.** Impact of Clinical Factors on Hospital Mortality Analyzed through Cox Proportional Hazards Model

| Cox's proportional hazard model on time to event (Hospital Mortality) | Univariate | | Multivariate | |
|---|---|---|---|---|
| | HR [95%CI] | p-value | HR [95%CI] | p-value |
| **Acute Kidney Injury Etiology:** *ref.=Cardiorenal Syndrome* | | | | |
| Sepsis | 2.40 [1.08 – 5.35] | **0.032** | 2.59 [1.21 – 5.57] | **0.014** |
| Malignancy | 1.49 [0.49 – 4.60] | 0.481 | 2.18 [0.86 – 5.49] | 0.099 |
| Nephrotoxic Drugs | 0.01 [0.01 – 0.02] | 0.997 | 0.01 [0.01 – 0.02] | 0.997 |
| Other | 0.92 [0.24 – 3.48] | 0.904 | 2.11 [0.66 – 6.72] | 0.205 |
| **Inotrope:** Yes vs. No | 3.42 [1.81 – 6.45] | **<0.001** | 1.96 [1.10 – 3.50] | **0.022** |
| **CRP 1** | 1.02 [0.99 – 1.06] | 0.172 | | |
| **CRP 2** | 1.03 [1.02 – 1.05] | **<0.001** | 1.04 [1.02 – 1.06] | **<0.001** |
| **NLR 1** | 1.01 [0.99 – 1.03] | 0.246 | | |
| **NLR 2** | 1.01 [1.01 – 1.02] | **0.029** | 1.01 [0.99 – 1.02] | 0.084 |
| **Creatinine 1** | 0.95 [0.84 – 1.07] | 0.376 | | |
| **Creatinine 2** | 1.11 [0.99 – 1.25] | 0.059 | 1.07 [0.98 – 1.18] | 0.134 |
| **MPV 1** | 1.02 [0.79 – 1.32] | 0.862 | | |
| **MPV 2** | 1.19 [0.92 – 1.52] | 0.181 | | |

Footnote: Table 8 presents the analysis of clinical factors on hospital mortality using the Cox Proportional Hazards Model. The model assesses the impact of factors such as Acute Kidney Injury (AKI) etiology, inotrope use, CRP, NLR, and creatinine levels on time to event (Hospital Mortality). Hazard Ratios (HR) with 95% Confidence Intervals (CI) are reported for both univariate and multivariate analyses, indicating the strength and direction of the association between each factor and hospital mortality. HRs greater than 1 indicate an increased risk of mortality. The 'ref.' denotes the reference category against which comparisons are made. P-values indicate the statistical significance of the associations, with values less than 0.05 considered significant.

**Table 9.** Impact of Clinical Factors on 28-Day Mortality Analyzed through Cox Proportional Hazards Model

| Cox's proportional hazard model on time to event (Mortality 28) | HR [95%CI] | | p-value | |
|---|---|---|---|---|
| | HR [95%CI] | p-value | HR [95%CI] | p-value |
| **Acute Kidney Injury Etiology:** *ref.=Cardiorenal Syndrome* | | | | |
| Sepsis | 2.80 [1.38 – 5.69] | **0.004** | 1.99 [1.03 – 3.85] | **0.042** |
| Malignancy | 1.47 [0.57 – 3.80] | 0.422 | 1.67 [0.76 – 3.68] | 0.201 |
| Nephrotoxic Drugs | 0.19 [0.02 – 1.47] | 0.112 | 0.19 [0.02 – 1.45] | 0.109 |
| Other | 1.39 [0.44 – 4.36] | 0.575 | 2.51 [0.92 – 6.88] | 0.073 |
| **Inotrope:** Yes vs. No | 3.01 [1.7 – 5.34] | **<0.001** | 2.37 [1.36 – 4.13] | **0.002** |
| **CRP 1** | 1.01 [0.99 – 1.04] | 0.292 | - | - |
| **CRP 2** | 1.03 [1.01 – 1.05] | **<0.001** | 1.04 [1.02 – 1.05] | **<0.001** |
| **NLR 1** | 1.01 [0.98 – 1.02] | 0.780 | - | - |
| **NLR 2** | 1.01 [1.01 – 1.02] | **0.022** | 1.01 [0.99 – 1.02] | 0.055 |
| **Creatinine 1** | 0.96 [0.87 – 1.06] | 0.372 | - | - |
| **Creatinine 2** | 1.13 [1.01 – 1.26] | **0.030** | 1.1 [1.01 – 1.21] | **0.031** |
| **MPV 1** | 0.97 [0.76 – 1.25] | 0.837 | - | - |
| **MPV 2** | 1.07 [0.85 – 1.35] | 0.559 | - | - |

Footnote: In Table 9, the Cox Proportional Hazards Model is utilized to determine the impact of various clinical factors on 28-Day Mortality. This model provides insights into the risk factors influencing the likelihood of mortality within 28 days post-hospitalization. It includes variables such as AKI etiology, inotrope use, CRP, NLR, and creatinine levels. The table displays HRs and their respective 95% CIs, elucidating the proportional impact of each variable on 28-day mortality. Statistical significance is denoted by p-values, where a value below 0.05 indicates a statistically significant effect on mortality risk. The 'ref.' denotes the reference category against which comparisons are made.

