Review Article
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Case Report
Podocyte Disease Following Treatment with Intravenous Ibandronate in an Older Patient

Letter to the Editor
Survey of Awareness of Terminology Related to Functional Impairment and Muscle Health among Rehabilitation Healthcare Staff
Aims and Scope
Annals of Geriatric Medicine and Research (Ann Geriatr Med Res, AGMR) is a peer-reviewed journal that aims to introduce new knowledge related to geriatric medicine and to provide a forum for the analysis of gerontology, broadly defined. As a leading journal of geriatrics and gerontology in Korea, one of the fastest aging countries, AGMR offers future perspectives on policymaking for older adults, clinical and biological science in aging researches especially for Asian emerging countries. Original manuscripts relating to any aspect of geriatrics, including clinical research, aging-related basic research, and policy research related to senior health and welfare will be considered for publication. Professionals from a wide range of geriatric specialties, multidisciplinary areas, and related disciplines are encouraged to submit manuscripts for publication.

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Enhancing Footwear Safety for Fall Prevention in Older Adults: A Comprehensive Review of Design Features

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Background: Falls are a global concern affecting people of all ages; however, older adults are particularly vulnerable to age-related factors and foot-related issues. Footwear is critical for preventing falls, as it provides stability and protection against slips, trips, and falls (STFs). However, a significant gap exists in the systematic exploration of the safety aspects of footwear design for fall prevention in older adults.

Methods: This comprehensive review applied a meticulous search strategy encompassing prominent databases, including Google Scholar, ScienceDirect, SCOPUS, MEDLINE, ResearchGate, and PubMed. This review synthesized and analyzed existing research to bridge knowledge gaps and provide insights into optimal footwear choices for older adults in terms of design features such as fit, fixation, heel height, collar height, slip resistance, and sole/insole hardness.

Results: The results underscore the importance of specific design features for preventing falls among older adults. A proper fit, secure fixation, appropriate heel and collar heights, slip resistance, and sole/insole hardness significantly contributed to fall prevention. These findings offer valuable guidance for optimizing footwear designs to enhance comfort, stability, and safety in the daily lives of older individuals.

Conclusion: This comprehensive review fills a critical knowledge gap regarding the safety of footwear designs for fall prevention in older adults. The identified design features play a vital role in reducing the risk of falls and offer practical recommendations for the development of safer footwear. Ultimately, this study contributes to the existing knowledge base and supports efforts to prevent STFs in older adults through improved footwear design.

Key Words: Falls in elderly, Footwear safety, Footwear fit, Safe footwear design, Slip resistance

INTRODUCTION

A profound demographic shift is underway as the global population ages, driven by increasing life expectancy. Projections indicate that individuals aged 65 years and older will comprise 12% of the world’s population by 2030 and 16.7% by 2050. An aging workforce across diverse industries mirrors this demographic transformation, a trend anticipated to persist in coming years. Along with these changes, the societal and healthcare ramifications of falls among older adults have become increasingly apparent.

Approximately 37.3 million fall incidents necessitating medical attention are reported annually globally. According to the World Health Organization, falls will be the second-leading cause of unintentional injury deaths, trailing only road traffic injuries. Although falls can affect individuals of all age groups, older people are particularly vulnerable and face the highest risk of sustaining severe injuries and fatalities. Alarmingly, over 30% of adults aged ≥ 65 years experience a fall each year, with 50% of these cases experiencing recurrences. The surge in fall-related hospitalizations not only escalates the economic burden on patients, caregivers, and healthcare systems but also affects the psychological well-being of older adults. Strikingly, 60% of older individuals with a fall...
history report a fear of falling, which can subsequently have deleterious effects on their overall functionality and quality of life.\textsuperscript{5,6} Given these pressing challenges, this comprehensive review aimed to delve into the multifaceted problem of falls among older adults. By synthesizing existing research and insights, this study sought to address critical questions concerning the role of footwear design in mitigating the risk of falls by examining key features of footwear such as fit, fixation, heel height, collar height, slip resistance, and sole/insole hardness. Through a meticulous analysis of the literature, the findings from this review may contribute to the current knowledge base, offering valuable recommendations for optimizing footwear choices to enhance comfort, stability, and safety for older adults in their daily lives. This review further aimed to shed light on the complexities of fall prevention among older adults and provide guidance for researchers, healthcare practitioners, and policymakers to reduce the burden of falls in an aging world.

**BACKGROUND INFORMATION**

**Physical Factors - Frailty and Aging**

Frailty among individuals aged ≥ 65 years is a prevalent concern, with estimates ranging between 6.9% and 8.4% and a clear upward trend with increasing age.\textsuperscript{9} Older adults often have musculoskeletal disorders that diminish their functionality and mobility.\textsuperscript{10} These individuals may exhibit reduced foot sensitivity,\textsuperscript{11} weakness, limited range of motion, increased soft tissue stiffness, and postural pronation.\textsuperscript{12} Improper gait patterns, attributed to various medical conditions, are also common among older adults.\textsuperscript{10} Combined with their slower response time to sudden situations, these factors can impair balance control in this population and increase the risk of slip, trip, and fall (STF) incidents.\textsuperscript{13} Moreover, chronic illnesses and persistent pains are strongly associated with fall incidents,\textsuperscript{14} with many older adults concurrently managing multiple diseases and taking various medications, amplifying the risk of STFs.\textsuperscript{10,15}

**Footwear - Role of Footwear in Fall Prevention**

Most of the literature available on STF incidents affecting older adults primarily focuses on intrinsic risk factors such as activity levels; functional and cognitive disabilities; ambulatory status: chronic diseases; use of walking aids; medication use; and sociodemographic and socioeconomic factors such as sex, marital status, employment status, living conditions, and education.\textsuperscript{10,13,14} In contrast, evaluations of extrinsic risk factors often underestimate or overlook the impact of footwear features on safe ambulation and STF prevention. However, emerging evidence has highlighted the significant impact of footwear interventions on the static and dynamic stability and gait patterns of older adults.\textsuperscript{15} Footwear choices are crucial in fall prevention, influencing an individual’s balance and overall stability. As footwear modifications may be a relatively simple, efficient, and cost-effective means of enhancing safety, understanding the specific footwear characteristics that promote or compromise balance in older adults is essential. The key footwear features that have been studied for fall prevention include:

1) **Fit**: Properly fitting shoes are crucial. Loose or tight footwear can cause instability and discomfort.
2) **Fixation**: Shoes should provide adequate support and focus to prevent the foot from sliding within them, which can affect balance.
3) **Heel height**: Heel height can affect gait and balance. Higher heels may also increase the risk of falls.
4) **Collar height**: The shoe collar height around the ankle can influence ankle stability.
5) **Slip resistance**: The shoe outsole should have adequate slip resistance to prevent slipping on various surfaces.
6) **Sole/insole hardness**: The hardness of the sole or insole can affect shock absorption and comfort, which in turn can affect balance.

Understanding the interplay between footwear characteristics and the unique needs of older adults is crucial for developing strategies to reduce the incidence of footwear-related STF incidents. Footwear interventions can range from selecting appropriate off-the-shelf shoes to customizing orthopedic shoes depending on an individual’s needs. By investigating how footwear features can promote or compromise balance in older adults, researchers and healthcare practitioners can contribute more effective fall prevention strategies and improve the safety and well-being of the aging population. Fig. 1 illustrates the main features of shoe design that affect balance control and falls.

**Objectives**

The primary aim of this study was to comprehensively review the recent literature on footwear-related issues among older adults, with a specific focus on footwear fit, fixation, heel height, collar height, slip resistance, and sole/insole hardness. To achieve this aim, this study formulated the following research questions:

1) **Objective 1**: To conduct a comprehensive review of recent literature to determine the prevalence and availability of specific footwear features including fit, fixation, heel height, collar height, slip resistance, and sole/insole hardness in footwear designed for older adults.
2) **Objective 2**: To assess the prevalence of footwear features in older adults, based on existing research and data.
3) Objective 3: To analyze the impact of selected footwear features on various aspects of older adults’ well-being, including comfort, balance, gait, and slip resistance based on the findings of recent studies and publications.

4) Objective 4: To investigate the relationship between footwear features and the occurrence of STF incidents among older adults.

5) Objective 5: To synthesize the reviewed literature and provide evidence-based recommendations for optimal footwear features to enhance safety and reduce the risk of STF incidents among older adults, thereby contributing to the development of footwear design guidelines.

The above refined objectives and questions provide a clear and focused framework for this review, helping to systematically explore the relevant literature and providing valuable insights into the role of footwear in fall prevention among older adults.

MATERIALS AND METHODS

Literature Search Strategy
This review employed a meticulous and systematic search strategy to comprehensively address the primary research questions. We used the following five primary search keywords: “footwear properties,” “older adults,” “slips,” “trips,” and “falls.” These keywords were selected to capture relevant literature surrounding footwear issues in older adults and their relationship with STF incidents. We conducted this search across a carefully curated selection of well-established and respected academic databases; namely, Google Scholar, ScienceDirect, SCOPUS, MEDLINE, ResearchGate, and PubMed, to ensure the comprehensive retrieval of pertinent literature from various sources.

Inclusion Criteria
The following stringent inclusion criteria were applied to determine the quality and relevance of the studies included in this review.

1) Language: We considered only studies published in English. This criterion was chosen to ensure the accessibility and understanding of a broad readership.

2) Publication date: This review focused on studies published from 2011 onwards. This timeframe was chosen to prioritize the incorporation of the most current research findings and practices in the field. This approach allowed us to build on prior knowledge while keeping our review contemporary.

3) Study participants: To maintain consistency and relevance, the included studies featured adults aged ≥ 60 years as the primary participants. We adopted this age criterion to align with the target older adult population at a higher risk of STF.

4) Study outcomes: The selected studies investigated and reported at least one of the following aspects:

   - Prevalence of specific footwear properties.
   - Influence of footwear-related factors on comfort, balance, gait, and slip resistance.
   - Associated risks of STF incidents among older adults attributed to footwear characteristics.

Study Selection Process
The process of selecting eligible studies adhered to well-established systematic review guidelines to ensure rigor and objectivity. This process comprised several sequential stages.

1) Initial database search: We searched the designated databases using predefined search keywords.

2) Title and abstract screening: We systematically screened the titles and abstracts of the retrieved studies for relevance to our research questions and adherence to the inclusion criteria.

3) Full-text review: Studies that passed the initial screening underwent a thorough full-text review. This step was essential to ascertain their alignment with the inclusion criteria.

Data Extraction and Synthesis
This review extracted vital information from the selected studies, including the study design, sample characteristics, methodological approach, and footwear-related variables. We meticulously compiled and analyzed these data to facilitate a comprehensive understanding of the outcomes reported in the literature. Fig. 2 illustrates the selection procedure for research papers included in this review.
Shoe Fit

Shoe fit is a critical aspect of footwear that significantly affects comfort and functionality.\(^{17}\) While some older adults make appropriate choices regarding well-fitted footwear, ill-fitting shoes appear to be more common among this demographic.\(^{19}\) A descriptive observational study involving 100 older adults at an outpatient clinic reported that 83% wore improperly fitted footwear on at least one foot.\(^{20}\) Furthermore, a case-control study assessing fall risk factors in 333 older adults revealed that 34% of men and 50% of women wore excessively narrow footwear, leading to discomfort and foot-related issues.\(^{20}\)

This proclivity toward ill-fitting footwear selection among older adults can be attributed to several factors. One contributing factor is the reduced sensitivity of the feet of older individuals.\(^{19}\) Moreover, many older adults do not routinely check their feet, lack awareness of their correct shoe size, or have difficulties in selecting footwear that accommodates variations in foot morphology.\(^{21}\) O’Rourke et al.\(^{22}\) revealed parallel findings, indicating that 72% of older adults wore ill-fitting shoes. Notably, the percentage of those who experienced a fall in the previous 6 months was higher among individuals wearing ill-fitting footwear (56%) than among those wearing correctly fitting shoes on at least one foot (39%). However, this difference was not statistically significant.

Furthermore, a recent comparative study involving 153 older adult participants found that 60% wore ill-fitting footwear. In this group, 26% had experienced a fall in the past year, in contrast to only 15% of those who wore correctly fitted footwear. Those wearing ill-fitted shoes also exhibited lower scores on the Berg Balance Scale and reported higher levels of fear of falling, as measured by the Activities-Specific Balance Confidence Scale.\(^{23}\) Well-fitted footwear can enhance the stability, gait, and social engagement of older adults while reducing their fear of falling.\(^{17,23}\) This underscores the importance of recommending properly fitting footwear as a viable strategy for mitigating the risk of STF incidents.

Shoe Fixation

Shoe fit is a critical aspect of footwear that significantly affects comfort and functionality.\(^{17}\) Proper shoe fixation ensures that the foot remains securely positioned within the footwear, allowing for better control over potential trip hazards.\(^{24}\) A study investigating the gait of 20 older women, both barefoot and wearing various types of footwear, highlighted the importance of fixation. The participants wore backless slippers, less-fixed shoes with a nylon mesh upper and lenient heel counter, and well-fixed shoes with dorsal fixation, a belt, and a stiff heel counter. The results revealed notable alterations in the knee and ankle joint angles when walking in slippers and less-fixed shoes. These alterations indicated adjustments made to keep the footwear in place, potentially increasing the risk of trips and falls.\(^{25}\)

Further evidence comes from an analysis of 70,196 fall incidents among older adults conducted by Buchele et al.,\(^{26}\) in which the use of open slippers significantly predicted falls, resulting in hospital transfers for older women. The design of open slippers can impede the stepping motion, potentially contributing to falls. Additionally, gait assessments of 30 older women, both barefoot and wearing various types of footwear, highlighted the benefits of shoes with lace fixation.\(^{26}\) The use of such shoes resulted in increased walking speed, step length, and minimum foot clearance while reducing step width, step duration, and heel slippage compared to enclosed slippers lacking dorsal fixation. O’Rourke et al.\(^{22}\) assessed the common daily footwear choices of older adults, observing that 26% lacked proper fixation. However, Vass et al.\(^{14}\) reported a higher percentage, with 60% of footwear lacking adequate fixation. This variance may be attributed to differences in the sample size and types of footwear considered, encompassing indoor and outdoor options.

In conclusion, recommending footwear with adequate fixation
is crucial for enhancing foot clearance, gait, and stability in older adults.\textsuperscript{24} This measure helps mitigate the risk of trips and falls, thus contributing to fall prevention.\textsuperscript{24,25}

**Shoe Heel Height**

The height of the shoe heel is a critical factor to consider when assessing its effect on the biomechanics and stability of older adults during walking. This particular footwear characteristic can induce substantial alterations in various key parameters, including the trajectory of the center of pressure, the area of contact between the foot and ground, and the peak plantar pressure.\textsuperscript{27} Consequently, high-heeled shoes are associated with hallux valgus, musculoskeletal pain, and first-party injury.\textsuperscript{28}

Furthermore, a heel height exceeding approximately 2.5 cm can elevate and shift the body’s center of mass, leading to consequential adjustments in posture and kinematics, which can significantly affect overall stability.\textsuperscript{29} Given its profound influence on lower extremity function and balance, heel height is a pivotal consideration in footwear design for older adults.\textsuperscript{30} Moreover, an excessively high heel is a potential risk factor for falls.\textsuperscript{27,31}

A study assessed the effects of varying heel heights on plantar foot pressure in a cohort of older women.\textsuperscript{32} The participants wore shoes featuring heel elevations of 1 cm, 3 cm, and 5 cm. The findings revealed a relationship between heel height and gait stability. Specifically, individuals who wore shoes with 1 cm or 3 cm heel elevations exhibited improved gait stability compared to those wearing 5 cm heels. Thus, the lower elevations substantially reduced the fall risk.\textsuperscript{27}

High heels are unlikely to be the most common type of footwear worn by older women when they experience falls.\textsuperscript{33} This observation can be attributed to the decreasing prevalence of high-heeled footwear as women age. An examination of the most commonly worn outdoor footwear revealed that only 3.3% of older women wore high heels, consistent with the notion that the practice of wearing high heels with a very narrow toe box declines to < 10% in women aged ≥ 40 years.\textsuperscript{33}

These findings underscore the importance of considering heel height when designing safe footwear for older adults. Recommendations within established guidelines emphasize the prudence of restricting heel heights, focusing on limiting the elevation to ensure optimal balance and mitigate fall risks.\textsuperscript{17,30,34} A heel height of ≤ 4 cm is a reasonable threshold for maintaining balance and stability, thereby mitigating the associated risk of falls.\textsuperscript{35}

In summary, the multifaceted interplay between heel height, gait stability, and fall risk in older adults underscores the paramount importance of heeding recommendations for heel height limitations in footwear selection. Such considerations are a cornerstone of the broader strategy for mitigating the profound impact of STFs in the older adult population.

**Shoe Collar Height**

The consensus in the literature is that shoes with a high collar height and top line play a crucial role in enhancing the balance of older adults, making shoe collar height a vital consideration in the design of safe footwear.\textsuperscript{17,36,37} The underlying rationale is that materials covering all sides of the ankle provide mechanical stability to the ankle and subtalar joints in the coronal plane. Additionally, elevator collar height may enhance proprioceptive feedback, a vital sensory component for balance, compared to regular footwear.\textsuperscript{36}

These factors align with those of an experimental study that assessed the impact of three different footwear styles on gait parameters associated with falls among older adults. The three footwear styles included soft open-heel shoes with no collar or fastening and two closed-heel shoes with varying material hardness featuring a high collar and Velcro fastening. The results revealed significant improvements in walking speed, stride length, and step time for closed-heel shoes with high collars. The participants also rated these shoes as more comfortable and stable.\textsuperscript{37} Thus, incorporating high collar height and top-line designs into footwear design for older adults is a promising strategy for enhancing balance and stability, contributing to reduced fall risk. These findings underscore the importance of integrating high collar height into footwear design for older adults to improve their proprioceptive feedback, mechanical stability, and overall balance, thereby reducing the risk of falls.

**Shoe Slip Resistance**

Slips leading to falls often result from the delicate balance between a traction force and a vertical force applied to the ground, which ultimately determines the coefficient of friction (COF) between the footwear and the walking surface.\textsuperscript{38} Footwear lacking adequate slip-resistant properties can significantly contribute to falls among older adults, thus emphasizing the importance of addressing this aspect in footwear design and selection.\textsuperscript{40,41}

**Heel/sole tread**

The tread pattern on the soles of shoes plays a pivotal role in enhancing slip resistance. Effective channeling and dispersion of fluid pressure during ground contact mitigate the detrimental effects of liquid-induced reductions in the COF.\textsuperscript{42} Older adults tend to take broader steps during walking, increasing the demand for mediolateral (ML) and anteroposterior (AP) COF. Consequently, sole tread patterns should be designed to offer superior slip resistance in both the ML and AP directions to minimize the risk of sideways
slips, which are common in older adults.\textsuperscript{39}

Although slip tests involving older adults are infrequent because of their hazardous nature, insights gleaned from experiments conducted in young adults suggest a treded sole coupled with increased tread depth significantly enhances friction at the shoe-floor interface, thereby reducing the likelihood and severity of slip and fall incidents.\textsuperscript{42,43} Studies have consistently recommended incorporating an appropriate tread pattern in footwear design to enhance the safety of older adults.\textsuperscript{17,34,41}

Another critical factor to consider in sole profile design is wear caused by repeated use, as worn soles are frequently observed when evaluating older adults’ indoor and outdoor footwear. O’Rourke et al.\textsuperscript{22} reported wear in 90% of older adults’ footwear, whereas Vass et al.\textsuperscript{15} reported that 60% of older adults’ footwear had been owned for >1 year, with 48% showing partially to excessively worn soles. As the worn area of the shoe sole increases, the peak fluid pressure under the shoe increases, leading to a decrease in the available COF and an aggravated risk of slipping.\textsuperscript{45}

**Heel/sole material**

The choice of heel and sole materials in footwear design is important, particularly when addressing slip resistance and overall safety, especially for older adults. Rubber, a versatile and widely used material, has become the preferred option owing to its proven slip-resistant properties. However, other factors should be considered when evaluating the suitability of heel/sole materials for fall prevention in older adults.

1) Slip resistance: Rubber’s intrinsic characteristics make it a natural choice for enhancing traction and reducing the risk of slips and falls. Its high slip resistance on various surfaces, including wet or slippery surfaces, contributes significantly to its efficacy in preventing slip and fall incidents.\textsuperscript{40,41} The use of rubber in shoe heels/soles and, more recently, in anti-slip socks, underscores its role in providing stability and reducing the likelihood of accidents.\textsuperscript{38} Nevertheless, the nuances surrounding the effectiveness of anti-slip socks must be acknowledged. Hartung and Lalonde\textsuperscript{46} reported inconclusive evidence regarding the efficacy of anti-slip socks in averting falls, especially in hospitalized older adults. This ambiguity underscores the importance of discerning the precise conditions under which anti-slip socks are most efficacious. Moreover, concerns regarding the potential transmission of infections through shared hospital-provided anti-slip socks have been raised, necessitating a careful approach to their implementation. Furthermore, anti-slip socks provided by hospitals may not provide the requisite support to the heel, forefoot, or sole necessary to cultivate ideal gait and balance characteristics in older adults.\textsuperscript{30}

2) Material durability: Beyond slip resistance, material durability is paramount, especially for older adults who may wear footwear for extended periods. The resilience of rubber to wear and tear ensures that it maintains its slip-resistance properties over time. However, the initial slip resistance of the sole material and its ability to withstand prolonged use (wear and tear) without losing its effectiveness must be assessed.\textsuperscript{30,41,43}

3) Evaluating alternative materials: While rubber is a frontrunner, alternative materials with slip-resistant qualities must also be explored. Advances in material science and technology have led to the development of innovative sole materials with exceptional traction on various surfaces.\textsuperscript{41} These materials may present new possibilities for enhancing the safety and comfort of footwear in older adults.

4) Customization for specific settings: The heel and sole material choice should also consider the specific settings in which older adults wear their footwear. For instance, hospital environments may require different material characteristics due to hygiene concerns and the nature of hospital floors. Customized solutions such as slip-resistant coatings or hybrid materials may be required to satisfy the unique demands of healthcare settings.\textsuperscript{46}

5) User comfort: Achieving slip resistance must not compromise user comfort. Footwear with excessively rigid or uncomfortable heels and soles may discourage older adults from consistently wearing them. Striking a balance between slip resistance and comfort is a delicate but essential consideration in footwear design.\textsuperscript{47}

6) Future directions: Research on novel materials and technologies for enhancing footwear slip resistance and user comfort is ongoing. Collaborative efforts between material scientists, footwear designers, engineers, and healthcare professionals can yield innovative solutions tailored to the specific needs of older adults.

In conclusion, while rubber remains a steadfast choice for slip-resistant heel and sole materials, ongoing research and innovation can expand the array of materials available to enhance footwear safety and comfort for older adults. A holistic understanding of user needs, durability, and the unique demands of different settings should guide heel/sole material selection.

**Anti-slip devices**

Older adults are advised to use slip-resistant footwear to mitigate fall risk. For example, the use of anti-slip devices represents a practical and effective strategy for alleviating fall risk in this population, especially in icy or slippery environments.\textsuperscript{38,49} These devices, such
as studded footwear and ice cleats, enhance traction on challenging surfaces and provide users with a safer walking experience. By actively engaging older adults in the design and testing phases, anti-slip devices can be developed to meet their functional requirements and provide high user satisfaction and usability. This user-centered approach contributes to the overall effectiveness and acceptance of anti-slip solutions for older individuals. The following critical issues must be considered:

1) Multi-environment compatibility: This requires the design of anti-slip devices that perform exceptionally well on various surfaces commonly encountered by older adults, including wet floors, icy sidewalks, and uneven terrain. Thus, research should focus on developing materials and tread patterns that can adapt to different surface conditions to provide consistent slip resistance. Studies on surface interactions and material compatibility can provide insights into the optimization of anti-slip devices for multiple environments. Extensive testing on various surfaces, including laboratory-controlled conditions and real-world scenarios, is needed to ensure effectiveness.

2) Material selection: The slip resistance properties of shoe materials should be investigated by considering high-quality rubber, silicone, or thermoplastic elastomers to determine which materials offer the best grip on different surfaces. Comprehensive material testing is needed to understand friction coefficients and surface adhesion properties. Material science research on these factors can provide in-depth knowledge regarding the suitability of different materials. Detailed material testing involving tribology studies and surface characterization can help identify the most effective materials for slip resistance.

3) Customization and adjustability: Anti-slip devices should have adjustable features such as strap length and tightness to accommodate various shoe sizes and styles. Customization should enhance user comfort and usability. Thus, human factors and ergonomic research can guide the design of adjustable features that cater to the diverse footwear preferences of older adults. Detailed studies on foot anatomy and sizing should inform adjustable mechanisms to ensure a secure fit.

4) Ergonomic design: The design of slip-resistant footwear must incorporate ergonomic concepts considering elastic materials, adjustable straps, and user-friendly fasteners to ensure a secure and comfortable fit. The design should minimize pressure points or discomfort. Ergonomic studies provide insights into wearable device design, including considerations for pressure distribution and comfort. Detailed biomechanical research can help identify areas where pressure or discomfort may occur and guide design adjustments.

5) Tread patterns: Various tread patterns should be identified to optimize traction and stability during forward and lateral movements. Extensive research must be conducted using channels or grooves in the tread to effectively disperse liquids and debris. Tribology research has explored shoe surface texture and friction enhancement. Detailed studies should assess the performance of different tread patterns under various conditions to identify the most effective designs for better slip resistance.

6) Durability and longevity: Anti-slip devices prone to wear and tear must be reinforced to extend their lifespan. Materials and construction techniques that can withstand frequent usage must also be evaluated. Material engineering and product durability studies offer insights into the design of anti-slip devices that can withstand the rigor of daily use. Detailed testing should include accelerated wear tests and real-world simulations.

7) Compact and portable: Anti-slip devices must be compact and easily portable, allowing older adults to conveniently carry them in bags or pockets when not in use. A compact design should not compromise performance. Product design principles for portability and compactness can guide the development of compact anti-slip devices. Detailed engineering studies require the optimization of device size and weight without sacrificing effectiveness.

8) Non-intrusive profile: Anti-slip devices must not significantly alter the user’s gait or comfort. Biomechanical and gait analysis studies can provide insight into the impact of wearable devices on gait. Detailed testing involving older adults can assess the impact of these devices on their gait parameters.

9) Easy maintenance: Providing clear maintenance instructions and selecting materials that are resistant to degradation over time must also be considered. Anti-slip devices should be easy to clean and maintain. Older users should be able to maintain their slip-resistant properties. Material science research on aging and degradation resistance can inform material choices that resist wear and tear. Detailed maintenance guidelines should be developed based on user feedback and testing.

10) Accessibility and inclusivity: Anti-slip devices must be designed for accessibility that considers the needs of older adults with mobility challenges or specific health conditions. Devices should be inclusive and user-friendly for a diverse user base. Inclusive design principles for wearable assistive devices offer guidance for creating products that cater to this wide range of users. User testing involving older individu-
als with diverse abilities and needs should be conducted to assess accessibility.

11) User feedback and testing:
   (i) The real-world usability issues and preferences of older adults must be addressed during the design process through user testing and feedback. Engaging users from the target demographic is needed to ensure that anti-slip devices are tailored to their specific needs. We suggest the implementation of the following strategies for feedback and testing in older adults:
   - User-centered design workshops: Workshops or focus groups with older adults should be organized to gather insights into the daily challenges related to slipping and falling. Older participants should be encouraged to share their experiences, needs, and expectations regarding anti-slip devices.
   - Prototype testing: Prototypes of anti-slip devices should be constructed based on the initial designs. Older adults should be invited to evaluate these prototypes in controlled environments to simulate real-world conditions. Feedback on comfort, ease of use, and effectiveness in preventing slips and falls must also be collected.
   - Field trials: Field trials are needed, in which older adults use anti-slip devices in their natural living environments. Their experiences should be monitored over an extended period to assess the durability of the devices, as well as their long-term comfort, and overall user satisfaction.
   - Feedback loops: Continuous feedback loops with older adult participants should be established, in which the participants are encouraged to report issues, concerns, or suggestions during real-world use. This feedback should be regularly incorporated to refine and improve the design.
   - Usability testing: Formal usability testing sessions with older adults are needed to evaluate specific aspects of anti-slip devices, such as fastening mechanisms, adjustability, and maintenance, using established usability metrics to assess user interactions.
   (ii) Involving older adults in the design process ensures that anti-slip devices align with their preferences and requirements. This helps to identify potential usability issues early in the development cycle, leading to more user-friendly and effective products. User feedback and testing also enhance user acceptance and satisfaction, thereby increasing the likelihood of widespread adoption.

Shoe Hardness

Sole hardness

The concept of rugged soles in footwear has garnered attention as a potential tool for reducing the risks associated with STF incidents among older adults. Previous studies have shown improved balance and gait when rugged soles are incorporated into footwear design. However, more studies are needed to explicitly examine the role of sole hardness in fall prevention among older people. This scarcity can be attributed to the widely accepted validity of the recommendations. Furthermore, when advocating the use of footwear with stiff soles, it is imperative to consider the expected benefits of wearing such shoes. A study assessing the effects of wearing three identical shoes with varying sole hardness (Shore A25, A40, and A58) on forefoot pain in older adults surprisingly observed that while plantar pressure increased proportionally with hardness alone, the comfort scores did not differ significantly across the range of hardness levels.

Insole hardness

Incorporating insoles into footwear design serves a multifaceted purpose, including providing cushioning, facilitating uniform pressure distribution, and maintaining proper alignment of the lower extremities. Unlike soft insoles, which conform to the foot’s position, more rigid insoles may exert a corrective influence, aiding in the maintenance of a neutral foot position and, consequently, enhancing postural stability. Losa Iglesias et al. investigated the impact of insole hardness on the static balance of older subjects with eyes open and closed. Soft gel and rigid insoles (Shore A50) were assessed. The results indicated that the rigid insole improved postural sway when visual feedback was eliminated compared with the soft gel insole. Qiu et al. investigated the effects of textured insole surfaces on postural sway in ten younger and seven older participants performing standing balance tests on a force plate under three insole surface conditions: (1) barefoot; (2) with hard; and (3) soft textured insole surfaces. They suggested that textured insole surfaces could decrease postural sway in older people during demanding balance tasks. Additionally, Qiu explored the effects of different insole designs and materials on the static and dynamic balance of older adults and found that hard insoles made of polyurethane and ethylene-vinyl acetate (EVA) significantly increased the anteroposterior margin of stability, suggesting that stiffer insoles may enhance dynamic balance in the anteroposterior direction.

However, a study examining the effects of soft-textured (270-density EVA) and hard-textured (320-density EVA) insoles on postural sway in younger and older adults on foam and firm surfaces reported contradictory findings. Although the young participants generally performed better with hard insoles, the older participants did not evidence similar benefits. Moreover, older participants standing on hard insoles for extended durations reported discomfort. Although increased sole and insole hardness may improve stability,
the optimal materials and degree of hardness required to maintain the comfort of wear must be identified.

**Optimal Footwear Design**

Numerous studies have sought to incorporate specific features in the selection, design, and testing of footwear intended for safety to enhance balance, gait, slip resistance, and overall comfort in older individuals. The following important features were collectively integrated into this footwear.

**Spatiotemporal gait analysis and standard footwear**

A study conducted a spatiotemporal gait analysis of 57 older women performing various walking tasks, including single and double motor and cognitive tasks. During these assessments, the participants were observed barefoot and wearing three distinct types of footwear: backless slippers, high-heeled footwear (heels ≥ 3.5 cm), and a standard footwear option provided for the study. The traditional footwear was characterized by lace fixation, a mildly rounded low heel (< 2.5 cm), an EVA foam midsole, a solid 6.5 cm heel collar, and a treded sole. The results revealed that standard shoes consistently and significantly increased participants’ gait speed and stride length regardless of the conditions. These findings suggest that everyday footwear is the optimal choice for enhancing gait performance in older individuals.\(^{49}\)

**Effects of different footwear types on gait and balance**

A study investigated the effects of three distinct footwear types—regular socks, backless slippers, and enclosed slippers—on gait and balance control in older women.\(^{59}\) The backless slippers, characterized by a lack of fixation, featured a soft foam (Shore A15) sole with a uniform thickness of 25 mm. In contrast, the enclosed slippers included Velcro fixation, a hard rubber (Shore A50) sole.

### Table 1. Summary of published studies versus fall risk factors

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Study design and research methods</th>
<th>Fall risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Losa Iglesias et al.(^{61})</td>
<td>2012</td>
<td>Experiments</td>
<td>✓</td>
</tr>
<tr>
<td>Kim et al.(^{27})</td>
<td>2012</td>
<td>Experiments</td>
<td>✓</td>
</tr>
<tr>
<td>Qiu et al.(^{10})</td>
<td>2012</td>
<td>Experiments</td>
<td>✓</td>
</tr>
<tr>
<td>de Mettelinge et al.(^{30})</td>
<td>2013</td>
<td>Experiments</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td>Hatton et al.(^{50})</td>
<td>2013</td>
<td>Experiments</td>
<td>✓</td>
</tr>
<tr>
<td>Karlsson et al.(^{46})</td>
<td>2013</td>
<td>Literature review</td>
<td>✓</td>
</tr>
<tr>
<td>Kuhirunyaratn et al.(^{29})</td>
<td>2013</td>
<td>Case-control &amp; interviews</td>
<td>✓</td>
</tr>
<tr>
<td>Ziaei et al.(^{33})</td>
<td>2013</td>
<td>Semi-experimental</td>
<td>✓</td>
</tr>
<tr>
<td>Beschorner et al.(^{33})</td>
<td>2014</td>
<td>Experiments</td>
<td>✓</td>
</tr>
<tr>
<td>Buchele et al.(^{33})</td>
<td>2014</td>
<td>Prospective observational</td>
<td>✓</td>
</tr>
<tr>
<td>Lopez et al.(^{19})</td>
<td>2015</td>
<td>Descriptive observational</td>
<td>✓</td>
</tr>
<tr>
<td>Qi(^{10})</td>
<td>2015</td>
<td>Experiments</td>
<td>✓</td>
</tr>
<tr>
<td>Vass et al.(^{33})</td>
<td>2015</td>
<td>Observational survey &amp; interviews</td>
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</tr>
<tr>
<td>Aboutorabii et al.(^{33})</td>
<td>2016</td>
<td>Systematic review</td>
<td>✓ ✓ ✓ ✓</td>
</tr>
<tr>
<td>Davis et al.(^{24})</td>
<td>2016</td>
<td>Randomised control trial</td>
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</tr>
<tr>
<td>Van der Cammen et al.(^{30})</td>
<td>2017</td>
<td>Experiments &amp; questionnaire</td>
<td>✓ ✓</td>
</tr>
<tr>
<td>Hurst et al.(^{17})</td>
<td>2017</td>
<td>Systematic review</td>
<td>✓ ✓ ✓ ✓</td>
</tr>
<tr>
<td>Guidozzi(^{26})</td>
<td>2017</td>
<td>Literature review</td>
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<td>Hartung and Lalonde(^{46})</td>
<td>2017</td>
<td>Literature review</td>
<td>✓</td>
</tr>
<tr>
<td>Menz et al.(^{60})</td>
<td>2017a</td>
<td>Experiments &amp; questionnaire</td>
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</tr>
<tr>
<td>Menz et al.(^{60})</td>
<td>2017b</td>
<td>Experiments &amp; questionnaire</td>
<td>✓ ✓ ✓ ✓ ✓ ✓ ✓ ✓</td>
</tr>
<tr>
<td>Buldt and Menz(^{21})</td>
<td>2018</td>
<td>Systematic review</td>
<td>✓</td>
</tr>
<tr>
<td>Bonander and Holmberg(^{40})</td>
<td>2019</td>
<td>Quasi-experimental</td>
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</tr>
<tr>
<td>Yamaguchi and Masani(^{33})</td>
<td>2019</td>
<td>Data analysis</td>
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<td>O’Rourke et al.(^{23})</td>
<td>2020</td>
<td>Observational cross-sectional</td>
<td>✓ ✓</td>
</tr>
<tr>
<td>Sundaram et al.(^{43})</td>
<td>2020</td>
<td>Observational cross-sectional</td>
<td>✓</td>
</tr>
<tr>
<td>Amiez et al.(^{46})</td>
<td>2021</td>
<td>Crossover, controlled, randomised single-blind</td>
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</tr>
<tr>
<td>Maden et al.(^{33})</td>
<td>2021</td>
<td>Comparative observational single blind</td>
<td>✓</td>
</tr>
<tr>
<td>Hida et al.(^{33})</td>
<td>2021</td>
<td>Experiments</td>
<td>✓</td>
</tr>
<tr>
<td>Li(^{10})</td>
<td>2021</td>
<td>Systematic review &amp; interviews</td>
<td>✓ ✓ ✓</td>
</tr>
</tbody>
</table>

Total number of studies: 11 12 8 5 17 9

SFT, shoe fit; SFX, shoe fixation; SHH, shoe heel height; SCH, shoe collar height; SSR, shoe slip resistance; SHD, shoe hardness.
15 mm below the forefoot and 32 mm below the heel, and a solid heel counter. The results of the study demonstrated that enclosed footwear provided the most substantial support for gait and balance, leading to improved directional control and reduced postural sway, step width, and end sway. Furthermore, the participants consistently reported higher comfort, fit, and overall satisfaction with the enclosed slippers.

**Prototype footwear for enhanced performance**

Another study assessed the balance and gait performance of older women wearing three different types of footwear: outdoor footwear, flexible footwear (control), and prototype footwear designed to optimize performance. The prototype footwear featured a rubber sole with Shore A55 hardness and forefoot sole and heel thicknesses of 18 mm and 25 mm, respectively, and also incorporated both lace and Velcro fixation mechanisms. The design enhancements included a high collar, a firm heel counter, a 10° bevel in the heel area to improve slip resistance, and specific tread patterns. Additionally, a textured EVA insole with unique characteristics was designed. The results of these assessments demonstrated consistently better performance when the participants wore the prototype footwear, including a narrower step width and reduced end-postural sway. These improvements in lateral stability are particularly significant in mitigating the risk of STFs among older adults.

**Balance shoes for enhanced stability**

Other studies have explored the effects of balance shoes designed for stability, contrasting them with regular outdoor shoes. The balance-specific shoes featured a longitudinal track under the heel and a protective space within the midsole, strategically designed to mitigate potential balance disturbances caused by pebbles. The midsole further incorporated bands elevated 2 mm on both sides to improve balance. A metal shank was integrated into the sole to enhance rigidity, and a circular arc tread was bolstered to improve slip resistance. The findings consistently demonstrated that balance-specific shoes significantly enhanced leg stability, especially with the eyes closed. Moreover, the participants reported an increased sense of steadiness and security when wearing these specialized shoes. These studies collectively emphasize the importance of integrating specific footwear features to enhance balance, gait, and overall safety in older individuals. Thus, optimal footwear design considers factors such as fixation, sole properties, and tread patterns to reduce the risk of STFs in this vulnerable population.

Table 1 and Fig. 3 provide a comprehensive overview of the results of this review, summarizing the findings from published studies related to footwear features and their associations with fall risk, as discussed in the Results and Discussion Section. Fig. 3 shows the significant increase in research on shoe slip resistance over the past 12 years. However, as highlighted by Kim, the challenges of addressing wear and tear on shoe heel/sole surfaces due to friction remain an important concern that necessitates innovative engineering solutions. Therefore, we strongly recommend that future research aimed at developing safer footwear designs to prevent falls among older adults should adopt a holistic approach involving collaboration between clinicians, researchers, and engineers.

**CONCLUSION**

The results of this comprehensive review highlight the central role of footwear in preventing falls in older adults. Addressing this multifaceted challenge requires a thorough approach involving education, awareness, assessment, and innovation. Integrating these recommendations into clinical practice and public health initiatives can invigorate efforts to reduce the burden of STFs among older individuals, ultimately creating a safer and more secure environment for vulnerable populations.

**ACKNOWLEDGMENTS**

**CONFLICT OF INTEREST**

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, IJK; Funding acquisition, IJK; Investigation, IJK; Methodology, IJK, FH; Project administration, IJK, FH; Supervision, IJK, FH; Writing–original draft, IJK; Writing–review & editing, IJK, FH.

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INTRODUCTION

The rapid growth of digital technology in Korea leads to offline public and private service substitution with digital devices such as smartphones and computers. These changes have been accelerated by the coronavirus disease 2019 (COVID-19) impact, which started in 2020, and the Fourth Industrial Revolution. Digital literacy combines literacy, the ability to read and write, and proficiency in digital technology. Glister’s definition encompasses the ability to understand computer-mediated information, evaluate and integrate diverse information, and accurately use it.

Although digitalizing animate services brings convenience, it aggravates alienation among individuals vulnerable to such digitalized information, facing difficulty accessing digital information and tools. The National Information Society Agency provides reports on South Korea’s digital divide. According to their 2021 report, older adults are more vulnerable than low-income earners, disabled individuals, farmers, and fishermen. Despite the high demand for online services such as shopping and insurance claims, older adults may face discrimination due to difficulties in digital access.

Continuously excluding older people from the benefits of information society could degrade the quality of life of individuals with extended life expectancies. With Korea projected to become a super-aged nation by 2025, the number of socially isolated older adults is expected to increase owing to reduced social networks with advancing age. Thus, preventing social isolation among seniors and improving their quality of life requires fostering digital literacy.

Researchers’ definitions of social networks vary. Ell defined a social network as one encompassing an individual’s interpersonal contacts, spanning formal and informal support from family,
friends, neighbors, colleagues, and caregivers. This multidimensional concept involves network size, components, frequency of contact with family and friends, aid level, acceptance, and relationship satisfaction. Social network size decreases with age due to retirement, physical illness, or the death of friends. Maintaining good social networks enhances multiple aspects of older adults’ lives positively. Social networks are linked to cognitive, emotional, and mental health status for older adults. Moreover, strengthening social networks can help prevent suicide attempts among older adults. According to health indicators from the Organisation for Economic Cooperation and Development, Korea has the highest suicide rate among all countries. Korea’s suicide rate among those aged 65 years and older is twice the average, underscoring the growing need for research on social networks in older adults. Furthermore, older adults’ social networks affect health-promoting behaviors such as reducing smoking and alcohol consumption and life satisfaction.

Previous research on social networks in older Korean adults has focused on assessing the links between variables such as spouses, children, and friends and outcomes such as depression or health. However, recent research trends have aimed to elucidate the complex social network patterns in older adults. However, few studies have analyzed digital literacy discrepancies among older adults across various social network types. Therefore, this study aimed to categorize the social networks of older Korean adults and examine the characteristics and differences in digital literacy linked to these network types. The goal was to identify the most susceptible network type for digital devices and facilitate targeted interventions.

Materials and Methods

Study Data
This study used data from the 2020 National Survey on Older Koreans conducted by the Ministry of Health and Welfare of Korea. The survey was designed to understand the living conditions and needs of older individuals in South Korea, making it suitable for analyzing the characteristics of social networks and digital literacy disparities. This national survey employed a stratified two-stage cluster sampling method for community-dwelling older adults aged ≥ 65 years. Data were collected through in-person interviews conducted between September and November 2020.