**Table 10.** Impact of Clinical Factors on 90-Day Mortality Analyzed through Cox Proportional Hazards Model

| Cox's proportional hazard model on time to event (Mortality 90) | HR [95%CI] | | p-value | |
|---|---|---|---|---|
| | HR [95%CI] | p-value | HR [95%CI] | p-value |
| **Acute Kidney Injury Etiology:** *ref.=Cardiorenal Syndrome* | | | | |
| Sepsis | 1.94 [1.07 – 3.51] | **0.030** | 1.32 [0.75 – 2.32] | 0.333 |
| Malignancy | 1.17 [0.53 – 2.61] | 0.694 | 1.22 [0.61 – 2.43] | 0.572 |
| Nephrotoxic Drugs | 0.10 [0.01 – 0.78] | **0.027** | 0.09 [0.01 – 0.67] | **0.019** |
| Other | 0.8 [0.27 – 2.36] | 0.683 | 1.32 [0.52 – 3.38] | 0.556 |
| **Inotrope:** Yes vs. No | 2.64 [1.58 – 4.42] | **<0.001** | 2.27 [1.37 – 3.76] | **0.002** |
| **CRP 1** | 1.01 [0.99 – 1.04] | 0.241 | - | - |
| **CRP 2** | 1.03 [1.02 – 1.05] | **<0.001** | 1.03 [1.02 – 1.05] | **<0.001** |
| **NLR 1** | 1.01 [0.99 – 1.02] | 0.363 | - | - |
| **NLR 2** | 1.01 [1.01 – 1.02] | **0.017** | 1.01 [1.01 – 1.02] | 0.033 |
| **Creatinine 1** | 0.92 [0.84 – 1.02] | 0.103 | - | - |
| **Creatinine 2** | 1.11 [0.99 – 1.23] | 0.055 | 1.12 [1.03 – 1.22] | **0.010** |
| **MPV 1** | 0.99 [0.79 – 1.23] | 0.895 | - | - |
| **MPV 2** | 1.15 [0.93 – 1.42] | 0.189 | - | - |

Footnote: Table 10 focuses on analyzing the effects of clinical factors on 90-Day Mortality through the Cox Proportional Hazards Model. This analysis is critical for understanding long-term outcomes post-hospitalization. The table includes variables like AKI etiology, inotrope usage, and biomarker levels (CRP, NLR, creatinine, MPV) and their respective hazard ratios, reflecting their influence on 90-day mortality risk. The HRs, along with 95% CIs, provide a quantitative measure of risk associated with each factor, with p-values highlighting the statistical significance of these relationships. Values below 0.05 p-value signify significant effects on mortality risk over a 90-day period. The 'ref.' denotes the reference category against which comparisons are made.

a 2.27-fold increase in patients requiring inotropes. A one-unit rise in CRP (2), NLR (2), and creatinine (2) enhanced the 90-day mortality risk by 3%, 1%, and 12%, respectively (Table 9).

## DISCUSSION

This single-center retrospective cohort study describes the clinical characteristics, mortality, and factors associated with mortality in elderly patients who required acute hemodialysis during the course of AKI in the ICU. In-hospital mortality was 40.9% (n = 59), which is comparable to the results of other studies. In a retrospective analysis of 154 patients older than 80 years with AKI requiring dialysis, the overall mortality rate was 26.6% (13), but ICU patients were excluded. Other studies have reported mortality rates for elderly ICU patients with AKI of 63.5%–76.2% [11] and 53.1% (14). The highest mortality apart from these studies, reported by Chronopoulos et al., ranged from 31% to 80% (9). The definition of advanced age, treatment intensity, disease severity, and the unit in which the patient was followed have been suggested as reasons for the differing results (9). The lower in-hospital mortality in our study may be due to the inclusion of community-acquired AKI patients and the clinicians' experience in critical care management. The 28-day mortality was 47.2% (n = 68) and the 90-day mortality 56.2% (n = 81). The data are insufficient on the long-term outcomes of elderly people who develop AKI requiring hemodialysis. Coca reports that AKI is independently related to long-term mortality (10), and a prospective study including ICU patients determined that 66.7% of elderly patients with AKI progressing to dialysis treatment die within one year (15).

Comorbidities such as HT, DM, CAD, CKD, and HF have been reported as the most important risk factors for the development of AKI in elderly people (16). In a retrospective cohort study including 652 elderly patients, the most common comorbid



conditions were CVD (77.5%), HT (74.4%), and DM (35.8%) (17), but the same study observed no difference between survivors and non-survivors. Similarly, Santos et al. found no significant difference among comorbidities in terms of mortality (18); the most common comorbidities in their study were HT (80.5%), DM (43.7%), HF (40.2%), CVD (36.1%), and CKD (18.4%). Comorbidities were not associated with mortality.

The common causes of AKI in elderly ICU patients are hypotension of any cause (including hypovolemia and cardiac failure), sepsis, drug toxicity, obstructive causes, renal vascular disease, and glomerulonephritis. Sepsis has been reported to be involved in nearly half of all AKI cases (9, 17, 18). Duarte et al. found no difference in sepsis-related AKI mortality during hospitalization (13) when examining the relationship between etiology and mortality. Li et al. report that infections were significantly more frequent in the non-survival group at 90-day outcome (17). In a prospective observational study, the leading cause of etiology—sepsis—exhibited three times the death risk compared to pre-renal causes in the elderly (18). In our study, among etiologies, compared to cardiorenal syndrome, sepsis led to a 2.59-fold increase in in-hospital mortality and 1.99-fold increase in 28-day mortality.

Inotrope usage was significantly higher among non-survivors in in-hospital, 28-day and 90-day evaluations. Additionally, in univariate and multivariate analysis, mortality significantly increased in patients requiring inotropes for all three time periods. Our results are comparable with the current literature. Among 431 elderly patients with AKI, the use of vasopressors was associated with worse prognosis (19). Korula et al. (20) and Uchino et al. (1) also found the use of vasopressors to be associated with poor outcomes.

In recent studies, hypotension in AKI was associated with increased mortality (19, 21, 22). In the present study; among patients who required hemodialysis, we evaluated SBP across different time points and we found that SBP significantly decreased in patients with mortality. Considering that the leading etiology was sepsis, this may be related to the severity of the underlying disease. However, better perfusion of the kidney could be another reason, which warrants further investigation.

Regarding impact of temporal changes in laboratory parameters, laboratory parameter changes are notable findings of the current study. Additionally, in univariate and multivariate analysis, for all three time periods, we determined that increase in CRP indicated increased mortality. Among laboratory parameters, several factors are considered predictors of mortality in elderly patients with AKI. Serum albumin, CRP levels, and CRP/albumin ratio have been reported as mortality predictors in elderly patients with AKI requiring dialysis (13). Serum albumin, prealbumin, blood urea nitrogen levels, baseline estimated glomerular filtration rate, MAP, oliguria, and AKI severity were reported as 90-day mortality predictors in a retrospective study among 652 patients with AKI (17). Santos et al. report that mortality was significantly associated with an increase in urea and creatinine levels in elderly AKI patients (18). Although no distinction was made according to etiologies, the association of crp, a traditional marker, with mortality is not surprising and the demonstration of its temporal variation will guide the clinician in reviewing treatment options in practice.

The biochemical marker which we want to emphasize in detail is NT-proBNP. We found significant decrease in all three time periods among survivors. The prognostic significance of NT-proBNP has been demonstrated in HF (23). Moreover, NT-proBNP levels were associated with mortality in septic AKI patients receiving renal replacement therapy (24). Additionally, NT-proBNP and CRP were reported as independent predictors of mortality in sepsis patients older than 75 years of age (25). Although the present study includes heterogeneous etiology, our results reveals that in critical care

practice, NT-proBNP should be considered as a valuable marker for predicting mortality.

It is not surprising that critically ill elderly patients are susceptible to AKI, so age has drawn research interest, and advanced age has been independently associated with hospital mortality (1). Also, Bagshaw et al. observed a higher one-year mortality with advanced age (8), and older age has been identified as an independent risk factor for mortality in patients with AKI in the ICU (1, 26-28). Conversely, other studies did not find that increasing age had an impact on mortality (13, 17–19), nor did the present study identify age as a factor affecting mortality. Therefore, the survival of elderly patients with AKI in the ICU may be better than generally expected, and further studies should be considered to clarify the effect of age on mortality due to AKI. Finally, 16 of 93 surviving patients (17.2%) in our study were discharged on hemodialysis. Acuña et al. note that 18.9% of elderly patients with AKI progressed to dialysis treatment (15).

Although we presented highly selected patient group, it should be noted that our study has some limitations. First, it may not be appropriate to generalize our results, as this study had a retrospective design and was conducted at a single center. However, it may be considered as a pioneer for further research. In addition, the time from diagnosis of AKI to dialysis was not examined in our study, which may be considered another limitation. Finally, it was not possible to obtain long-term follow-up of renal function in patients who were discharged without dialysis, although we were able to report the number of patients on dialysis at discharge.

## CONCLUSION

Elderly hospitalized patients have a significant rate of in-hospital death owing to AKI. Although advanced age exacerbates this situation, its effect on mortality may not be as expected. Therefore, chronological age should not be evaluated alone when deciding on dialysis in elderly patients. Appropriate laboratory parameters should be used as a guide in the decision-making process, and treatment intensity should be decided on a case-by-case basis. As this was a single-center retrospective study, the results cannot be generalized; future research is thus needed to obtain long-term follow-up of renal function in patients who were discharged without dialysis.

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**Ethics approval and consent to participate:**

The study was approved by the Ege University Ethics Committee, number 19-5.2T/69 and adhered to the principles of the Declaration of Helsinki. All patients or their relatives provided written informed consent.

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