Participants
This study initially included 10,097 Korean adults aged ≥ 65 years. After excluding 185 individuals with missing digital literacy or social network values, the final analysis included a total of 9,377 individuals.

Study Variables

Social network typology indicator
Latent class analysis was used to identify network types based on earlier social network typology studies. This study included seven social network variables from the 2020 National Survey on Older Koreans, based on the typology described by Kang et al. These seven variables were spousal presence, child encounter frequency, child contact, friend encounter frequency, friend contact, club participation, and social activity engagement. For each variable, encounters refer to in-person encounters with a child or friend, whereas contact refers to remote contact with a child or friend, such as phone calls or texts. All variables were coded dichotomously, as follows.

Spousal presence was coded as 0 (no spouse) or 1 (spouse present). The frequency of child encounters was coded as 0 (less than once every three months) or 1 (more than once every three months). The frequencies of child contact, friend encounters, and friend contact were coded as 0 (less than once a week) or 1 (more than once a week). Club and social activity participation was coded as 0 (did not participate in the past year) or 1 (participated in the past year). Club participation refers to club involvement, while social activities involve engagement in social groups such as alumni associations and social gatherings.

Digital literacy
Older adults’ digital literacy was measured using five questions regarding challenges with information service devices. The question “Is online or internet-based information and services usage challenging?” was coded as 0 (yes) or 1 (no). The remaining four questions used a five-point Likert scale reflecting discomfort levels (1 = not uncomfortable at all, 2 = not uncomfortable, 3 = normal, 4 = uncomfortable, and 5 = very uncomfortable). However, for this analysis, we dichotomously coded the four questions (1 of 1–3 points, 0 of 4–5 points) to standardize the scales across the five questions. The four questions were related to (1) difficulty with online train/bus reservations, (2) difficulty with restaurant orders through kiosks (digital machines), (3) inconvenience caused by ATM usage at banks or fewer offline bank locations, and (4) difficulty caused by an increase in credit card-only establishments. We summed the responses to the five questions, with higher scores indicating higher digital literacy.

Demographic and health status
We used the respondents’ demographic characteristics and health-related variables to analyze disparities in attributes among older Korean adults based on their social network type. The demographic and sociological characteristics included age, sex.
(male = 0, female = 1), educational level (illiterate = 1, elementary school = 2, middle school = 3, and high school or higher = 4), residential area (large city = 1, small and medium-sized city = 2, and rural area = 3), and economic level (national basic livelihood security or medical benefit recipient = 1, if not = 0). We also measured subjective age, which refers to one’s self-perceived status as an older adult or otherwise.\textsuperscript{20,21} We determined the subjective age by subtracting perceived age from actual age\textsuperscript{22} based on responses to the question, “At what age do you consider someone an older adult?” A negative subjective age indicated self-perceived older status, whereas a positive value indicated the opposite.

Health status evaluations included functional independence, cognitive health, and depression indicators. First, the independence level of instrumental activities of daily living (IADL) was used to gauge daily life difficulties through 10 questions: grooming, housework, meal preparation, laundry, taking medicine on time, financial management, short-distance outings, making decisions on payment and changes, making phone calls, and using transportation. Questions #1–7 were rated on a three-point scale, whereas questions #8–10 were rated on a four-point scale. The coding was as follows: Questions #1–7 (complete self-reliance = 3, partial help = 2, and complete help = 1) and Questions #8–10 (complete self-reliance = 4, some help = 3, considerable help = 2, and complete help = 1). We used the scores for 10 IADL items in the analysis, with a higher score indicating greater functional independence. The Korean version of the Mini-Mental State Examination for Dementia Screening (MMSE-DS) was used to evaluate cognitive function. The MMSE-DS includes 19 questions and a 0–30-point scale, wherein a lower score indicates a lower cognitive function. The 15-item short form of the Geriatric Depression Scale (SGDS) measured depression over the past week using “yes” or “no” responses. The existing score scale was reverse-coded for this analysis, in which the higher the SGDS score, the lower the depression level.

**Instruments for Validation of the Data Analyses**

For the latent class analysis, we used Mplus version 8.0 (https://www.statmodel.com/) to categorize older adults into groups based on their social relationships involving family, friends, and social activities. Latent class analysis employs the maximum likelihood estimation method for continuous variables while simultaneously assessing an individual’s likelihood of belonging to a group and the overall group model.\textsuperscript{23,24} This approach classifies groups similarly to conventional cluster analysis.\textsuperscript{25} This employs an objective approach to determine the optimal number of groups using a model-based stochastic analysis method.\textsuperscript{26}

To determine the optimal number of groups, goodness-of-fit indices were used, including the Akaike information criterion (AIC),\textsuperscript{27} Bayesian information criterion (BIC),\textsuperscript{28} and sample-size adjusted Bayesian information criterion (SABIC).\textsuperscript{29} Lower values indicated a better-fit model. Additionally, we assessed the classification quality of the latent groups using the entropy index,\textsuperscript{30} which ranged in values from 0 to 1. An entropy index closer to 1 indicates a more accurate profile, and values of ≥ 0.8 are considered favorable.\textsuperscript{31,32} We used the Lo–Mendell–Rubin likelihood ratio test (LMR-LRT) to assess statistical significance by comparing the k and k-1 latent profile group models.\textsuperscript{33}

We analyzed the digital literacy differences within detailed social network types using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). The frequency and descriptive statistics provided an overview of the respondents’ characteristics. Chi-square and Welch’s F analyses were performed to confirm each group’s characteristics in the case of no equality of variances based on Levene’s test, followed by the Games–Howell post-hoc test to determine the significance of differences between groups. Statistical significance was set at p < 0.05. We further analyzed whether the differences in digital literacy varied according to social network type by stratifying confounding factors such as education level, sex, and age.

**Ethical Considerations**

Participants in the National Survey on Older Koreans provided written informed consent before enrolling in the survey. This national survey was approved by the Institutional Review Board of the Korea Institute for Health and Social Affairs (IRB No. 2020-36). This study obtained a review exemption from the Institutional Review Board of Yonsei University Mirae Campus (No. 1041849-202210-SB-180-01).

**RESULTS**

The participants’ demographic and sociological characteristics are summarized in Table 1.

**Social Network Typologies of Older Adults: Latent Class Analysis**

**Determination of latent classes of social network**

We performed latent class analysis using the presence of a spouse, child encounters (at least once a week), child contact (at least once a week), friend encounters (at least once a week), club participation, and engagement in social activities as dependent variables to confirm the social network types of the older adults. The analysis compared the information criterion indices and likelihood ratio verification statistics as the number of latent classes increased from
two to four (Table 2). Information reference values, including AIC, BIC, and SABIC, decreased as the fit of the four-class model improved. The statistical significance of the LMR-LRT signified that the current number of k-groups was more suitable than that of k-1 groups. In this estimation, all four classes were statistically significant (p = 0.001). The second and third classes exhibited excellent entropy values of ≥ 0.8. The number of latent classes for older adults’ social networks was determined based on statistical information and a comprehensive consideration of class interpretability and case counts. Consequently, three latent classes were determined to be optimal.

**Social network types in older adults**

We classified the latent classes based on the response patterns to each question within seven categories (spouse, child, child, friend, friend, club, and social activity). The latent class demonstrating substantially high encounter and contact frequency with children was labeled the “child-centered type.” Similarly, the class with elevated encounter and contact frequencies with friends and children was designated the “child-friend type.” Finally, the latent class showing a high frequency of encounters and contact with friends was termed the “friend-centered type.” Fig. 1 shows the conditional response probabilities for each latent class using average values. The specific values of the response probabilities for each class are presented in Supplemental Table S1. Figs. 2–4 show the latent classes.

**Characteristics of the social network types**

We analyzed the differences in demographics, health status, and digital literacy factors among the social network types of older adults (Table 3).

First, our examination of demographic factors, including age, sex, educational level, residential area, economic status, and degree of older adult perception, according to the social network type, revealed significant differences in all items. Regarding age, the friend-centered and child-friend types showed the highest and lowest average ages, respectively. The proportions of women were higher than those of men for all types.

Regarding education level, the child-centered type exhibited the highest proportion of high school graduates or those with higher education, whereas the child-friend and friend-centered types showed high ratios of elementary school graduates. Regarding residential areas, the child-centered and child-friend types had the highest percentages of individuals living in large cities and the lowest in towns. However, the friend-centered type was characterized by a low percentage of residents in large cities and a high percentage in rural areas. Regarding economic conditions, the rate of non-recipients of government support was high for all three types. The friend-centered type comprised the highest proportion of individuals who perceived themselves as older adults.

We analyzed functional independence, cognitive health, and depression as health status factors with significant differences in all items. Regarding functional independence, the child-centered type experienced the most difficulties, whereas the child-friend type showed the fewest challenges. Regarding cognitive health, the

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**Table 1.** Demographic and sociological characteristics (n=9,377)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
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<tbody>
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<td>Age (y)</td>
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</tr>
<tr>
<td>Sex  Male</td>
<td>3,817 (40.1)</td>
</tr>
<tr>
<td>Female</td>
<td>5,621 (59.9)</td>
</tr>
<tr>
<td>Educational attainment</td>
<td></td>
</tr>
<tr>
<td>Illiteracy</td>
<td>1,072 (11.4)</td>
</tr>
<tr>
<td>Elementary school</td>
<td>3,126 (33.3)</td>
</tr>
<tr>
<td>Middle school</td>
<td>2,192 (23.4)</td>
</tr>
<tr>
<td>High school and above</td>
<td>2,987 (31.9)</td>
</tr>
<tr>
<td>Region</td>
<td></td>
</tr>
<tr>
<td>Large city</td>
<td>3,841 (41.0)</td>
</tr>
<tr>
<td>Small and medium-sized city</td>
<td>2,821 (30.1)</td>
</tr>
<tr>
<td>Rural area</td>
<td>2,715 (29.0)</td>
</tr>
<tr>
<td>Economic level</td>
<td>291 (31.4)</td>
</tr>
<tr>
<td>National basic livelihood security or medical benefit recipients</td>
<td>617 (6.6)</td>
</tr>
<tr>
<td>Not applicable</td>
<td>8,760 (93.4)</td>
</tr>
<tr>
<td>Elderly perception degree</td>
<td>3.27 ± 7.93</td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation or number (%).

---

**Table 2.** A comparison of the fit statistics of different latent class models

<table>
<thead>
<tr>
<th>Class</th>
<th>AIC</th>
<th>BIC</th>
<th>SABIC</th>
<th>Entropy</th>
<th>LMR-LRT</th>
<th>Proportions for the class (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>68628.216</td>
<td>68735.649</td>
<td>68687.981</td>
<td>1.000</td>
<td>4266.448***</td>
<td>72.68</td>
</tr>
<tr>
<td>3</td>
<td>67150.092</td>
<td>67314.822</td>
<td>67241.732</td>
<td>0.849</td>
<td>1474.014***</td>
<td>23.14</td>
</tr>
<tr>
<td>4</td>
<td>66589.534</td>
<td>66811.563</td>
<td>66713.049</td>
<td>0.717</td>
<td>568.797***</td>
<td>21.82</td>
</tr>
</tbody>
</table>

AIC, Akaike information criterion; BIC, Bayesian information criterion; SABIC, sample-size-adjusted Bayesian information criterion; LMR–LRT, Lo–Mendell–Rubin likelihood ratio test.

*p < 0.05, **p < 0.01, ***p < 0.001.
Fig. 1. Profile of latent classes. Conditional response probabilities for each latent class are shown using the averages.

Fig. 2. Characteristics of the child-centered type.

Fig. 3. Characteristics of the child-friend type.

Fig. 4. Characteristics of the friend-centered type.

child-friend and friend-centered groups scored the highest and lowest, respectively. Regarding depression, older adults were less depressed in the order of child-friend, child-centered, and friend-centered relationships.

Finally, the digital literacy factors differed significantly according to the social network type. The friend-centered type was the most vulnerable to digital literacy, whereas the child-centered type was the most competent. We performed additional analysis to determine whether there were differences in digital literacy according to social network type when stratifying potential confounding factors such as education level, sex, and age (Table 4). When stratified by sex, the friend-centered and child-centered types were the most vulnerable in both men and women. This finding was similar to the results obtained without stratification. In terms of education level, the difference in digital literacy according to social network type was significant at all levels except for illiteracy. At the other
Table 3. Characteristics of social network types

<table>
<thead>
<tr>
<th></th>
<th>Child-centered type (a)</th>
<th>Child-friend type (b)</th>
<th>Friend-centered type (c)</th>
<th>F (Games-Howell)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (y)</strong></td>
<td>73.53 ± 6.91</td>
<td>73.38 ± 6.43</td>
<td>74.24 ± 6.25</td>
<td>8.659*** (c &gt; a, b)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td>67.586***</td>
</tr>
<tr>
<td>Male</td>
<td>1,009 (47.3)</td>
<td>2,319 (37.4)</td>
<td>428 (40.3)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1,111 (52.7)</td>
<td>3,872 (62.6)</td>
<td>638 (59.7)</td>
<td></td>
</tr>
<tr>
<td><strong>Educational attainment</strong></td>
<td></td>
<td></td>
<td></td>
<td>30.935***</td>
</tr>
<tr>
<td>Illiteracy</td>
<td>272 (13.3)</td>
<td>655 (10.7)</td>
<td>145 (13.7)</td>
<td></td>
</tr>
<tr>
<td>Elementary school</td>
<td>664 (31.7)</td>
<td>2,090 (33.7)</td>
<td>372 (35.1)</td>
<td></td>
</tr>
<tr>
<td>Middle school</td>
<td>476 (22.3)</td>
<td>1,446 (23.4)</td>
<td>270 (25.2)</td>
<td></td>
</tr>
<tr>
<td>Over high school</td>
<td>708 (32.7)</td>
<td>2,000 (32.1)</td>
<td>279 (26.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Region</strong></td>
<td></td>
<td></td>
<td></td>
<td>167.864***</td>
</tr>
<tr>
<td>Large city</td>
<td>965 (45.4)</td>
<td>2,583 (41.6)</td>
<td>293 (27.9)</td>
<td></td>
</tr>
<tr>
<td>Small and medium-sized city</td>
<td>713 (33.7)</td>
<td>1,756 (28.5)</td>
<td>352 (32.8)</td>
<td></td>
</tr>
<tr>
<td>Rural area</td>
<td>442 (21.0)</td>
<td>1,852 (29.8)</td>
<td>421 (39.3)</td>
<td></td>
</tr>
<tr>
<td><strong>Economic level</strong></td>
<td></td>
<td></td>
<td></td>
<td>51.969***</td>
</tr>
<tr>
<td>National basic livelihood or medical benefit recipients</td>
<td>173 (8.1)</td>
<td>331 (5.3)</td>
<td>113 (10.5)</td>
<td></td>
</tr>
<tr>
<td>Not applicable</td>
<td>1,947 (91.9)</td>
<td>5,860 (94.7)</td>
<td>953 (89.4)</td>
<td></td>
</tr>
<tr>
<td><strong>Subjective age</strong></td>
<td>3.00 ± 8.66</td>
<td>3.22 ± 7.71</td>
<td>4.02 ± 7.66</td>
<td>6.251** (c &gt; a, b)</td>
</tr>
<tr>
<td><strong>Functional independence</strong></td>
<td>3.19 ± 0.36</td>
<td>3.26 ± 0.20</td>
<td>3.24 ± 0.27</td>
<td>61.146*** (b, c &gt; a)</td>
</tr>
<tr>
<td><strong>Cognition</strong></td>
<td>24.26 ± 7.88</td>
<td>24.86 ± 6.56</td>
<td>23.41 ± 6.12</td>
<td>21.082*** (b &gt; a, c)</td>
</tr>
<tr>
<td><strong>Depression</strong></td>
<td>11.16 ± 3.61</td>
<td>11.92 ± 3.15</td>
<td>11.09 ± 4.00</td>
<td>50.604*** (b &gt; a, c)</td>
</tr>
<tr>
<td><strong>Digital literacy</strong></td>
<td>1.94 ± 1.66</td>
<td>1.79 ± 1.62</td>
<td>1.49 ± 1.47</td>
<td>30.363*** (a &gt; b &gt; c)</td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation or number (%).

Subjective health indicates subtracting perceived age from actual age; Functional independence, daily life difficulties score of 10 instrumental activities of daily living questions; Cognition, Korean version of the Mini-Mental State Examination for Dementia Screening; Depression, the 15-item short form of the Geriatric Depression Scale; and Digital literacy, five questions on challenges with information service devices.

*p<0.05, **p<0.01, ***p<0.001.

Table 4. Digital literacy difference of social network types

<table>
<thead>
<tr>
<th></th>
<th>Digital literacy</th>
<th></th>
<th>Friend-centered type (c)</th>
<th>F (Games-Howell)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Education</strong></td>
<td>Digital literacy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illiteracy</td>
<td>0.68 ± 1.02</td>
<td>0.74 ± 1.13</td>
<td>0.74 ± 1.08</td>
<td>0.319</td>
</tr>
<tr>
<td>Elementary school</td>
<td>1.52 ± 1.50</td>
<td>1.24 ± 1.37</td>
<td>1.23 ± 1.39</td>
<td>9.290*** (a &gt; b, c)</td>
</tr>
<tr>
<td>Middle school</td>
<td>1.92 ± 1.63</td>
<td>1.81 ± 1.51</td>
<td>1.49 ± 1.50</td>
<td>7.160*** (a, b &gt; c)</td>
</tr>
<tr>
<td>Over high school</td>
<td>2.83 ± 1.55</td>
<td>2.70 ± 1.60</td>
<td>2.23 ± 1.44</td>
<td>17.023*** (a, b &gt; c)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2.19 ± 1.65</td>
<td>2.14 ± 1.67</td>
<td>1.71 ± 1.48</td>
<td>17.082*** (a, b &gt; c)</td>
</tr>
<tr>
<td>Female</td>
<td>1.71 ± 1.64</td>
<td>1.58 ± 1.56</td>
<td>1.35 ± 1.44</td>
<td>11.801*** (a, b &gt; c)</td>
</tr>
<tr>
<td><strong>Age group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Youngest old (65–74 y)</td>
<td>2.42 ± 1.62</td>
<td>2.26 ± 1.62</td>
<td>1.94 ± 1.49</td>
<td>19.342*** (a &gt; b &gt; c)</td>
</tr>
<tr>
<td>Middle old (75–84 y)</td>
<td>1.33 ± 1.48</td>
<td>1.12 ± 1.34</td>
<td>1.05 ± 1.28</td>
<td>6.917* (a &gt; b, c)</td>
</tr>
<tr>
<td>Oldest old (≥ 85 y)</td>
<td>0.58 ± 1.05</td>
<td>0.84 ± 1.27</td>
<td>0.53 ± 0.94</td>
<td>4.029* (b &gt; a, c)</td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation.

*p<0.05, **p<0.01, ***p<0.001.

levels, the results were comparable to the findings without stratification. Moreover, the differences in digital literacy were significant after classifying the participants into three age groups. The youngest old and middle old groups demonstrated results similar to those without stratification. However, for the oldest old, friend-centered behavior remained the most vulnerable, whereas the child-friend type was the most competent.
DISCUSSION

This study aimed to understand social network types based on the frequency and size of social networks among older Korean adults, analyze each type’s characteristics, and examine digital literacy disparities among these types. The summary and implications of the results are as follows.

First, the social network types were classified according to the frequency and size of the social network of older Korean adults into three latent classes: “child-centered type,” “child-friend type,” and “friend-centered type.” The child-friend type accounted for the most participants, followed by the child-centered and friend-centered types. All three types exhibited lower engagement in club participation and social activities among the seven areas used to determine the social network types. This deviated from the patterns reported in other countries, where more diverse networks involve connections among relatives, friends, and communities and reflects the family-centered culture in Korea. These findings are partially consistent with those of Im et al. who highlighted the prominence of social networks centered on cohabiting partners and non-cohabiting children among the oldest Korean adults. In contrast, in their 2014 national survey data analysis, Park et al. reported higher club or social group participation among older Koreans. This result reflects the unique situation posed by the COVID-19 pandemic, which reduced social networks and activities during the survey period.

Second, the results of this study revealed significant differences in the descriptive characteristics of each social network type. A comparative analysis revealed a relatively high average age for the friend-focused type among social network types. In contrast, the child-focused group was younger. While the terminology may differ, these findings align with those of Park et al. demonstrating higher average age among restricted and friend-focused types. Kang et al. added that with aging, the proportions of the friend-focused types tend to shrink due to factors such as death or health deterioration, in contrast to the expansion of child-centered types due to family care. Moreover, institutional support is required to form and maintain diverse social networks. Sex differences were also apparent in the present study, with the child-friend type showing a significantly higher proportion of women. This is consistent with earlier research demonstrating women’s broader and more diverse networks and heightened social support exchanges. In addition, distinctions in residential areas according to social network type revealed higher proportions of older adults of child-centered and child-friend types living in large cities, whereas the friend-centered type was marked by higher rural residence. This might stem from younger generations migrating to urban areas, leading to depopulation and aging in the rural areas of Korea. Economic status varied across social networks in the present study, with the child-friend type showing fewer national basic livelihood security support beneficiaries than the friend-centered and child-centered types. This implies that older adults with better economic standing are more likely to engage in diverse social networks, consistent with the findings of previous studies.

These results suggest the need to reinforce various social networks, particularly for older adults in rural areas and beneficiaries of the national basic livelihood security support. Expanding social networks through public support or developing visiting programs to facilitate interaction with local neighbors is crucial.

Third, the social network type was associated with health outcomes. Regarding the health sub-areas, the child-friend type was healthier in terms of functional independence, cognition, and depression. This finding was consistent with those previous studies showing that broader social networks are correlated with more positive health outcomes. Differentiating between child-centered and friend-centered health statuses proved complex due to inconsistencies across health sub-areas. This mirrors earlier studies that reported varying findings on this topic. Regarding functional independence, previous studies suggested that the friend-centered type is healthier than the child-centered type. However, the disparities in depression between friend-centered and child-centered types in the present study were not statistically significant. Research on older adults from Western cultures has revealed a better depressive status for the friend-centered type. In contrast, studies from Eastern cultures such as Hong Kong and Japan have reported no significant differences in depression. This distinction might stem from the cultural emphasis on family bonds in Eastern societies, compared to the value placed on independence in Western cultures. Based on the finding that diverse social network types affect health status, fostering various networks is vital. This could involve creating opportunities for older adults to participate in community gatherings and social activities rather than relying solely on traditional family support.

Fourth, the results of the present study demonstrated that the child-centered type was the most competent, whereas the friend-centered type was the most vulnerable in digital literacy. This indicates that children adopt digital devices, and family composition is a learning environment for digital device usage. Since older adults in Korea are an information-vulnerable group and the digital divide rate is 68.6%, digital literacy among older Korean adults is generally low. Consequently, interventions and institutional alternatives should be developed to enable older adults to use digital devices without relying on their families. The results of this study demonstrated lower digital literacy among illiterate...
individuals, regardless of the social network type. This may occur due to the combined difficulty of learning new digital skills and understanding or using text. Therefore, strategies for digital device utilization among seniors must be tailored to the diverse situations of older adults.

During the pandemic, the importance of social isolation and digital literacy increased. The results of the present study are valuable for identifying which types of older adults are most at risk during this unprecedented time by collecting data during a period when older adults were experiencing both social and digital isolation. Particularly, the friend-centered type appeared to be the most vulnerable in terms of health and digital literacy. During the pandemic, when social distancing was required, friend-centered individuals with less interaction with their families may have been at a greater risk of isolation.

This study has several limitations. First, due to the use of secondary data, the variables were limited in selection and validation when identifying social network types and digital literacy in older adults. The study’s understanding of digital literacy levels in older adults was also hindered by the limited scope of items addressing digital use and the difficulties faced by this population. Therefore, follow-up research requires analysis and verification, including more comprehensive and diverse digital items. Second, analyzing social network types in older adults relied on cross-sectional data from 2020 onwards. Therefore, it is difficult to rule out the effects of COVID-19 on older adults’ social activities and networks. Furthermore, owing to aging, the distinct social network patterns among the youngest, middle-aged, and oldest participants necessitate further investigation through longitudinal data analysis. Finally, measuring social network types in older adults was primarily quantitative, focusing on network presence, frequency, and participation. Future studies should consider incorporating qualitative aspects of social networks, such as relationship satisfaction, for a more comprehensive understanding of social network types. Given the current analysis of the distinct characteristics of each network type, follow-up studies applying regression models to investigate the relationships between social network types and digital literacy are needed.

In conclusion, this study categorized the social networks of older adults in Korea into three distinct types and explored their general characteristics and differences in digital literacy. Among these, the child-friend type emerged as the most healthy, underscoring the significance of a wider social network in health preservation. Conversely, the friend-centered type was the most vulnerable to digital literacy. These findings suggest the need to prioritize digital literacy intervention programs and services for friend-centered older adults in South Korea.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

AUTHOR CONTRIBUTION

Conceptualization, HL, MKK; Data curation, HL, MKK, KHP; Investigation, HL; Methodology, MKK; Project administration, HL, HYP; Supervision, HYP, KHP; Writing—original draft, HL, MKK; Writing—review & editing, HL.

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SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4235/agmr.23.0174.

REFERENCES


Global Research on Centenarians: A Historical and Comprehensive Bibliometric Analysis from 1887 to 2023

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2Colombian Centenarians Alliance, Cartagena, Colombia
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Background: Centenarians are considered the most successful human biological aging model. However, the characteristics and patterns of research among centenarians have not been described or analyzed. Thus, this study aimed to disclose the historical landscape of global research on centenarians. Methods: This bibliometric study investigated historical evidence on centenarian research published in the Scopus database. The bibliometrix package in R was used to perform visual and quantitative analyses of research metrics, trends, and patterns. Results: Of the 2,061 documents included between 1887 and 2023, 84.2% (n=1,736) were published as articles with primary data. We identified international collaboration and annual growth rates of 21.4% and 3.15%, respectively. The United States published the highest number of papers on centenarians (n=786), whereas the publications from Italy had the highest impact (h-index of 90). Based on the frequency of keywords, mortality, genetics, dementia, Alzheimer’s disease, and immunosenescence are a few of the most studied topics among centenarians, with emerging research related to mitochondrial DNA and comparison of results between nonagenarians and centenarians. Italy, the United States, and China lead the global research collaboration network, collaborating most frequently with Japan and European countries. Conclusion: Global research on centenarians has grown over the last 20 years, primarily led by Italy, the United States, and China. Latin American and African countries have conducted little or no research on centenarians. The most widely studied topics include mortality, cognition, immunosenescence, and genetics.

Key Words: Centenarians, Longevity, Aged, Research, Bibliometrics

INTRODUCTION

The world is currently facing a critical demographic transition with the acceleration of population aging, which is linked to an increase in the incidence and prevalence of age-related chronic diseases.1 These conditions result in a substantial disease burden and high healthcare costs.2,3 Therefore, international consensus recommendations emphasize designing and implementing health strategies and plans to promote healthy aging.4 This emphasis aims to optimize healthy lifespans in the older adult population, along with other health indicators such as functional capacity, quality of life, and self-satisfaction during aging.5 Centenarians are the most successful biological aging model in humans.6 This population is characterized by a low prevalence of age-related chronic diseases, favorable functionality and independence, adequate social resilience, and life satisfaction.6,7 Studying this population is important for understanding the physiological and pathophysiological mechanisms of aging and the determinants associated with these outcomes.6,7,10 Various studies have used centenarians as super-control groups for comparing clinical phenotypes, biomarker expression, and immunological resilience.12 These results, based on precision medicine, show promising out-

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comes, such as the identification of genetic polymorphisms that protect against certain diseases or conditions.\textsuperscript{13}

Despite the notable advantages provided by research on populations, what has been studied regarding the centenarian population, how it has been studied, and where, has not been examined. The heritability of extreme longevity is approximately 30%.\textsuperscript{14} Therefore, lifestyle, environmental factors, and social determinants of health are crucial for understanding the evolution and health phenotypes of centenarians.\textsuperscript{15} These characteristics vary between regions, making the study of centenarians tailored to social and cultural contexts essential for understanding the risks and benefits of specific signatures in each population.\textsuperscript{16}

Globally, just over 2,000 or 3,000 articles related to centenarian research have been published.\textsuperscript{17,18} However, this scientific production has never been characterized, highlighting a significant gap in knowledge regarding what has been researched and what remains to be investigated in centenarians. This limitation hinders the development of evidence-based road maps. To address this and provide useful and actionable data for researchers in longevity, healthy aging, and centenarian studies, we aimed to describe the historical landscape of global research on centenarians, highlighting their characteristics and future priorities.

**MATERIALS AND METHODS**

**Study Design**

Bibliometric cross-sectional study.

**Source Database**

We performed a broad search of the Scopus database, which is the largest peer-reviewed literature database and provides access to numerous metrics related to authors, citations, and scientific articles. Currently, Scopus includes > 15,000 indexed medicine journals and has been previously used to perform bibliometric analyses.\textsuperscript{7,18}

**Search Strategy**

Our search identified all scientific articles on centenarians published worldwide. We used Medical Subject Headings terms and synonyms to construct the search. After pilot testing, to identify the largest amount of related evidence, we used the following search: TITLE-ABS-KEY (centenarian) OR TITLE-ABS-KEY (centenarians) OR TITLE-ABS-KEY (centenar*).

**Standardization and Data Collection**

No language restrictions were applied regarding article inclusion. The database yielded results that encompassed diverse data, including the year of publication, article title and type, journal details, keywords, affiliations, author information, citations, and collaborations. We performed the search through November 26, 2023, with a focus on filters labeled “Journals.” Subsequently, two authors performed a manual review using Microsoft Office Excel 2016 to eliminate duplicates and articles that did not meet the research scope (centenarians) based on their titles, abstracts, and keywords.

Subsequently, two authors performed another manual review to standardize the data. Then, a few variables were recategorized by article typology. We classified all original studies, regardless of their observational or experimental designs, as “original studies.” The “review” category included narrative, systematic reviews, and meta-analyses. The “editorial” category comprised all articles published under that specific typology. In contrast, the “letter” category encompassed any other typologies distinct from the previous ones, including comments, correspondences, letters to the editor, etc. The same procedure was applied to study affiliations.\textsuperscript{18}

**Indicators and Metrics**

To assess the impact of the scientific production of authors, affiliations, and countries, we used the h-index, m-index, and g-index, along with the aggregate count of citations, when precise data were available for such calculations. The h-index is a quantitative bibliometric index that measures the impact of scientific output based on the number of citations in published articles.\textsuperscript{19,20} For instance, an author has an h-index if h of their p papers have received at least h citations. Mathematically, this is expressed as follows:

\[
h = \max \{ C_i \geq i \}, \quad i = 1, 2, \ldots, p \land C_i \geq C_{i+1}
\]

where p is the number of documents published by the author and \( C_i \) denotes the number of citations for the \( i \)-th document, organized in descending order. Consequently, an h-index of 20 indicates no fewer than 20 articles, each with a minimum of 20 citations.

The m-index (also known as Hirsch’s m-quotient) is a quantitative index that assesses the linear correlation of an investigator’s impact over time.\textsuperscript{19,20} This value is calculated using the following equation:

\[
m = h^p = h/Y_{aa}
\]

where \( h \) denotes the h-index of the author and \( Y_{aa} \) represents the author’s academic age, which is determined by subtracting the present year from the year of the author’s first publication. Hence, in 2024, an author with an h-index of 20 with a first publication in 2020 would have an m-index of 5 (20/4 years [2024–2020]).
The g-index is an additional quantitative measure that emerges from the distribution of the accumulated citations of an author (the g-value), structured such that when positioned in descending order, they correspond to the $g^2$ ranking. A g-index of 10 requires at least 100 citations ($g^2$) from the ten most-cited articles (g), although not all must have a minimum of 10 citations. 

### Data Analysis and Visualization

We applied bibliometric and network metrics. All the publications that satisfied the inclusion criteria were exported and downloaded. The bibliometrix package in R (version 4.3.1) was used to calculate the quantitative bibliometric indicators and perform visual analyses.\(^\text{23}\) Owing to the potential for differences in names, spellings, or variants (e.g., plurals and synonyms) in the thesaurus.txt files, we performed manual standardization to integrate authors, institutions, and keywords. We used Microsoft Office Excel 2016 to calculate the frequencies and percentages of the qualitative variables.

We investigated scientific production and annual scientific growth and assessed the average number of citations per year, publication frequency, and impact indicators adjusted for journals. The most prolific authors were identified, and Lotka’s law was employed to visualize the distribution of publications among the authors. Furthermore, we visualized the most-studied topics among centenarians worldwide, as well as collaborative networks among countries and affiliations.

### Ethical Statement

Ethical approval was not required for this study as it did not include human subjects, animals, or clinical records. However, this study was part of the Coosalud EPS centenarian project.

### RESULTS

Among the 3,089 documents initially identified, we selected 2,061 published between 1887 and 2023. Of these, 84.2% ($n = 1,736$) were published as articles with primary data, followed by 8.4% ($n = 173$) as reviews. International collaboration and annual growth rates were identified at 21.4% and 3.15%, respectively, with an average document age of 15 years (Table 1). The first postmortem description of a centenarian was published in 1887.\(^\text{22}\) Subsequently, not until 1947 were two documents published describing the clinical and surgical histories of centenarians in the United States and the United Kingdom.\(^\text{23,24}\) Since then, the number of publications related to research on centenarians has shown fluctuating growth, with a significant and sustained increase since the 1990s, peaking in 2020 ($n = 116$). In contrast, while citation behavior has fluctuated over time, peaking in 1993 (average of 73 citations per article), we observed a noticeable decline in the last 20 years (Fig. 1). Applying Lotka’s law, 72.3% of authors published only one document, followed by 12.7% with two publications.

Our analysis of the authors, affiliations, and countries with the highest scientific production related to research on centenarians revealed that the five most prolific authors were located in Italy, the United States, and Japan, with Claudio Franceschi (Italy) being the most prolific author with the highest impact to date (13,489 citations; h-index = 64, g-index = 75.5, m-index = 2.04). Regarding affiliations, four of the most prolific are located in Italy, and the remainder are located in the United States, with the Università di Bologna being the most prominent, with 207 documents related to research on centenarians. The United States had the highest number of articles published in the field (786 documents), followed by Italy (654 documents), although the latter had the highest impact (h-index = 90) (Table 2).

Regarding the behavior and impact of journals derived from publications on centenarians, The Journal of Gerontology Series A: Biological Sciences and Medical Sciences had the highest number of published articles (86) and the highest impact in all metrics (h-index = 36, g-index = 61, m-index = 1.38), including the number of citations (3,936) (Fig. 2A–2E). The number of articles published annually in the top five journals on centenarians varied, with significant peaks in different years, especially from Archives of Gerontology and Geriatrics, Mechanisms of Aging and Development, and Experimental Gerontology, which published at least 14 papers per

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**Table 1. General characteristics of global research on centenarians (n=2,061)**

<table>
<thead>
<tr>
<th>Document types</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Articles with primary data</td>
<td>1,736 (84.2)</td>
</tr>
<tr>
<td>Reviews</td>
<td>173 (8.4)</td>
</tr>
<tr>
<td>Editorials</td>
<td>22 (1.1)</td>
</tr>
<tr>
<td>Letters</td>
<td>130 (6.3)</td>
</tr>
<tr>
<td>Authors</td>
<td></td>
</tr>
<tr>
<td>Authorships</td>
<td>6,427</td>
</tr>
<tr>
<td>Authors of single-authored docs</td>
<td>199 (3.09)</td>
</tr>
<tr>
<td>Author collaboration</td>
<td></td>
</tr>
<tr>
<td>Single-authored documents</td>
<td>228 (2.7)</td>
</tr>
<tr>
<td>Co-authors per document</td>
<td>6.49</td>
</tr>
<tr>
<td>International co-authorships (%)</td>
<td>21.4</td>
</tr>
<tr>
<td>Document contents</td>
<td></td>
</tr>
<tr>
<td>Keywords</td>
<td>2,968</td>
</tr>
<tr>
<td>Journals</td>
<td>801</td>
</tr>
<tr>
<td>Annual growth rate (%)</td>
<td>3.15</td>
</tr>
<tr>
<td>Document average age (y)</td>
<td>15</td>
</tr>
<tr>
<td>Average citations per document</td>
<td>28.9</td>
</tr>
</tbody>
</table>

Values are presented as numbers (%).
Based on the frequency of keyword use, mortality, genetics, dementia, Alzheimer's disease, and immunosenescence were the most studied topics among centenarians (Fig. 3A). The main co-occurrence of these topics was related to (1) mortality, hip fracture, and risk factors; (2) immunosenescence linked to inflammation, inflammaging, and cytokines; (3) cognition related to dementia, neuropathology, personality, depression, and Alzheimer’s disease; and (4) genetics related to Okinawa (a blue zone in Japan) (Fig. 3B). Thus, these constitute foundational topics, with emerging research related to mitochondrial DNA and the comparison of results between nonagenarians and centenarians (Fig. 3C). In the last 20 years, interest has increased in genetics, mortality, and dementia in centenarians (Fig. 3D). Compared to the 2000s, increasing studies have focused on genetic polymorphisms, inflammation, immunosenescence, and dementia. The last decade has seen an emerging interest in publishing on gut microbiota, quality of life, environment, nutritional status, resilience, and frailty (Fig. 3E, 3F).

Regarding research collaboration networks, we observed significant endogamous collaborations among Italian, American, and American-Japanese affiliations (Fig. 4A). The global research collaboration network is essentially led by Italy, the United States, and China, which collaborate most frequently with Japan and European countries (Fig. 4B). However, weak or no international collabo-
Fig. 2. Impact of journals and publication frequency on centenarians in the most popular journals. (A) Frequency of published articles. (B) Total citations received. (C) h-index derived from the articles. (D) g-index derived from the articles. (E) m-index derived from the articles. (F) Yearly frequency of articles published in most popular journals.
Fig. 2. Continued
Fig. 3. Topics evolution and research patterns in global research on centenarians. (A) Wordcloud of most frequent keywords. (B) Co-occurrence network of keywords. (C) Thematic map with relevance and development degree of topics. (D) Frequency of occurrence of the most studied topics over time. (E) Trend topics from 2003 to 2012. (F) Trend topics from 2013 to 2023.
Fig. 3. Continued
Affiliations and countries collaboration network. (A) Affiliation collaboration network (with minimum number of five edges). (B) Countries collaboration network (with minimum number of five edges). (C) Countries’ collaboration world map (with minimum number of two edges).

Fig. 4. Affiliations and countries collaboration network. (A) Affiliation collaboration network (with minimum number of five edges). (B) Countries collaboration network (with minimum number of five edges). (C) Countries’ collaboration world map (with minimum number of two edges).

Affiliations were identified between countries in Latin America, Africa, and the rest of the world (Fig. 4C).

Finally, the articles that have achieved the highest impact to date, based on the number of citations, were (1) “Through ageing and beyond: gut microbiota and inflammatory status in seniors and centenarians” (1,068 citations, published in PLOS ONE in 2010; https://doi.org/10.1371/journal.pone.0010667); (2) “Age-related changes in gut microbiota composition from newborn to centenarian: a cross-sectional study” (799 citations, published in BMC Microbiology in 2016; https://doi.org/10.1186/s12866-016-0708-5); and (3) “Distinct DNA methylomes of newborns and centenarians” (583 citations, published in Proceedings of the National Academy of Sciences in 2012; https://doi.org/10.1073/pnas.1120658109).

DISCUSSION

The results of this study revealed the characteristics, trends, and collaborations in global research on centenarians. Previous bibliometric studies have addressed subtopics including physical exercise, cognition during aging, and the scientific growth of re-
search on healthy aging, but have not focused on centenarians.

The description of centenarians as a novel and infrequent finding in the general population occurred > 120 years ago. However, growth in research from 1887 to the 1950s was modest. Since then, compared with other medical disciplines, the annual growth rate in this area of research has been low, primarily focusing on countries where blue zones have been described, possibly facilitating the design and execution of studies owing to access to the target population. Nevertheless, the research gap between regions is evident, as indicated by the distribution of publications according to Lotka’s law, where 85% of the identified authors have published only up to two documents, suggesting occasional research or publication rather than massive centenarian research groups worldwide.

Italy, the United States, China, and Japan have led scientific research on centenarians, which may be linked to decades-old prospective centenarian cohorts such as the Italian Multicenter Study on Centenarians, Italian Longitudinal Study on Ageing, or the AKEA study in Italy, the New England Centenarian Study, Georgia Centenarian Study in the United States, China Hainan Centenarian Cohort Study in China, Okinawa Centenarian Study, and Tokyo Centenarian Study in Japan. These studies have allowed an extensive examination of this population in these countries. Many studies derived from these prospective cohorts have been published, contributing significantly to our understanding of variables related to healthy aging, characteristics that confer properties to centenarians as super-controls, and the heritability of longevity that protects against certain diseases in centenarian offspring.

This evidence suggests that the creation of large prospective cohorts characterizing variables specific to each region can help elucidate a few unanswered questions about centenarians, such as the absence of certain conditions despite decades-long exposures to risk factors or stressors, or proper proteodynamics, resilience, and immunological remodeling, depending on the epidemiology and common microorganisms among different global regions.

The frequency of keywords and research patterns demonstrates a significant mix of designs in centenarian studies. For example, the frequency of the keyword “mortality” related to hip fractures and risk factors suggests clinical research focused on the surgical field. However, hospital- or home-based research on cognition, dementia, and Alzheimer’s disease has been reported. Additionally, the use of terms such as genetics and immunosenescence, which are related to inflammation, cytokines, and inflammation, suggests the need for basic or translational research.

As population genetics can influence up to 30% of the longevity mark, studies in regions where racial, ethnic, and cultural characteristics differ significantly from those of countries with traditional cohorts (the United States, Europe, and Asia) are crucial. This highlights the absence of extensive research in Latin America and Africa, which show low frequencies of publications on centenarians and few collaborative networks. Multicarial research is critical for determining differences in race, ethnicity, and ancestry in genetics and genomics, which are closely related to proteomic and metabolomic markers (whose signatures are unique to centenarians and reflect the favorable organic adaptive capacity during aging to reduce inflammation and promote a healthy lifespan). Therefore, these data are the basis for proposing an innovative roadmap for these two continents to provide evidence to improve the care of this population and explore new biomarkers and protective factors for extreme longevity and healthy aging.

Despite the number of studies on longevity, healthy aging, comorbidities, sociodemographic characteristics, and a few biomarkers, more centenarian-specific studies are needed. Although existing research has shed light on various aspects of aging, evidence is required regarding how the environment affects centenarians, the type of care these individuals require, the public protection policies that affect them, and the health resources available to this population. Furthermore, understanding the social behaviors and cultural roles of centenarians and how these factors influence their health and well-being is essential. In this regard, normality parameters for specific biomarkers in this population must be established, and cognitive tests and functional constructs adapted to their unique needs and capabilities must be developed. The exploration of how centenarians relate to their environment, lifestyle, and interactions with the environment is essential, as these aspects can significantly impact their quality of life and ability to remain healthy and active at an older age. In short, focusing on specific studies of centenarians will enable us to better understand the factors contributing to their longevity and well-being and design more effective interventions to promote healthy aging in this unique population.

Finally, a hot topic in centenarian research is the absence of clinical practice guidelines and randomized controlled trials. To date, no registered clinical trials registered on ClinicalTrials.gov (http://tinyurl.com/5n875sx6) are related to pharmacological or non-pharmacological interventions in centenarians, and fewer than five registered studies are focused on nonagenarians. Considering the forecasted increasing life expectancy, advancing potential interventions for nonagenarians and centenarians who can maintain a good health phenotype and continue to play a useful role at the social and family levels is imperative. Therefore, despite progress in global research on centenarians, much work remains.

The major limitation of this study was the analysis of only the Scopus database. However, Scopus covers a wider journal range.
and provides help in keyword search and citation analysis. Additionally, the metadata recorded in the database is inherently biased. However, we standardized the analysis and performed manual reviews to reduce the margin of error.

In conclusion, global research on centenarians has grown over the last 20 years, primarily led by Italy, the United States, and China. However, research in Latin American and African countries is scarce. The most studied topics are mortality, cognition, immunosenescence, and genetics. Approximately 85% of the authors published up to two documents, indicating the absence of a continuous line of research on centenarians. Moreover, scientific collaboration is necessary to share data, create biorepositories, and robustly answer questions to identify the factors and determinants of successful and healthy aging.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST
The researchers claim no conflicts of interest.

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None.

AUTHOR CONTRIBUTIONS
Conceptualization, IDLM; Data curation, IDLM, MCDG; Investigation and Methodology, IDLM, SCT, JMA; Writing–original draft, IDLM, MCDG, SCT, JMA; Writing–review & editing, IDLM, MCDG, SCT, JMA.

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Factors Associated with the Deterioration of Intrinsic Capacity among Older Adults in Mexico and Colombia

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\textsuperscript{2}Facultad de Enfermería de Tampico, Universidad Autónoma de Tamaulipas, Tamaulipas, Mexico
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Background: Intrinsic capacity (IC) is defined as “all the physical and mental attributes possessed by the older person.” This concept has gained momentum in recent years because it provides insights into the changes in the functional capacity of individuals during their life. This study examined common factors associated with IC decline among older adults in Mexico and Colombia.

Methods: This cross-sectional, correlational study included 348 community-dwelling older adults. Sociodemographic, clinical, and family conditions were assessed as possible associated factors, and IC was analyzed across five domains: cognitive, locomotor, psychological, vitality (malnutrition through deficiency and excess), and sensory (visual and auditory). Parametric and non-parametric statistical analyses were performed.

Results: The common factors associated with impairment according to domain were family dysfunctionality (cognitive domain); myocardial infarction, family dysfunctionality, age >80 years, home occupation, and not having a partner (locomotor domain); dysfunctional family and risk of falls (psychological domain); age >80 years and not having a partner (malnutrition by deficiency domain); age 60–79 years, walking <7,500 steps/day, and peripheral vascular disease (malnutrition by excess domain); risk of falling and being female (visual sensory domain); risk of falling (auditory sensory domain); and dysfunctional family and risk of falling (total intrinsic capacity).

Conclusion: Both populations had common sociodemographic, clinical, and familial factors that directly affected total IC stocks and their domains.

Key Words: Intrinsic capacity, Risk factors, Geriatric assessment, Older adult

INTRODUCTION

The World Health Organization operationally defines intrinsic capacity (IC) as “all the physical and mental attributes possessed by the older person.”\textsuperscript{3} This construct is based on a longitudinal pattern consistent with the continuous process of individual aging, which must be assessed through multiple observations over time rather than a single assessment.\textsuperscript{3} This concept has gained momentum in recent years because it provides an understanding of changes in the functional capacity of individuals during their life. IC is also based on a positive health perspective and although its clinical application always seeks to measure deficits, its main objective is to guide preventive interventions tailored to the individual needs of older adults, overcoming limiting paradigms such as chronological age or the presence of diseases.\textsuperscript{3}

Reserves and deficits in IC occur in different ways among older adults, making them difficult to study and address. Recently, studies have analyzed the five IC domains (cognitive, locomotor, psychological, vitality, and sensory) and their relationship with sociodemographic\textsuperscript{4} and clinical conditions\textsuperscript{5-11} in older adults. IC has
also been identified as a predictor of all-cause mortality and adverse events as well as incidents in older people. Likewise, three patterns of IC in community-dwelling older people have been identified: (1) those who are relatively healthy, (2) those with acute decline in the sensory domain, and (3) those with acute decline in the locomotion, psychological, cognitive, and vitality domains, a finding that is considered valuable for better stratification of groups of older people.

In Latin American countries such as Mexico, all IC domains tend to decline with age, especially among women. Self-rated health, chronic diseases, number of doctor visits in the last year, and ≥2 affected activities of daily living are consistently associated with more affected IC domains. In contrast, in Colombia, individuals with optimal grip strength have better IC compared with their weaker counterparts; likewise, altered IC domains act as mediators between a fear of falling and the built environment, with increasing fear of falling reported among people living in neighborhoods with structural limitations and social problems.

While some clinical factors associated with IC decline have been identified separately in Mexico and Colombia, sociodemographic and familial determinants that may influence the decline in IC reserves have not been explored. Moreover, whether similar factors of decline exist in both countries among community-dwelling older adults who are independent in their daily living basic and instrumental activities but live in different conditions and culture remains undetermined.

Therefore, this study assessed IC considering the personal, clinical, and family characteristics of people > 60 years of age living in Colombia and Mexico.

MATERIALS AND METHODS

Participants
Older community members were enrolled from Ciudad Madero, Tamaulipas (Mexico) and Manizales (Colombia). Participants from Mexico were recruited through the community clubs for older adult members of the “Adults in Action Programme.” Participants from Colombia were recruited from the Primary Care Programs operating in the city’s health centers. All participants were characterized by age > 60 years and regular attendance of primary care programs. We determined a random sample by applying the formula for the estimation of averages with a known sampling frame, assuming a type I error of 0.05, precision of 0.03, and standard deviation of 0.3. Therefore, minimums of 280 and 297 individuals from Mexico and Colombia, respectively, were required. The final sample included a total of 348 older people (226 from Mexico and 122 from Colombia) who participated in this study.

Measurements
Sociodemographic, clinical, and family characteristics
We investigated sociodemographic characteristics including age, sex, marital status, and level of schooling. Clinical variables were identified by asking about the presence or absence of diseases with a predominance of cardiovascular, brain, and vascular diseases, as well as alcohol and tobacco consumption. Additionally, we assessed fall risk using the Downie scale. The number of steps walked per day was determined by providing pedometer and recording for 7 days, using the cut-off points proposed by Tudor-Locke as reference. We assessed family functionality and support using the Family Functionality Effectiveness Scale A-EFF-22 by Chavez et al.

Intrinsic capacity
We analyzed the five domains separately. Each domain was interpreted by considering the cutoff points established in the validated instruments and subsequently recoded as a dichotomous response to identify preservation or impairment in each domain as follows: the cognitive domain was assessed using the Pfeiffer questionnaire, in which some level of intellectual impairment was considered cognitive impairment and normal scores as preserved cognitive domain. The locomotion domain was assessed using the Tinetti Scale, with minimal and high risks defined as balance or gait impairment and no risk as preserved locomotor domain. The psychological domain was assessed using the Yesavage scale, in which levels of mild and established depression were considered depressive symptoms, and the absence of symptoms was considered preserved psychological domain. The vitality domain was assessed using the Mini Nutritional Assessment (MNA) and anthropometric measurements (weight/height) were used to determine the body mass index (BMI; as the MNA does not identify overweight or obesity). After each result was obtained separately, two new variables were created to determine malnutrition deficiency and excess. The first was obtained by defining MNA scores < 24 and BMI scores < 27 kg/m² as deficit malnutrition and the remaining scores as not having deficit malnutrition. The second variable defined MNA results > 24 and BMI scores ≥ 27 kg/m² as excess malnutrition, with the remaining scores defined as no excess malnutrition. The sensory domain was assessed by self-reporting the presence or absence of visual and auditory impairments. Finally, the total IC was calculated by summing all the domains under a theoretical scale of 0–7 points (considering that two aspects were assessed in the sensory domain), where each impaired domain contributed one point (0 and 1 points for the preserved and impaired domains, respectively). Thus, the higher the score, the greater the IC impairment. The variable was then dichotomized.

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using the following cutoff points: 0–2, "preserved IC (for those with up to two impaired domains)" and > 3 points, "impaired IC (for those with three or more impaired domains)."

**Ethical aspects**

This project was developed under the ethical and legal considerations for research in Mexico and Colombia. This proposal was approved by the ethics committees of the educational institutions of the authors (Colombia IRB No. 122 / 25 /06/2018, Mexico IRB No. 301.511-6/17-7700). We obtained informed consent from the participants and complied with bioethical principles (autonomy, beneficence, non-maleficence, and justice). This study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.23

**Data analysis**

Data were processed using IBM SPSS Statistics for Windows, version 24.0 (IBM, Armonk, NY, USA). Sociodemographic, clinical, and family characteristics were analyzed as frequencies, percentages, and measures of central tendency (for scale variables), and cross-tables were constructed by comparing the proportions for each country and applying the chi-square test. We proceeded in the same way for the characterization of the IC domains to identify the proportions of deterioration or conservation of each domain according to country. Finally, to identify the associated factors as possible predictors, we explored binary logistic regression models using the backward method and only the independent variables that were statistically significant in the bivariate analysis. We identified predictors jointly for both populations.

**RESULTS**

For the whole sample, the age range was 60–92 years (average 70 ± 6 years, median 69 years). Age discrimination by category showed statistically significant differences, with a higher proportion of older people in the 60–79-year age group in both countries. We also observed significant differences in the distributions by sex and level of education, with higher proportions of women and individuals with a low level of education (no education or primary education) in both countries. Marital status and occupation did not differ significantly between countries (Table 1). Regarding the clinical conditions of older people in each country, Mexico had significantly higher prevalence rates of peripheral vascular disease (43.4%) and alcohol consumption (25.2%), whereas older adults in Colombia demonstrated significantly higher prevalence rates of hypertension (75.4%) and dyslipidemia (46.7%) (Table 1). The IC domains showed no significant sex differences, except in

| Table 1. Characteristics of participants discriminated by country |
|----------------------|------------------|----------------------|------------------|
| Variable | Mexico (n = 226) | Colombia (n = 122) | p-value |
| Age group (y) | | | |
| 60–79 | 214 (94.7) | 105 (86.1) | 0.005* |
| ≥ 80 | 12 (5.3) | 17 (13.9) | |
| Sex | | | |
| Female | 180 (79.6) | 80 (65.6) | 0.004* |
| Male | 46 (20.4) | 42 (34.4) | 0.144 |
| Marital status | | | |
| With partner | 113 (50.0) | 51 (41.8) | 0.144 |
| Without partner | 113 (50.0) | 71 (58.2) | |
| Schooling | | | < 0.0001** |
| None/Elementary school | 144 (63.7) | 103 (84.4) | |
| Junior high/Technician/University | 82 (36.3) | 19 (15.6) | |
| Lives | | | 0.001* |
| Alone | 206 (91.2) | 122 (100) | |
| Accompanied | 20 (8.8) | 0 (0) | |
| Occupation | | | 0.130 |
| House care/Retired | 163 (72.1) | 97 (79.5) | |
| Works or study | 63 (27.9) | 25 (20.5) | |
| Alcohol consumption | | | < 0.0001** |
| Yes | 57 (25.2) | 3 (2.5) | |
| No | 169 (74.8) | 119 (97.5) | |
| Arterial hypertension | | | < 0.0001** |
| Yes | 117 (51.8) | 92 (75.4) | |
| No | 109 (48.2) | 30 (24.6) | |
| Dyslipidemia | | | < 0.0001** |
| Yes | 45 (19.9) | 57 (46.7) | |
| No | 181 (80.1) | 65 (53.3) | |
| Peripheral vascular disease | | | < 0.0001** |
| Yes | 98 (43.4) | 28 (23.0) | |
| No | 128 (56.6) | 94 (77.0) | |
| Tobacco consumption | | | 0.053 |
| Yes | 12 (5.3) | 14 (11.5) | |
| No | 214 (94.7) | 108 (88.5) | |
| Ischemia and/or myocardial infarction | | | 0.104 |
| Yes | 7 (3.1) | 9 (7.4) | |
| No | 219 (96.9) | 113 (92.6) | |
| Epilepsy | | | 0.351 |
| Yes | 0 (0) | 1 (0.8) | |
| No | 226 (100) | 121 (99.2) | |
| Cerebrovascular disease | | | 0.246 |
| Yes | 3 (1.3) | 4 (3.3) | |
| No | 223 (98.7) | 118 (96.7) | |
| Psychiatric disorder | | | 0.348 |
| Yes | 2 (0.9) | 3 (2.5) | |
| No | 224 (99.1) | 119 (97.5) | |
| Parkinson disease | | | 0.950 |
| Yes | 2 (0.9) | 1 (0.8) | |
| No | 224 (99.1) | 121 (99.2) | |
| Heart failure | | | 1.000 |
| Yes | 7 (3.1) | 4 (3.3) | |
| No | 219 (96.9) | 118 (96.7) | |

(Continued to the next page)
Table 1. Continued

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mexico (n = 226)</th>
<th>Colombia (n = 122)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of falls</td>
<td></td>
<td></td>
<td>&lt; 0.0001**</td>
</tr>
<tr>
<td>Risk of falls</td>
<td>173 (76.5)</td>
<td>70 (57.4)</td>
<td></td>
</tr>
<tr>
<td>No risk of falls</td>
<td>53 (23.5)</td>
<td>52 (42.6)</td>
<td></td>
</tr>
<tr>
<td>Family functionality</td>
<td></td>
<td></td>
<td>0.032*</td>
</tr>
<tr>
<td>Dysfunctional family</td>
<td>59 (26.1)</td>
<td>45 (37.2)</td>
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</tr>
<tr>
<td>Functional family</td>
<td>167 (73.9)</td>
<td>76 (62.8)</td>
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<td>Family support</td>
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<td></td>
<td>0.546</td>
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<tr>
<td>Low family support</td>
<td>23 (10.2)</td>
<td>15 (12.3)</td>
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<td>Moderate or high family support</td>
<td>203 (89.8)</td>
<td>107 (87.7)</td>
<td></td>
</tr>
<tr>
<td>Average steps per day</td>
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<td></td>
<td>0.001*</td>
</tr>
<tr>
<td>&lt; 7,499</td>
<td>177 (78.3)</td>
<td>112 (91.8)</td>
<td></td>
</tr>
<tr>
<td>&gt; 7,500</td>
<td>49 (21.7)</td>
<td>10 (8.2)</td>
<td></td>
</tr>
</tbody>
</table>

Values are presented as number (%). *p≤0.05, **p≤0.01 using the chi-square test.

Table 2. Comparison of total intrinsic capacity (IC) and altered and preserved domains in study participants

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mexico (n = 226)</th>
<th>Colombia (n = 122)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive domain (Questionnaire Pfeiffer)</td>
<td></td>
<td></td>
<td>&lt; 0.0001**</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>15 (6.6)</td>
<td>34 (27.9)</td>
<td></td>
</tr>
<tr>
<td>Preserved</td>
<td>211 (93.4)</td>
<td>88 (72.1)</td>
<td></td>
</tr>
<tr>
<td>Locomotor domain (Tinetti Scale)</td>
<td></td>
<td></td>
<td>&lt; 0.0001**</td>
</tr>
<tr>
<td>Balance/gait disturbance</td>
<td>59 (26.1)</td>
<td>57 (46.7)</td>
<td></td>
</tr>
<tr>
<td>Preserved</td>
<td>167 (73.9)</td>
<td>65 (53.3)</td>
<td></td>
</tr>
<tr>
<td>Psychological domain (Yesavage Scale)</td>
<td></td>
<td></td>
<td>0.059</td>
</tr>
<tr>
<td>Depressive symptoms</td>
<td>32 (14.2)</td>
<td>27 (22.1)</td>
<td></td>
</tr>
<tr>
<td>Preserved</td>
<td>194 (85.8)</td>
<td>95 (77.9)</td>
<td></td>
</tr>
<tr>
<td>Vitality domain (MNA+BMI)</td>
<td></td>
<td></td>
<td>0.004*</td>
</tr>
<tr>
<td>Malnutrition due to deficit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>27 (11.9)</td>
<td>29 (23.8)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>199 (88.1)</td>
<td>74 (76.2)</td>
<td></td>
</tr>
<tr>
<td>Malnutrition by excess</td>
<td></td>
<td></td>
<td>&lt; 0.0001**</td>
</tr>
<tr>
<td>Yes</td>
<td>134 (59.3)</td>
<td>39 (32.0)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>92 (40.7)</td>
<td>83 (68.0)</td>
<td></td>
</tr>
<tr>
<td>Sensory domain</td>
<td></td>
<td></td>
<td>0.026*</td>
</tr>
<tr>
<td>Visual disturbances (Self-report)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>130 (57.5)</td>
<td>55 (45.1)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>96 (42.5)</td>
<td>67 (54.9)</td>
<td></td>
</tr>
<tr>
<td>Hearing impairment (Self-report)</td>
<td></td>
<td></td>
<td>0.010*</td>
</tr>
<tr>
<td>Yes</td>
<td>34 (15.0)</td>
<td>7 (5.7)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>192 (85.0)</td>
<td>115 (94.3)</td>
<td></td>
</tr>
<tr>
<td>Total IC</td>
<td></td>
<td></td>
<td>0.359</td>
</tr>
<tr>
<td>Deterioration</td>
<td>67 (29.6)</td>
<td>42 (34.4)</td>
<td></td>
</tr>
<tr>
<td>Preserved</td>
<td>159 (70.4)</td>
<td>80 (65.6)</td>
<td></td>
</tr>
</tbody>
</table>

Values are presented as number (%). MNA, Mini Nutritional Assessment; BMI, body mass index. *p≤0.05, **p≤0.01 using the chi-square test.

The visual sensory domain, where self-reported visual impairment prevailed in 56.9% of women (p = 0.016). Total IC was impaired in 32.3% and 28.4% of females and males, with no statistically significant differences. We observed statistically significant differences for all domains according to country, except for the psychological domain. In older adults in Mexico, the three domains that reported the greatest deterioration were vitality (excess malnutrition, 59.3%), followed by the sensory (self-reported visual impairment, 57.5%) and locomotor (balance/gait impairment, 26%) domains. In Colombia, the main impaired domains were the locomotor (balance/gait impairment, 46.7%), sensory (self-reported visual impairment, 45.1%), and vitality (malnutrition due to excess, 32.0%) domains. We observed no significant differences in total IC impairment between the countries (Table 2).

Binary regression (for all participants) revealed factors associated with impairment in all domains and total IC. The locomotor domain had the highest number of associated factors, followed by excess malnutrition. Fall risk was the most frequent clinical condition associated with impairment in four of the eight models. Similarly, within the family-related variables, family dysfunctionality was associated with impairment in four predictor models, followed by sociodemographic characteristics such as age, sex, and marital status (Table 3).

DISCUSSION

This study identified sociodemographic, family, and clinical factors that synergistically increased the deterioration of individual domains and total IC. A dysfunctional family environment was the main factor in the cognitive domain, which is consistent with recent findings in another study showing a lower prevalence of family functioning among groups of families with older people with mild cognitive impairment compared with their counterparts without cognitive impairment (59.3% vs. 89.7%). Family functionality implies coherence between the relationships of its members; individuation mechanisms that improve communication, knowledge, and growth of its members; and adaptation to changes in situations to guarantee security, independence, and greater autonomy. Thus, older individuals present a decline in cognition when they lack sufficient resources within their family group to conserve and enhance the individual’s cognitive reserve.

The locomotor domain showed the highest number of factors in this study. Among these factors, myocardial infarction demonstrated the greatest effect. Myocardial infarction has been reported as a cause of physical deterioration (especially in females) and presents as slower walking speed and frailty. Herein, the prevalence of myocardial infarction in the two countries was only 10.5%; howev-
er, 66.7% of these patients were females. We identified family functionality as the second factor, in which 16.4% of people living with dysfunctional family processes showed impairments in this domain. The third factor associated with locomotor impairment was age, in which 5.5% of people aged > 80 years had impaired balance and gait. Another factor associated with the deterioration of this domain was related to dedicating oneself solely to household chores (vs. working or studying). In this case, the decrease in locomotion is explained by restricted mobility in the living space, with the consequent limitation of instrumental and social activities in the neighborhood and city in which the individual lives.26 However, herein, being single was associated with increased locomotor deterioration. The influence of a partner on the performance of physical activity and, consequently, on the conservation of locomotor reserves, has been demonstrated27; likewise, physical activity interventions for older people in which a partner participates facilitate a substantial increase in this activity over time, more so than when it is performed alone.28 Hence, living as a couple and engaging in all types of activities (not just physical activity) together can promote a lifestyle that is active enough to preserve locomotor reserve.

The main associated factor in the psychological domain was living in a dysfunctional family. Other studies have demonstrated a relationship between family functionality, the perception of health, and the presence of depressive symptoms in nonagenarians and centenarians.2931 Our findings demonstrated a dysfunctional family environment was associated with a 6.7-fold increased likelihood of deterioration in the psychological domain in older adults, making this a significant finding. Likewise, the risk of falls was associated with the deterioration of the psychological domain, which is consistent with other studies reporting two-way associations, in which the risk of falls increases depressive symptoms over time, which subsequently, increases the incidence of multiple falls.32 In the vitality domain, we observed a greater number of factors associated with excess malnutrition, including age (60–79 years), which is consistent with the findings of another study in South America reporting a higher risk of obesity in women in the same age group (odds ratio [OR] = 1.88; 95% confidence interval [CI] 1.16–3.04).33 We observed a higher risk in the present study, (OR = 4.1), which can be explained by the fact that the overweight and obese groups were analyzed together. Another factor related to deterioration in this domain was walking < 7,499 steps/day,

Table 3. Factors associated with intrinsic capacity (IC) deterioration for both countries

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimation</th>
<th>ES</th>
<th>p-value</th>
<th>OR (95% IC)</th>
<th>R² Nagelkerke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1: cognition domain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysfunctional family</td>
<td>1.272</td>
<td>0.322</td>
<td>&lt; 0.0001</td>
<td>3.5 (1.900–6.707)</td>
<td>0.099</td>
</tr>
<tr>
<td>Model 2: locomotor domain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1.738</td>
<td>0.803</td>
<td>0.030</td>
<td>5.6 (1.179–24.429)</td>
<td>0.254</td>
</tr>
<tr>
<td>Dysfunctional family</td>
<td>1.291</td>
<td>0.265</td>
<td>&lt; 0.0001</td>
<td>3.6 (2.161–6.112)</td>
<td></td>
</tr>
<tr>
<td>Age &gt; 80 y</td>
<td>1.202</td>
<td>0.443</td>
<td>0.007</td>
<td>3.3 (1.397–7.923)</td>
<td></td>
</tr>
<tr>
<td>Occupation: home</td>
<td>1.035</td>
<td>0.335</td>
<td>0.002</td>
<td>2.8 (1.460–5.427)</td>
<td></td>
</tr>
<tr>
<td>No partner</td>
<td>0.723</td>
<td>0.261</td>
<td>0.006</td>
<td>2.0 (1.236–3.439)</td>
<td></td>
</tr>
<tr>
<td>Model 3: psychological domain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysfunctional family</td>
<td>1.915</td>
<td>0.330</td>
<td>&lt; 0.0001</td>
<td>6.7 (3.556–12.950)</td>
<td>0.284</td>
</tr>
<tr>
<td>Risk for falls</td>
<td>1.228</td>
<td>0.475</td>
<td>0.010</td>
<td>3.4 (1.346–8.660)</td>
<td></td>
</tr>
<tr>
<td>Model 4: vitality domain (deficiency malnutrition)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &gt; 80 y</td>
<td>1.477</td>
<td>0.446</td>
<td>0.001</td>
<td>4.3 (1.829–10.489)</td>
<td>0.144</td>
</tr>
<tr>
<td>Not having a partner</td>
<td>0.786</td>
<td>0.326</td>
<td>0.016</td>
<td>2.1 (1.159–4.157)</td>
<td></td>
</tr>
<tr>
<td>Model 5: vitality domain (malnutrition by excess)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age 60–79 y</td>
<td>1.420</td>
<td>0.457</td>
<td>0.002</td>
<td>4.1 (1.690–10.124)</td>
<td>0.073</td>
</tr>
<tr>
<td>Walking less than 7,499 steps/day</td>
<td>0.638</td>
<td>0.297</td>
<td>0.032</td>
<td>1.8 (1.057–3.388)</td>
<td></td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>0.565</td>
<td>0.231</td>
<td>0.015</td>
<td>1.7 (1.118–2.769)</td>
<td></td>
</tr>
<tr>
<td>Model 6: sensory domain (visual)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk for falls</td>
<td>1.474</td>
<td>0.261</td>
<td>&lt; 0.0001</td>
<td>4.3 (2.618–7.280)</td>
<td>0.174</td>
</tr>
<tr>
<td>Being a woman</td>
<td>0.585</td>
<td>0.266</td>
<td>0.028</td>
<td>1.7 (1.066–3.025)</td>
<td></td>
</tr>
<tr>
<td>Model 7: sensory domain (hearing)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk for falls</td>
<td>2.287</td>
<td>0.735</td>
<td>0.002</td>
<td>9.8 (2.331–41.581)</td>
<td>0.100</td>
</tr>
<tr>
<td>Model 8: total IC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysfunctional family</td>
<td>1.750</td>
<td>0.264</td>
<td>&lt; 0.0001</td>
<td>5.7 (3.432–9.654)</td>
<td>0.249</td>
</tr>
<tr>
<td>Risk for falls</td>
<td>1.126</td>
<td>0.327</td>
<td>&lt; 0.0001</td>
<td>3.0 (1.626–5.850)</td>
<td></td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval.
which, according to Tudor-Locke et al., corresponds to a group of people with basal or low physical activity, in whom the number of steps is not sufficient for weight control. Finally, peripheral vascular disease was a predictor of overweight or obesity, which may be explained by the relationship between peripheral vascular disease and cardiometabolic syndrome.

Two factors were associated with malnutrition deficiency: first, age > 80 years, which is a condition arising from the aging process, such that as time progresses, anorexia, underweight, sarcopenia, and frailty develop. Second, single adults were at a higher risk of deficit malnutrition, which is consistent with the findings of another South American study. This is explained by the lifestyle and different eating habits of older persons living alone, which may involve cultural practices, personal tastes, or simply not having sufficient resources or independence to care for themselves during the feeding process.

Factors such as being female and at a higher risk of falls were significantly related to impairment in the sensory domain. The causes of visual impairment (cataracts and corrected refractive errors) are associated with demographic transition; likewise, women aged ≥ 50 years show a higher prevalence of visual impairment. In the present study, 80% of older adults who reported having some type of visual impairment were females. Regarding the risk of falls, the relationship between visual and hearing impairments and postural control is well known. However, in this study, these two conditions showed the opposite relationship, in which the risk of falls could be a factor that does not allow sufficient physiological integration between movement, vision, and hearing to perform daily activities.

Finally, the results of the total IC revealed three factors, the most significant being a dysfunctional family environment. Family living conditions can be a protective factor that contributes to member support and well-being; however, problematic conditions are also associated with stress and health impairment. The results of the present study revealed that family dysfunctionality can lead to a 5.7-fold higher probability of IC deterioration in older individuals. These findings provide significant data to inform health interventions, particularly nursing interventions that aim to preserve the intrinsic reserves necessary for adaptation to the environment and performance of the maximum number of possible activities in daily life. Moreover, not having a partner decreased the total IC; thus, this condition can lead to unfavorable or disadvantageous situations over time, with the consequent loss of intrinsic and health reserves. Previous studies have reported higher relative mortality rates among divorced, widowed, and single individuals compared with married individuals. Additionally, the risk of falls increased the probability of the deterioration of total IC by 3.0-fold; however, this was the only geriatric syndrome that was considered a possible risk factor. Therefore, additional studies comparing the most prevalent geriatric conditions in their entirety are needed to identify those conditions with the greatest impact on IC.

In summary, our results provide new evidence regarding the deterioration of intrinsic reserves via socio-demographic and family variables that synergize with different health changes, enhancing dependence in various domains. Therefore, health promotion and maintenance should be performed on different fronts and not only from the therapeutic aspects. Moreover, interventions should address aspects related to the family environment of older individuals, considering that the loss of reserves is an individual and heterogeneous phenomenon that is not only attributed to comorbidities and clinical conditions.

The limitations of this study are that, as it is a cross-sectional study with a small sample population per country, the validity of the predictors observed may be reduced. The factors found for each domain of IC show a synergistic phenomenon in the area in which older people live.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, CLVR, NHGQ, SMCV; Data curation, CLVR, NHGQ, SMCV; Investigation & methodology, CLVR, NHGQ, SMCV; Project administration, LGCO, HCH, LFR; Writing–original draft, CLVR, NHGQ, SMCV; Writing–review & editing, LGCO, HCH, LFR.

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Geriatric Nutritional Risk Index as a Possible Predictor of Decline in Kidney Function in Older People

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This study’s preliminary results and abstract were presented at the 42nd Annual Meeting of the Korean Society of Nephrology.

Background: The Geriatric Nutritional Risk Index (GNRI) is associated with morbidity and mortality in older individuals. Our study explored the relationship between GNRI, decline in kidney function, and all-cause mortality in older individuals. Methods: This retrospective cohort study analyzed data from participants aged ≥60 years who underwent a general health checkup between 2002 and 2018. The primary exposure was the GNRI, divided into quartiles. The primary and secondary outcomes were a decline in kidney function assessed using the 5-year estimated glomerular filtration rate (eGFR) and all-cause mortality, respectively. Results: The analysis included a total of 1,599 participants (median age, 63 years; interquartile range [IQR], 61–67; 54% males). The mean±standard deviation of GNRI was 114±7. Compared with the highest GNRI quartile, the lower GNRI quartiles were associated with steeper 5-year slopes in eGFR, with a fully adjusted beta coefficient and 95% confidence intervals (CIs) of −0.50 (−0.86, −0.14), −0.29 (−0.63, 0.05), and −0.19 (−0.53, 0.14) for the first, second, and third GNRI quartiles, respectively. The median follow-up duration was 7.4 years (IQR, 4.6–12.4). During this period, we identified 108 deaths (7.8 per 1,000 person-years). The first GNRI quartile was associated with all-cause mortality compared to the highest GNRI quartile (hazard ratio of 2.20; 95% CI 1.23, 3.95). Conclusion: Nutritional status, as evaluated using the GNRI, was associated with 5-year changes in kidney function and all-cause mortality in older individuals.

Key Words: Older individual, Kidney, Mortality, Nutrition

INTRODUCTION

With the aging of the population, the number of older individuals is gradually increasing. The World Health Organization reported that individuals aged ≥60 years account for 12% of the global population; by 2050, this number is expected to rise to nearly 22%. Older adults, compared to younger individuals, have age-specific illnesses, various types of chronic diseases, and the after-effects of these diseases, which can accumulate over time, leading to polypharmacy. Malnutrition is common among older individuals. Along with the aforementioned health conditions, social and environmental issues, inadequate food intake, and impaired physical function may contribute to the development of malnutrition in this population. Malnutrition is associated with poor health outcomes, such as cardiovascular disease and mortality in older adults, and is currently considered a modifiable prognostic factor for these outcomes.

In older people, kidney function tends to decline with age, due to complications from acute and chronic diseases, and depending on the medications used. This decline in kidney function may lead to clinical and public health burdens. Therefore, kidney function must be monitored in older adults to ensure that they are not at risk for health issues associated with declining kidney function.

The Geriatric Nutritional Risk Index (GNRI) was originally developed as a tool for assessing the nutritional status of hospitalized older individuals. Moreover, it is calculated using serum albumin...
levels and body weight. A low GNRI is associated with an increased risk of morbidity and mortality in hospitalized older patients or patients with various diseases, including end-stage renal disease (ESRD), heart failure, cancer, and traumatic injuries.\(^{14-18}\)

Studies examining the relationship between nutritional status and kidney function are limited.\(^{15,19}\) Although studies have reported an association between a lower GNRI and progression to ESRD in patients with chronic kidney disease (CKD), studies showing the relationship between the GNRI and decline in kidney function assessed by estimated glomerular filtration rate (eGFR) changes in older adults are lacking.\(^{11,20}\) Therefore, this study investigated the association of GNRI with the decline in kidney function and all-cause mortality over time in older individuals.

**MATERIALS AND METHODS**

**Study Participants and Data Collection**

This retrospective cohort study used de-identified data from participants who underwent a general health checkup at Samsung Changwon Hospital between January 1, 2002, and December 31, 2018. We included participants aged \(\geq 60\) years after excluding those without data on baseline body weight, height, serum albumin, and creatinine levels. Additionally, we excluded participants with a baseline eGFR < 15 mL/min/1.73 m\(^2\) or those without a follow-up examination on kidney function within 5 years.

Baseline information on age, sex, comorbidities (diabetes, hypertension, coronary artery disease, and stroke), current smoking status, body weight, height, systolic blood pressure (SBP), diastolic blood pressure (DBP), and laboratory variables, including hemoglobin, serum albumin, total cholesterol, serum glucose, serum creatinine, and albuminuria, was collected from the database. Albuminuria was defined as a urine protein dipstick test reading of \(\geq 1\).

This study was approved by the Institutional Review Board of Samsung Changwon Hospital (IRB No. SCM2022-01-008), which waived the requirement for informed consent from the participants because our study only retrospectively accessed a de-identified dataset based on the health screening cohort of the epidemiological research center at Samsung Changwon Hospital for analysis purposes.

This study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.\(^{21}\)

**Exposures and Outcomes**

The primary exposure measure in this study was the GNRI, which was divided into quartiles. The primary outcome was a change in kidney function 5 years after baseline, which was assessed using the 5-year slope of eGFR. The secondary outcome was all-cause mortality 5 years after baseline. The GNRI was calculated using the following formula: \(14.89 \times \text{serum albumin (g/dL)} + 41.7 \times \text{(actual body weight [kg])} / \text{(ideal body weight [kg])}\). The ideal body weight was calculated using the following formula: \(\text{height [m]}^2 \times 22 \text{ (kg/m}^2\)). The eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation.\(^{22}\) A negative slope indicates a decline in eGFR.

**Statistical Analyses**

Continuous and categorical variables for baseline characteristics were expressed as mean \(\pm\) standard deviation or median (inter-quartile range [IQR]) and count (%), respectively. We determined the significance of the trends in the variables across the GNRI quartiles using linear regression analysis or the Wilcoxon-type nonparametric trend test, as appropriate. For the primary outcome variable, the 5-year slope of eGFR was estimated in participants with at least one follow-up eGFR data point measured between follow-up years 2 and 6, in addition to the baseline eGFR, using a linear mixed-effects model with adjustment for baseline eGFR, allowing for a random intercept and slope using an unstructured covariance matrix. We conducted linear regression analyses to assess the association between the categorized GNRI and the 5-year slope of eGFR, using the highest GNRI quartile as the reference. The analyses were hierarchically adjusted for baseline covariates including age, sex, presence of diabetes or hypertension, systolic blood pressure (SBP), diastolic blood pressure (DBP), and levels of serum hemoglobin, total cholesterol, serum glucose, and serum creatinine as follows: (1) unadjusted model; (2) model 1, which included age, sex, presence of diabetes or hypertension, SBP, DBP, and levels of serum hemoglobin, total cholesterol, and serum glucose; and (3) model 2, which included serum creatinine in addition to all variables included in model 1. The association between all-cause mortality and categorized GNRI was estimated using Cox proportional hazards regression models with the aforementioned adjustments. The survival curve was calculated using the Kaplan–Meier method to compare the cumulative incidence of all-cause mortality across the GNRI quartiles. Differences among groups were determined using the log-rank test.

Missing baseline parameters included diabetes, hypertension, coronary artery disease, stroke, smoking status, hemoglobin, total cholesterol, and albuminuria. The frequency of missing data was < 0.7% for hemoglobin, total cholesterol, and albuminuria, whereas those for comorbidities and smoking status were < 20.0% and 25.6%, respectively. Multiple imputations were performed using a multivariate normal model. The imputation model included all the variables of the fully adjusted model and an outcome variable using
50 imputed datasets. All statistical analyses were performed using STATA version 14.2 (StataCorp LLC, College Station, TX, USA).

RESULTS

Participant Characteristics

Data from 403,677 participants who received a health check-up between 2002 and 2018 were extracted from a de-identified data-set for analysis, and 22,632 participants aged 60 years and older were included in our study cohort. After excluding participants with missing data on baseline body weight, height, serum albumin, and serum creatinine, those with baseline eGFR less than 15 mL/min/1.73 m\(^2\), and those without follow-up serum creatinine data, data from 1,599 participants were finally available for analysis. A flowchart of the cohort construction is shown in Supplementary Fig. S1.

Baseline characteristics of the participants in the GNRI quartiles are discussed in Table 1. The median age of the participants was 63 years (IQR, 61–67), and 54% were male. The mean GNRI scores were 113.7 ± 6.9. The median serum creatinine and eGFR levels were 0.9 mg/dL (IQR, 0.7–1.0) and 81 mL/min/1.73 m\(^2\) (IQR, 72–93), respectively. The group with a higher GNRI was slightly younger, had a higher proportion of patients with diabetes and hypertension, and had a higher SBP and DBP.

Association between GNRI and the 5-Year Slope of eGFR

The median value of the eGFR slope was −0.44 mL/min/1.73 m\(^2\) (IQR, −1.34 to 1.17) per year. The median values of the actual eGFR changes over 5 years by group were −3.36 (IQR, −7.48 to 1.12), −2.88 (−4.86 to 5.30), −2.65 (−7.46 to 7.67), and −1.91 (−3.67 to 8.42) mL/min/1.73 m\(^2\) for the first, second, third, and fourth quartiles of GNRI, respectively (p < 0.001). In the linear regression analyses, the lower GNRI groups were associated with steeper 5-year eGFR slopes, as compared with the highest GNRI group (the reference group). The fully adjusted beta coefficients (β) and 95% confidence intervals (CIs) were −0.50 (−0.86, −0.14), −0.29 (−0.63, 0.05), and −0.19 (−0.53, 0.14) for the first, second, and third quartiles of GNRI, respectively (Fig. 1). Each 10-point decrease in GNRI level was associated with a steeper decline in the 5-year slope of eGFR by 0.26 mL/min/1.73 m\(^2\) per year. The fully adjusted β and 95% CI were –0.26 (–0.45, –0.08).

In subgroup analyses, the association between the GNRI and 5-year eGFR slope was not modified by age, sex, presence of diabetes or hypertension, SBP, DBP, and levels of serum hemoglobin, total cholesterol, and serum creatinine (all for interaction p > 0.5).

Table 1. Baseline characteristics of 1,599 participants aged ≥60 years stratified by baseline Geriatric Nutritional Risk Index

<table>
<thead>
<tr>
<th>Geriatric Nutritional Risk Index</th>
<th>Total</th>
<th>Quartile 1 (81.3–109.1)</th>
<th>Quartile 2 (109.1–113.6)</th>
<th>Quartile 3 (113.6–118.0)</th>
<th>Quartile 4 (118.0–137.2)</th>
<th>p-value for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of participants</td>
<td>1,599</td>
<td>399</td>
<td>400</td>
<td>400</td>
<td>400</td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>64 (61–67)</td>
<td>64 (61–68)</td>
<td>64 (61–67)</td>
<td>63 (61–66)</td>
<td>63 (61–66)</td>
<td>0.031</td>
</tr>
<tr>
<td>Sex, male (%)</td>
<td>54</td>
<td>55</td>
<td>55</td>
<td>52</td>
<td>55</td>
<td>0.643</td>
</tr>
<tr>
<td>Comorbidities (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>14.1</td>
<td>11.2</td>
<td>14.0</td>
<td>13.0</td>
<td>18.2</td>
<td>0.022</td>
</tr>
<tr>
<td>Hypertension</td>
<td>36.8</td>
<td>24.3</td>
<td>32.7</td>
<td>37.7</td>
<td>52.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>6.0</td>
<td>5.9</td>
<td>4.2</td>
<td>6.2</td>
<td>7.6</td>
<td>0.225</td>
</tr>
<tr>
<td>Stroke</td>
<td>2.8</td>
<td>1.3</td>
<td>3.2</td>
<td>3.4</td>
<td>3.4</td>
<td>0.114</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>9.9</td>
<td>15.8</td>
<td>5.4</td>
<td>7.7</td>
<td>10.8</td>
<td>0.095</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>131 ± 18</td>
<td>127 ± 20</td>
<td>129 ± 17</td>
<td>133 ± 16</td>
<td>136 ± 18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>77 ± 11</td>
<td>74 ± 13</td>
<td>76 ± 10</td>
<td>78 ± 10</td>
<td>79 ± 12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>63 ± 10</td>
<td>56 ± 8</td>
<td>61 ± 8</td>
<td>64 ± 8</td>
<td>71 ± 9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>161 ± 9</td>
<td>161 ± 8</td>
<td>161 ± 9</td>
<td>161 ± 9</td>
<td>162 ± 9</td>
<td>0.937</td>
</tr>
<tr>
<td>Laboratory parameters</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>14 ± 1</td>
<td>14 ± 1</td>
<td>14 ± 1</td>
<td>14 ± 1</td>
<td>15 ± 1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum albumin (g/dL)</td>
<td>4.6 ± 0.3</td>
<td>4.3 ± 0.3</td>
<td>4.5 ± 0.2</td>
<td>4.6 ± 0.2</td>
<td>4.8 ± 0.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>204 ± 40</td>
<td>197 ± 37</td>
<td>204 ± 38</td>
<td>207 ± 40</td>
<td>207 ± 43</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum glucose (mg/dL)</td>
<td>94 (87–104)</td>
<td>90 (83–99)</td>
<td>93 (87–103)</td>
<td>94 (88–103)</td>
<td>99 (90–111)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>0.9 (0.7–1.0)</td>
<td>0.9 (0.7–1.0)</td>
<td>0.9 (0.7–1.0)</td>
<td>0.9 (0.8–1.0)</td>
<td>0.9 (0.8–1.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Proteinuria (%)</td>
<td>1.2</td>
<td>2.3</td>
<td>0.5</td>
<td>0.8</td>
<td>1.3</td>
<td>0.253</td>
</tr>
</tbody>
</table>

Values are presented as median (interquartile range) or mean ± standard deviation.

SBP, systolic blood pressure; DBP, diastolic blood pressure.
Among the 1,599 participants, the median follow-up duration was 7.4 years (IQR, 4.6–12.4). During this period, we identified 108 (7.8 per 1,000 person-years) all-cause deaths. The Kaplan–Meier curve for cumulative all-cause mortality stratified by GNRI quartiles is shown in Fig. 2. All-cause mortality significantly increased in the first GNRI quartile (log-rank p < 0.001). The Cox regression analyses showed similar results: compared to the highest quartile of GNRI, the fully adjusted hazard ratios and 95% CIs were 2.20 (1.23, 3.95), 0.65 (0.33, 1.27), and 1.06 (0.57, 2.00) for the first, second, and third quartiles of GNRI, respectively (Table 2).

**DISCUSSION**

We conducted this study to investigate the association between GNRI, changes in kidney function over time, and all-cause mortality in older adults. Our findings indicated that individuals with lower GNRI values experienced a more rapid 5-year decline in eGFR. However, this significant association was observed only in the first GNRI quartile after adjusting for baseline kidney function. In addition, we observed that the first GNRI quartile was associated with an increased risk of all-cause mortality.

Previous research on the relationship between the GNRI and clinical outcomes has primarily focused on hospitalized older individuals or patients with various illnesses. Few studies have examined the relationship between GNRI and kidney function, particularly as assessed by eGFR changes, in older adults. While studies have suggested a relationship between a low GNRI and an increased risk of progression to ESRD in patients with CKD, other studies, such as that by Kiuchi et al., did not find such an association. We observed that a lower GNRI was associated with a
A steeper decline in kidney function in older individuals, which is consistent with the findings of previous studies. However, our study is distinct in that it specifically focused on changes in kidney function as assessed by eGFR. We observed that individuals with lower GNRI values experienced a more rapid decline in kidney function than those with higher GNRI values, despite having fewer traditional risk factors for CKD, such as diabetes and hypertension. Our findings indicate that the nutritional status assessed by the GNRI may be a valuable tool for predicting the decline in kidney function in older individuals, regardless of other comorbidities.

The mechanisms driving the relationship between GNRI and kidney function are currently unclear. However, inflammation is one potential cause. The GNRI is calculated using albumin and body weight as its main components, both of which are associated with malnutrition and inflammation. Low-grade inflammation is observed in many older individuals and can contribute to kidney fibrosis. Therefore, inflammation may link low GNRI to a decline in kidney function in older individuals.

We observed a significant association between a low GNRI and all-cause mortality only in the first quartile among the GNRI quartiles. This may be because our study population consisted of relatively healthy older individuals who underwent regular health checkups and had higher GNRI levels than those in previous studies. Additionally, the number of all-cause deaths in our cohort was relatively small (6.8%). As a result, our study may not have had sufficient power to detect a more gradual relationship between the GNRI and all-cause mortality.

Our study has several limitations. First, as our study was observational in nature, confounding factors may remain unaccounted for even after adjustment. We did not consider the participants’ dietary intake, health behaviors, and socioeconomic status, all of which are associated with nutritional status. These factors may affect kidney function. Second, while we used multiple imputations to address missing data and adjusted for blood pressure and serum glucose, a significant amount of information was missing regarding comorbidities, such as diabetes and hypertension, in our population. This may have introduced bias into our data analysis. Finally, our results may not be generalizable to older individuals, as only 14% of the participants were > 70 years of age. In addition, changes in medical standards during the long-term follow-up period may have affected the health status and outcomes of our population.

In conclusion, our study suggests that a lower GNRI is associated with a steeper decline in eGFR over 5 years and a higher risk of all-cause mortality in older individuals. Therefore, the assessment of nutritional status using the GNRI as a modifiable risk factor should be considered a predictor of kidney function decline in older individuals. However, these findings require validation in larger populations of older individuals, and future studies are needed to determine whether improving nutritional status can prevent kidney function decline in these populations.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST
The researchers claim no conflicts of interest.

FUNDING
None.

AUTHOR CONTRIBUTIONS
Conceptualization, YJL; Data curation, YJL, NGK; Investigation and Methodology, YJL, NGK; Writing–original draft, SMY, NGK, YJL; Writing–review & editing, YJL.

SUPPLEMENTARY MATERIALS
Supplementary materials can be found via https://doi.org/10.4235/agmr.23.0215.

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Predicting Mortality Risks Using Body Mass Index and Weight Loss at Admission in Patients with Heart Failure

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Background: The association of the combination of body mass index (BMI) and weight change at admission with prognoses in patients with heart failure (HF) is unclear. Therefore, we investigated whether BMI and weight changes at admission affect mortality in patients with HF.

Methods: This retrospective cohort study lasted 99 months, starting in April 2014, and included 4,862 patients with HF from a Japanese real-world database. Cubic and thin-plate smoothing spline analyses were performed to investigate the association of BMI and weight changes with mortality. The percentage weight change was calculated every 6 months. The study outcome was the presence or absence of death.

Results: The patients’ mean age was 81.5±9.6 years, and 1,239 (25.5%) patients died. Cubic spline analysis revealed a negative correlation of BMI with mortality hazard ratio (HR) (BMI of 18.5 kg/m² and 25 kg/m²; HR=1.3 [1.2–1.4] and 0.8 [0.7–0.9], respectively). Cubic spline analysis of weight change showed that weight loss tended to increase the mortality HR (each 6% decrease in weight change rate was associated with a 1.1 times higher mortality risk (95% CI [1.0–1.2]). Thin-plate smoothing spline analysis showed that the odds ratio (OR) negatively correlated with BMI (1-year mortality: BMI of 18.5 kg/m², 22 kg/m², and 25 kg/m²; OR at 0% weight change=1.5, 1.0, and 0.7, respectively; 2-year mortality: BMI=18.5 kg/m², 22 kg/m², and 25 kg/m²; OR at 0% weight change=1.4, 0.9, and 0.7, respectively). Conclusion: A low BMI in patients with HF was associated with a higher risk of mortality. Weight loss in patients, regardless of BMI, was associated with a higher OR for mortality.

Key Words: Cachexia, Heart failure, Asian, Prognosis, Obesity paradox

INTRODUCTION

Heart failure (HF) primarily manifests as a symptom associated with aging and is a significant public health concern. Advanced HF is associated with severe muscle wasting known as cardiac cachexia. The prognosis of patients with cardiac cachexia is poor, with mortality reaching 50% by 18 months. A high body mass index (BMI) is a risk factor for HF; hence, obese patients in the general population are advised to lose weight to prevent HF. However, a recent study reported a better life prognosis in patients with a high
BMI compared with normal-weight patients after HF diagnosis. This phenomenon is termed the “obesity paradox,” and the role of weight loss in patients with HF has been debated. Most studies conducted to support the obesity paradox in HF have considered only patient weight or BMI at enrollment; however, few studies have examined the impact of changes in BMI over time on prognosis. Moreover, while several studies have investigated the association between weight loss and the prognosis of patients with HF, few studies have investigated the association between the combination of BMI, weight change at admission, and patient prognosis. Therefore, this study investigated the effects of BMI and weight change at admission on mortality in patients with HF.

MATERIALS AND METHODS

Ethics Statements
The Ethics Committee of Hospital, National Center for Geriatrics and Gerontology determined that an ethical review was not required owing to the use of a publicly available database (No. 1639). The requirement for informed consent was waived because the patient data were anonymized. This study complied the ethical guidelines for authorship and publishing in the Annals of Geriatric Medicine and Research.

Study Design and Data Source
This retrospective cohort study used the administrative claims database compiled by the Japan Medical Data Center Inc., which is one of the most frequently used sources of real-world data. In the database, each patient is assigned a unique anonymized identification number, and data associated with visits to medical facilities is chronologically traced using this anonymized personal ID. Thus, information on outcomes, such as death, can be obtained. We received data containing these unique identification numbers; however, patient personal information, including name or address, could not be obtained.

Patient Selection
This study included data from patients hospitalized between April 2014 and June 2022. The participants were defined as those who met the following inclusion criteria: patients (i) assigned the International Classification of Disease-10 code I50 (HF) and with New York Heart Association classification information, (ii) with available BMI information at admission, (iii) with a history of hospitalization 3–12 months before the hospitalization in (i), and (iv) who were ≥ 40 years of age. Data from patients with similar BMIs at admission and 3–12 months prior were excluded because they were unreliable.

Variables
Patient data, including age, sex, BMI, weight change, New York Heart Association classification, comorbidities, and Barthel Index, were collected. The BMI of each patient was calculated by dividing their weight by the square of their height. The percentage weight change was derived from the BMIs at admission and 3–12 months and was calculated every 6 months. The New York Heart Association classification of each patient was determined on a 4-point scale based on subjective symptoms produced by physical exertion. Comorbidities were scored using the Charlson Comorbidity Index. The Barthel Index was used to assess activities related to daily living on a 100-point scale for all 10 items, with higher scores indicating greater independence. The outcomes measured in this study were the presence or absence of (1) death during the observation period, (2) in-hospital death, (3) death within 1 year of admission, and (4) death within 2 years of admission.

Statistical Analyses
We determined quantitative variables using histograms, with parametric variables presented as mean ± standard deviation and non-parametric variables presented as median (interquartile range). The data were analyzed using the Mann–Whitney U test. Categorical data are expressed as frequency (percentage). We modeled nonlinear associations by fitting a four-knot restricted cubic spline for BMI and weight change using a Cox regression model to determine their association with mortality or in-hospital mortality. Four knots were used in the 5th, 25th, 75th, and 95th percentile quartiles of the BMI and weight change distributions. The reference points were 22.0 kg/m² for BMI and 0% for weight change.

Moreover, we used thin-plate smoothing splines to generate contour plots of the odds ratios (ORs) of BMI and weight change for mortality within 1 and 2 years after admission. The reference point for the thin-plate smoothing spline analysis was set as the mean. Patients who survived within 1 or 2 years of admission and were censored within the same period were excluded from the analyses. We adjusted for age, sex, Charlson Comorbidity Index, Barthel Index, and New York Heart Association classification in the multivariate analysis. In a sub-analysis, we limited the study population to individuals aged ≥ 65 years and conducted a thin-plate smoothing spline analysis. We also modeled nonlinear associations by fitting a cubic spline with mortality during the observation period and in-hospital death as outcomes to determine the association between weight change and prognosis in patients repeatedly hospitalized for HF.

All statistical analyses were performed using R statistical software (version 4.2.1; The R Project for Statistical Computing, Vi-
RESULTS

Among 5,432 individuals considered eligible for inclusion in this study, we excluded 570 for having the same BMI at admission and 3–12 months previously; thus, the final analysis included 4,862 patients.

The patients’ mean age was 81.5 ± 9.6 years, and 2,174 (44.7%) and 2,688 (55.3%) were women and men, respectively (Table 1). Overall, 1,239 (25.5%) patients died during the observation period. Cubic spline analysis of BMI showed that BMI was negatively correlated with the mortality hazard ratio (HR) (BMI of 18.5 kg/m², HR = 1.3 [1.2–1.4]; BMI of 25 kg/m², HR = 0.8 [0.7–0.9]) (Fig. 1). Cubic spline analysis showed that, with 0% weight change as the reference rate, weight gain had a low mortality HR of approximately 0%–10% (weight change rate of +5%, HR = 1.0 [0.9–1.0]). However, with weight change > 10%, the mortality HR was high, and weight loss tended to increase the mortality HR by approximately -6% (weight change rate of -6%, HR = 1.1 [1.0–1.2]).

In the thin-plate smoothing spline analysis, 1,327 patients were censored within 1 year of admission for reasons other than death, while 1,869 patients were censored within 2 years of admission, resulting in a final analysis of 3,535 and 2,993 patients, respectively. Of the patients analyzed, 166 (4.7%) and 312 (10.4%) died within 1 and 2 years, respectively. In the unadjusted model, the OR increased with decreasing BMI regardless of mortality (1-year mortality: BMI of 18.5 kg/m², 22 kg/m², and 25 kg/m², OR at 0% weight change of 1.5, 1.0, and 0.7, respectively; 2-year mortality: BMI of 18.5 kg/m², 22 kg/m², and 25 kg/m², OR at 0% weight change of 1.4, 0.9, and 0.7, respectively) (Fig. 2). The adjusted models also showed a higher OR with decreasing BMI regardless of mortality (1-year mortality: BMI of 18.5 kg/m², 22 kg/m², and 25 kg/m², OR at 0% weight change of 1.2, 1.0, and 0.8, respectively; 2-year mortality: BMI of 18.5 kg/m², 22 kg/m², and 25 kg/m², OR at 0% weight change of 1.2, 0.9, and 0.8, respectively) (Fig. 3). For all BMIs, a mild weight gain of approximately 0%–10% resulted in a lower mortality OR, whereas weight loss resulted in a higher mortality OR (Figs. 2, 3). Moreover, 1-year and 2-year mortality analyses of 3,311 and 2,805 individuals aged ≥ 65 years showed a trend similar to that of the initial analysis, irrespective of the adjustment. In both the 1-year and 2-year mortality analyses, lower BMI and weight loss were associated with higher ORs for mortality (unadjusted model, 1-year mortality: BMI of 18.5 kg/m², 22 kg/m², and 25 kg/m², OR at 0% weight change of 1.3, 0.9, and 0.7, respectively; 2-year mortality: BMI of 18.5 kg/m², 22 kg/m², and 25 kg/m², OR at 0% weight change of 1.3, 0.9, and 0.7, respectively) (Supplementary Fig. S1). The results obtained in the adjusted model were as follows: 1-year mortality (BMI of 18.5 kg/m², 22 kg/m², and 25 kg/m², OR at 0% weight change of 1.2, 1.0, and 0.8, respectively) and 2-year mortality (BMI of 18.5 kg/m², 22 kg/m², and 25 kg/m², OR at 0% weight change of 1.2, 0.9, and 0.8, respectively) (Supplementary Fig. S2).

During the study period, we observed 1,259 hospitalizations for HF. Overall, 316 patients (25.1%) died during the observation period, 99 (7.9%) of whom died in the hospital. Cubic spline analysis of weight change showed that weight gain had a low mortality HR of approximately 0%–7% but a high mortality HR of > 7%. Weight loss tended to have a high mortality HR of approximately -8% when death within the observation period was the outcome (weight change rate of -8%, HR = 1.2 [1.0–1.5]) (Fig. 4). When in-hospital mortality was used as the outcome, a weight gain of approximately 0%–8% was associated with a lower mortality HR; however, a weight gain of > 8% was associated with a higher mortality HR, while a weight loss of approximately 9% tended to increase the mortality HR (weight change rate of -9%, HR = 1.6 [1.0–2.3]) (Fig. 4). We observed the highest HR for the mortality

---

**Table 1.** Patient characteristics (n=4,862)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>81.5 ± 9.6</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>2,174 (44.7)</td>
</tr>
<tr>
<td>Male</td>
<td>2,688 (55.3)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.0 ± 3.5</td>
</tr>
<tr>
<td>Weight change rate (%)</td>
<td>-1.2 (-5.6–3.1)</td>
</tr>
<tr>
<td>NYHA classification</td>
<td></td>
</tr>
<tr>
<td>Class 1</td>
<td>254 (5.2)</td>
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<tr>
<td>Class 2</td>
<td>1,227 (25.2)</td>
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<tr>
<td>Class 3</td>
<td>1,885 (38.8)</td>
</tr>
<tr>
<td>Class 4</td>
<td>1,496 (30.8)</td>
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<tr>
<td>CCI score</td>
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<tr>
<td>Barthel Index (%)</td>
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<tr>
<td>≥ 0 and &lt; 50</td>
<td>1,680 (34.6)</td>
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<tr>
<td>≥ 50 and &lt; 100</td>
<td>1,181 (24.3)</td>
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<tr>
<td>100</td>
<td>1,361 (28.0)</td>
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<td>Missing</td>
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</tr>
<tr>
<td>Death</td>
<td>1,239 (25.5)</td>
</tr>
<tr>
<td>1-year death</td>
<td>166 (3.4)</td>
</tr>
<tr>
<td>2-year death</td>
<td>312 (6.4)</td>
</tr>
<tr>
<td>Survival time (mo)</td>
<td>28 (7–63)</td>
</tr>
</tbody>
</table>

Values are presented as mean ± standard deviation or number (%) or median (interquartile range).

BMI, body mass index; NYHA, New York Heart Association; CCI, Charlson Comorbidity Index.
Fig. 1. Restricted cubic splines for mortality. (A, B) The association between BMI/weight change and mortality hazard ratios allowed for non-linear effects with 95% CIs. The model fitted with four knots restricted the cubic spline to BMI/weight change. The bar graph shows the histogram. BMI, body mass index; CI, confidence interval.

Fig. 2. Body mass index (BMI) and weight change in mortality odds ratio (OR) using a contour map (unadjusted model): (A) 1-year mortality and (B) 2-year mortality. The solid black line indicates an OR of 1.0. The dashed-and-dotted, dashed, and dotted lines indicate ORs of 0.8, 1.2, and 1.4, respectively. There is a higher OR for mortality with a lower BMI and weight gain/loss.
Fig. 3. Body mass index and weight change in mortality odds ratio (OR) using a contour map (adjusted model): (A) 1-year mortality and (B) 2-year mortality. The model was adjusted for age, sex, Charlson Comorbidity Index, Barthel Index, and New York Heart Association classification.

Fig. 4. Restricted cubic spline analysis of patients repeatedly hospitalized for heart failure. The association between weight change and mortality hazard ratios allowed for nonlinear effects with 95% CIs: (a) restricted cubic splines for (A) mortality and (b) in-hospital mortality. CI, confidence interval.
risk predicted by weight loss in patients with repeated hospitalizations for HF (HR = 1.2 and 1.6 for mortality and in-hospital mortality, respectively) compared with those without repeated hospitalization for HF (HR = 1.1).

DISCUSSION

This retrospective cohort study examined BMI and the rate of weight change in relation to mortality in patients with HF using real-world data. The results demonstrated that a low BMI in patients with HF was associated with a higher mortality risk; moreover, weight loss, regardless of BMI, was associated with a higher mortality. Weight loss in patients repeatedly hospitalized for HF was associated with a higher mortality risk. Additionally, the combination of low BMI and weight loss predicted death in patients with HF.

In one meta-analysis, Oreopoulos et al. (1) reported a lower mortality risk in obese or overweight individuals with chronic heart failure (CHF) than those with normal weight and CHF. In contrast, underweight patients had significantly higher mortality rates than those with a normal BMI. Anker et al. (2) also reported that a weight loss of ≥ 6% during follow-up was the strongest predictor of decreased survival. Several studies have examined the associations between BMI and prognosis; weight loss and prognosis; and a combination of BMI, weight loss, and prognosis. Pocock et al. (3) observed a > 150% increase in mortality in patients with CHF who were lean (mean baseline and 6-month BMI < 22.5 kg/m²) and had weight loss (> 5% weight loss over 6 months) compared with patients who were heavier and had little weight change. Tager et al. (4) reported the best prognosis for patients with CHF and 5% weight gain, although gradual weight loss was associated with increased mortality. Konishi et al. (5) observed higher mortality rates in patients with reduced weight in all baseline BMI subgroups (< 18.5 kg/m², 18.5–24.9 kg/m², and 25.0 kg/m²). As previously reported, the survival benefits of obesity in patients with HF may be explained by several mechanisms. (6) For example, a higher BMI may indicate a higher metabolic reserve, allowing patients to withstand the catabolism caused by chronic diseases. Patients with a higher BMI may have greater muscle mass, strength, and cardiopulmonary function than those with a lower BMI. Although the mechanism remains controversial, the results of this study are consistent with those of previous reports, with a high BMI indicating a low mortality risk and vice versa. Additionally, we observed increased mortality risk with weight loss and decreased mortality risk with gradual weight gain, regardless of patient BMI at admission.

To the best of our knowledge, this study is the first to investigate and identify a nonlinear association between the combination of continuous BMI and weight change values and prognosis. The difference between the present study and previous reports is the lack of categorization of BMI and weight loss rates. Previous reports on the association between BMI and weight change combinations and prognosis categorized participants according to BMI and rate of weight change. (7,12,13) Categorization using BMI or weight loss cutoffs could lead to the grouping of patients at different degrees of risk. For example, as observed in the present study, participants with BMIs of 18.5 kg/m² and 22 kg/m² demonstrated different mortality risks, with a higher risk for a BMI of 18.5 kg/m² (Fig. 1). As highlighted in a previous report, this trend may be overlooked when grouped and analyzed. The cutoff values for BMI and weight loss rate varied from study to study, with no uniformity. (7,12,13) In contrast, we observed a nonlinear relationship between BMI and weight change using continuous values without categorization.

Weight loss is associated with a high risk of mortality in patients with repeated hospitalizations for HF. In patients with repeated hospitalization for HF, in-hospital mortality was reportedly higher among those with weight loss or gain > 5.0% compared with those with stable weight (-2.0% to +2.0%; OR = 1.46 and 1.23, respectively). (7) We observed an HR of 1.6 for the association of weight loss with in-hospital mortality in patients admitted with repeated HF. Furthermore, the HR for the association between weight change and death during the observation period in patients with repeated HF hospitalizations was higher than that in patients without repeated HF hospitalizations (1.2 vs. 1.1). Progressive HF leads to cardiac cachexia (15) and a poor prognosis due to weight loss. Therefore, patients with repeated hospitalizations for HF were more likely to have cachexia than those without such repeated hospitalizations; hence, the mortality rate may have increased with weight loss.

This study has several limitations. First, the data did not indicate whether weight loss was intentional. Second, BMI was used as an index of body composition; however, it was not considered with respect to detailed body composition, such as muscle mass, fat storage, and water content. However, BMI may be a good surrogate for lean body mass (16,17) and is a practical index that is easily collected clinically without expensive equipment.

In conclusion, low BMI and weight loss on admission were associated with mortality in patients with HF. Future studies are required to determine whether weight loss, even if intended, is associated with a poor prognosis.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.
FUNDING
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AUTHOR CONTRIBUTIONS
Conceptualization, YI, K Maeda, K Murotani, AS, JU, AN, TI, NM; Funding acquisition, K Maeda; Methodology, YI, K Maeda, K Murotani; Supervision, K Maeda, NM; Writing–original draft, YI, K Maeda; Writing–review & editing, YI, K Maeda, K Murotani, AS, JU, AN, TI, NM.

SUPPLEMENTARY MATERIALS
Supplementary materials can be found via https://doi.org/10.4235/agmr.23.0213.

REFERENCES
Association of Olfactory and Gustatory Function with Memory among Community-Dwelling Independent Older Adults

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INTRODUCTION

Impairments in sensory functions, such as olfactory function and taste, are features of several neurodegenerative disorders. Poor olfactory function occurs in patients with mild cognitive impairment (MCI) and Alzheimer disease (AD). A longitudinal study with 5-year follow-up indicated that olfactory tests in patients with MCI could help predict AD conversion. Gustatory disorders also occur in AD. However, studies on gustatory disorders in patients with MCI have yielded inconsistent results. Thus, gustatory function may be maintained during the early stages of AD.

Olfactory and taste abilities decrease with advancing age, and many neurodegenerative conditions and health statuses may be associated with olfactory or gustatory dysfunction. Impairments in odor and taste identification are features of several neurodegenerative disorders. Although moderate or severe reductions in olfactory and gustatory function may correlate with cognitive impairment, few healthy older adults are aware of slight reductions in olfactory and gustatory function. Thus, the assessment of hyposmia and hypogeusia may be useful for identifying early cognitive deficits in independent older adults.

Memory deficits are early symptoms of AD and other types of dementia. Older adults without dementia but with problems related to memory have an increased risk for dementia compared with those with challenges in other cognitive dimensions, attention, and executive function. Memory plays a specific role in olfactory perception; however, few studies have assessed gustatory function, with conflicting results. For instance, a previous study that included patients with MCI, AD, and controls did not identify group differences in olfactory threshold, gustatory function, or food preferences. In contrast, poor memory, rather than other domains of cognitive function, was associated with poor odor discrimination.

Background: This study examined the association between memory function and reduced olfactory and gustatory function among independent community-dwelling older adults. Methods: This cross-sectional study included 127 older adults (65.4% women). We assessed their memory, odor, and taste identification skills. Open essence (OE) test and taste strips (TS) were used to identify hyposmia (OE test ≤6) and hypogeusia (TS test ≤8), respectively. Results: Participants with severe hyposmia had significantly poorer memory functions compared to participants without severe hyposmia. After adjusting for covariates, multivariate logistic regression models revealed a significant association between immediate recognition performance and a decreased likelihood of severe hyposmia (odds ratio=0.65; 95% confidence interval 0.47–0.90). We observed no significant association between taste function and memory. Conclusion: Memory function may be associated with olfactory impairment in older adults.

Key Words: Olfactory perception, Taste perception, Memory
The association of memory with olfactory and gustatory functions remains unclear, particularly in independent community-dwelling older adults. This cross-sectional study investigated the association between memory function and reduced olfactory as well as gustatory function in the sample population.

MATERIALS AND METHODS

Participants
This study included cross-sectional data from 134 independent older adults who participated in community-based blood pressure management classes after participating in the Tarumizu Study 2019 a health check survey. The Tarumizu Study was conducted in collaboration with Kagoshima University’s, Faculty of Medicine, Tarumizu City Office, and Tarumizu Chuo Hospital. Participants aged ≥ 40 years were recruited via mail reply-paid postcards from Tarumizu City, Japan, a residential suburb of Kagoshima City. Totally, 1,024 citizens participated in the Tarumizu Study 2019, conducted between June and December 2019, of which 687 were older adults. Of the participants aged ≥ 65 years who had participated in blood pressure management classes after a health check survey, 137 participated in additional assessments of odor and taste function. Flyers were distributed to those who were participating in the blood pressure management class to recruit them for this study. Participants who required support in activities of daily living and those with missing data on odor and taste assessments were excluded. This study was approved by the Ethics Committee of Kagoshima University Faculty of Medicine (No. 190090). All participants provided informed consent. Also, this study complied with the ethical guidelines for authorship and publishing in the Annals of Geriatric Medicine and Research.

Olfactory Functioning
We assessed olfactory functioning using the open essence (OE) test (Wako Pure Chemical Industries Ltd., Osaka, Japan), which included 12 odor items known to people in Japan (Indian ink, perfume, wood, orange, menthol, curry, rose, cooking gas, Japanese cypress “hinoki,” sweaty clothes, condensed milk, and roasted garlic). Each of the 12 cards contained one odorant and was folded into halves. Microencapsulated test odorants were applied to the left half of the card instead of glue. Six choices, including four alternative odor names, “detectable, but not recognized,” and “no smell detected” were printed in Japanese on the opposite side of the card. The participants chose their answers after opening each card. One of the four odor names was the correct choice, with one point awarded for each correct answer. Herein, we defined hyposmia as participants with an OE test score of ≤ 6 out of 12.

Gustatory Functioning
We used taste strips (TS) to assess the gustatory function of the whole mouth. Sixteen TS were impregnated with sweet, sour, bitter, and salty solutions at four different concentrations—sweet (0.05, 0.1, 0.2, and 0.4 g/mL sucrose), sour (0.05, 0.09, 0.165, and 0.3 g/mL citric acid), bitter (0.0004, 0.0009, 0.0024, and 0.006 g/mL quinine-HCl), and salty (0.016, 0.04, 0.1, and 0.25 g/mL NaCl). The strips were presented in a predetermined order: sweet, salt, sour, and bitter, starting with the weakest concentration. Each TS was placed on the tongue and the participants were asked to close their mouths. The participants then categorized each strip as sweet, salty, sour, bitter, unidentified, or tasteless. The participants rinsed their mouths with water before tasting each strip. Each taste score ranged from 0 to 4 points (1 point for each correct answer). Thus, the total TS score ranged from 0–16. A total TS score ≤ 8 indicated hypogeusia in this study.

Memory Assessment
We applied a subitem (word-list memory) of the National Center for Geriatrics and Gerontology Functional Assessment Tool (NC-GG-FAT) to assess memory function. The wordlist memory tasks involved immediate recognition and delayed recall of a 10-word target list. The participants were asked to memorize 10 words. Each target word was presented for 2 seconds on a tablet computer. Subsequently, 30 words, including 10 and 20 target and distraction words, respectively, were presented. We requested that the participants choose 10 target words immediately, and the trial was repeated three times. The average number of correct answers in the three trials yielded the total score for the immediate recognition task. For the delayed recall score, we asked the participants to recall the 10 target words after approximately 20 minutes. The high test-retest reliability and moderate-to-high validity of the NC-GG-FAT have been confirmed in community-dwelling older adults.

Statistical Analysis
All data were analyzed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Since the data were not normally distributed, we used the Mann–Whitney U and chi-square tests (for sex and smoking status) to compare data between participants with and without hyposmia (OE test ≤ 6 and ≥ 7, respectively). We also tested the differences between participants with (TS test ≤ 8) and without (TS test ≥ 9) hypogeusia. Spearman correlation coefficients were calculated to test the simple as-
sociations between age, olfactory function, gustatory function, and memory test performance. We tested the associations of hyposmia and hypogeusia with memory function using logistic regression analyses, with hyposmia (OE test ≤ 6) and hypogeusia (TS test ≤ 8) as dependent variables, and memory performance scores (immediate recognition and delayed recall) as independent variables. The odds ratios (ORs) for hyposmia and hypogeusia in the memory performance tests were adjusted for age, sex, education, and smoking status. Statistical significance was set at p < 0.05.

RESULTS

The participant demographics are reported in Table 1. The mean (interquartile range) age of the participants was 74.0 (70.0–79.0) years and 66.4% were female.

Participants with hyposmia (OE test ≤ 6) were significantly older and had lower memory performance scores for immediate recognition and delayed recall compared with participants without hyposmia. Sex and smoking status but not memory performance differed significantly between participants with (TS test ≤ 8) and without hypogeusia (Table 2).

Table 3 shows the correlations among age, olfactory function, gustatory function, and memory. We observed significant simple correlations between OE test scores and age (Spearman’s ρ = -0.292, p < 0.001), immediate recognition (Spearman’s ρ = 0.327, p < 0.001), and delayed recall (Spearman’s ρ = 0.295, p < 0.001). TS test scores were not significantly correlated with age, immediate recognition, or delayed recall. In addition, we observed no significant correlation between OE and TS test scores (Spearman’s ρ = 0.150, p = 0.083).

Table 4 presents the results of the multivariate logistic regression models. Improved performance scores for immediate recognition were significantly associated with hyposmia after controlling for

<table>
<thead>
<tr>
<th>Table 1. Participant demographics (n=134)</th>
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<tbody>
<tr>
<td><strong>Value</strong></td>
</tr>
<tr>
<td>Age (y)</td>
</tr>
<tr>
<td>74.0 (70.0–79.0)</td>
</tr>
<tr>
<td>Sex, female</td>
</tr>
<tr>
<td>89 (66.4)</td>
</tr>
<tr>
<td>Education (y)</td>
</tr>
<tr>
<td>12.0 (9.0–12.0)</td>
</tr>
<tr>
<td>Medical history</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>78 (58.2)</td>
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<tr>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td>34 (25.4)</td>
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<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>15 (11.2)</td>
</tr>
<tr>
<td>Arthritis</td>
</tr>
<tr>
<td>4 (3.0)</td>
</tr>
<tr>
<td>Osteoporosis</td>
</tr>
<tr>
<td>3 (2.2)</td>
</tr>
<tr>
<td>Medications per day</td>
</tr>
<tr>
<td>4.0 (2.0–6.89)</td>
</tr>
</tbody>
</table>

Values are presented as mean (interquartile range) or number (%).

<table>
<thead>
<tr>
<th>Table 2. Comparisons of characteristics between participants with hyposmia or hypogeusia and those without</th>
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<tbody>
<tr>
<td><strong>Number of participants</strong> 134</td>
</tr>
<tr>
<td><strong>Age (y)</strong> 74.0 (70.0–79.0)</td>
</tr>
<tr>
<td><strong>Sex, female</strong> 89 (66.4)</td>
</tr>
<tr>
<td><strong>Education (y)</strong> 12.0 (9.0–12.0)</td>
</tr>
<tr>
<td><strong>Smokers (current and ever)</strong> 32 (23.9)</td>
</tr>
<tr>
<td><strong>Body mass index (kg/m²)</strong> 22.6 (20.7–24.9)</td>
</tr>
<tr>
<td><strong>Immediate recognition</strong> 8.2 (7.3–9.0)</td>
</tr>
<tr>
<td><strong>Delayed recall</strong> 5.0 (4.0–6.0)</td>
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<table>
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<tr>
<th><strong>Odor function</strong></th>
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</thead>
<tbody>
<tr>
<td><strong>Hyposmia</strong> (OE test ≤ 6) 51</td>
</tr>
<tr>
<td><strong>Non-hyposmia</strong> (OE test ≥ 7) 83</td>
</tr>
<tr>
<td><strong>p-value</strong> 0.01</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th><strong>Taste function</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypogeusia</strong> (TS test ≤ 8) 41</td>
</tr>
<tr>
<td><strong>Non-hyposmia</strong> (TS test ≥ 9) 93</td>
</tr>
<tr>
<td><strong>p-value</strong> 0.01</td>
</tr>
</tbody>
</table>

| **Immediate recognition** 8.2 (7.3–9.0) |
| **Delayed recall** 5.0 (4.0–6.0) |

Values are presented as mean (interquartile range) or number (%).

OE, open essence; TS, taste strips.

<table>
<thead>
<tr>
<th>Table 3. Correlation coefficients (Spearman’s ρ) between age, olfactory function, gustatory function, and memory (n=134)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td>1.000</td>
</tr>
<tr>
<td><strong>Olfactory function (OE test)</strong></td>
</tr>
<tr>
<td>-0.292**</td>
</tr>
<tr>
<td><strong>Gustatory function (TS test)</strong></td>
</tr>
<tr>
<td>-0.069</td>
</tr>
<tr>
<td><strong>Memory (immediate recognition)</strong></td>
</tr>
<tr>
<td>-0.378**</td>
</tr>
<tr>
<td><strong>Memory (delayed recall)</strong></td>
</tr>
<tr>
<td>-0.325**</td>
</tr>
</tbody>
</table>

**p<0.001.**
age, sex, education, and smoking status (adjusted OR = 0.65, 95% confidence interval [CI] 0.47–0.90). An improved delayed recall performance score was associated with hyposmia, however the association was not statistically significant after controlling for covariates (adjusted OR = 0.89; 95% CI 0.72–1.10). The results of multivariate logistic regression analyses showed no significant association between hypogeusia and memory.

**DISCUSSION**

The primary finding of this study was the association of poor memory scores with olfactory impairment. However, taste function and memory were not associated in independent community-dwelling older adults. Even in a relatively healthy aging stage, olfactory impairment may be associated with lower memory performance but not taste function.

Sensory systems, including taste and smell, are affected by aging. Sensory impairment progresses slowly with advancing age, and smell and taste deficits are highly prevalent in older adults. Impaired sensory function affects quality of life in older people. For instance, olfactory impairment complicates danger detection in our environment (e.g., gas, smoke, and spoiled food), while taste impairment increases the risk of foodborne illnesses, alter food choices, impairing nutritional status, and elevate the risk of allergic reactions. Olfactory impairment may also be a marker related to age-associated frailty status, such as sarcopenia and brain shrinking. Our findings demonstrated an association between olfactory function and memory. The current observational study could not assess these mechanisms, although olfactory loss could reflect age-related changes in the physiological system that are more sensitive than gustatory function.

A previous study analyzing data from a nationally representative sample of older adults reported that gustatory dysfunction was associated with dementia, while olfactory dysfunction was associated with MCI and dementia. In addition, middle-aged and older individuals with gustatory and olfactory dysfunction had worse global cognitive function than either alone. Herein, we observed no significant association between taste function and memory, while olfactory dysfunction was related to memory function. Those results confirmed the associations between poor memory function and olfactory impairment in the early stage of age-related sensory dysfunction.

Several interventional studies including older adults, MCI, and dementia have examined the effects of olfactory training on brain function. These intervention studies demonstrated the positive effects of training the sense of smell to improve olfactory function; however, the interventions showed a limited effect on cognition. A randomized controlled trial which conducted intensive olfactory training twice daily for 15 days (30 sessions) to older adults with dementia reported improved memory. Neurofibribrillary tangles in the olfactory bulb and the projection pathways from the olfactory bulb to the secondary olfactory brain regions are the earliest pathological features of AD and a damaged olfaction. Despite evidence from well-designed intervention studies, training and improvement in olfactory function may positively impact the prevention of cognitive decline.

Olfactory and gustatory functions are essential in the activities of daily living in older people. For instance, the loss of olfactory function may lead to poor flavor perception, reduced food enjoyment, reduced appetite, and difficulties with cooking as well as detection of spoiled food. The loss of gustatory function may lead to health consequences such as metabolic syndrome through unhealthy dietary patterns. In addition, olfactory function and physical activity are strongly related, with better olfactory performance observed in older adults with active lifestyles. An active lifestyle is an important protective factor that reduces the risk of cognitive deficits. Therefore, the interaction with lifestyle indicated an association between olfactory function and memory. Thus, the association between gustatory function and lifestyle may be limited in older adults.

This study has several limitations. First, causal inferences could not be made because of the cross-sectional study design. Future longitudinal studies should investigate how changes in memory over time are associated with changes in olfactory and gustatory function. Second, other cognitive aspects such as attention, executive function, and spatial perception should be considered. Third,
although specific tests for olfactory and gustatory functions were conducted, odor sensitivity and identification may have different characteristics and roles in older adults.\(^{30}\) Finally, more possible factors associated with order and taste function, such as comorbidities,\(^{30}\) socioeconomic status,\(^{30}\) and dietary intake\(^{37}\) should be considered to comprehensively understand the association of olfactory and gustatory function with memory.

In conclusion, community-dwelling, independent older adults with poor olfactory function had lower memory performance scores. While olfactory dysfunction was related to memory function, we observed no significant association between taste function and memory. Our findings suggest that memory function may be closely associated with olfactory impairment but not with gustatory function in this population. Thus, older adults showing loss of olfactory function should be carefully observed. Additional research is needed to determine the specific role of olfactory and gustatory functions in memory in older adults.

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**CONFLICT OF INTEREST**

The authors declare that they have no conflict of interest.

**FUNDING**

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**AUTHOR CONTRIBUTIONS**

Conceptualization, HM, SM; Data curation, HM, YN, SA, YT; Investigation, HM, YN, SA, YT; Methodology: HM, YN; Project administration: HM, YN, SM; Supervision, TM, SM; Writing–original draft: HM; Writing–review & editing: YN, SA, YT, TM, SM.

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Evaluation of Factors Influencing Handgrip Strength Asymmetry in Older Peruvian Adults

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²Centro de Investigación del Envejecimiento (CIEN), Facultad de Medicina Humana, Universidad de San Martín de Porres, Lima, Perú

Background: Sarcopenia is a musculoskeletal disease involving the reduction of muscle mass, strength, and performance. Handgrip strength (HGS) measurements included in frailty assessments are great biomarkers of aging and are related to functional deficits. We assessed the association between potential influencing factors and HGS asymmetry in older Peruvian adults.

Methods: We used a database of the Peruvian Naval Medical Center “Cirujano Santiago Távara” located in Callao, Peru. All the patients included were ≥60 years old and had an HGS measurement in the dominant and non-dominant hand.

Results: From a total of 1,468 patients, 74.66% had HGS asymmetry. After adjustment, calf circumference weakness (adjusted prevalence ratio [aPR]=1.08; 95% confidence interval [CI], 1.01–1.15), falls risk (aPR = 1.08; 95% CI, 1.02–1.16), and an altered Lawton index (aPR=0.92; 95% CI, 0.84–0.99) were associated with HGS asymmetry.

Conclusion: Our findings suggest that HGS asymmetry should be measured along with other geriatric assessments used to evaluate health outcomes in the elderly to enhance health promotion and prevention aimed at preserving muscle strength to curb functional limitations in the elderly.

Key Words: Sarcopenia, Hand strength, Aging, Geriatric assessment

INTRODUCTION

As skeletal muscles undergo age-related changes, anabolic impairments contribute to declines in muscle mass, strength, and overall performance.¹ This deterioration not only disrupts physical function but also plays a role in the development of geriatric syndromes and conditions such as sarcopenia, falls, frailty, and functional decline.²³ One crucial aspect linked with these disorders is handgrip strength (HGS). The HGS test is widely utilized to evaluate mobility, balance, and independent activities of daily living (ADL).⁴

Within the context of clinical tests for assessing muscle strength in older adults, HGS is a reliable measure heavily dependent on neuromuscular function.⁵ HGS measurements are significant biomarkers of aging and are included in frailty assessments.⁶ McGrath et al. defined HGS asymmetry as a function of the HGS ratio, which is the ratio of maximum non-dominant HGS to maximum dominant HGS.⁷ Asymmetry of muscle strength is related to functional deficits in older adult populations; however, no studies have demonstrated the variability in risk factors that may increase the risk of decreased muscle strength in this population, although some studies have demonstrated the consequences.⁸

Clinicians may encounter HGS asymmetry when assessing physical performance. This occurs when HGS differs significantly between the non-dominant and dominant hands. The strength of both hands must be assessed because good strength may bias sarcopenia diagnosis. Indeed, HGS asymmetry is associated with increased instances of disability in ADLs and future accumulation of morbidity and mortality.⁹ Therefore, we assessed factors associated with HGS asymmetry in older adults from a Latin American city.
MATERIALS AND METHODS

Patients and Design
This observational cross-sectional study involved the secondary analysis of a database created using data collected in a primary study conducted between 2010 and 2015, which reported the prevalence of factors associated with frailty in older adults treated at the Peruvian Naval Medical Center, Círculo Mayor Santiago Távara, located in Callao, Peru. We excluded patients with cancer, acquired immunodeficiency syndrome, disabilities, or dementia. Although the original study was conducted to study factors associated with frailty, not all patients in the database met the criteria for frailty. After applying the eligibility criteria, 1,468 individuals were selected from a population of 1,896 older adults.

Selection Criteria
The inclusion criteria were age ≥ 60 years and availability of data on HGS measurements in the dominant and non-dominant hands. We excluded 428 patients with missing data on sex (n = 5); HGS of the dominant hand (n = 9); drug use (n = 89); Lawton Index (n = 72); Functional Reach Test (n = 77); body mass index (BMI, n = 89); and history of diabetes (n = 23), hypertension (n = 7), chronic obstructive pulmonary disease (n = 23), depression (n = 15), and stroke (n = 19).

Variables
We evaluated sociodemographic characteristics, such as age and sex. In Peru, due to retirement, the cutoff point defining older adults is 60 years, despite The American College of Sports Medicine suggesting a cutoff point of > 65 years. We categorized age into 60–79 and > 80 years, according to the definitions of the Medical Subject Headings terms in MEDLINE. We also constructed a multimorbidity variable, which included a history of diabetes mellitus type 2; chronic kidney disease; arterial insufficiency; arterial hypertension; heart failure; periodontal disease; chronic obstructive pulmonary disease; depression; tobacco use; hip fracture; fractures of the upper and lower limbs and spine; hypothyroidism; stroke; number of falls in the last year; and osteoarthritis of the hand, knee, wrist, and lower back. This variable was divided into categories of < 2 and ≥ 2 comorbidities. We calculated obesity using BMI, which was calculated as weight (kg)/height² (m) and categorized as < 30.00 kg/m² and ≥ 30.00 kg/m². We defined reduced muscle mass as a calf circumference ≤ 31 cm. Likewise, we evaluated the numbers of drugs received, and defined polypharmacy as the consumption of ≥ 5 drugs. A sedentary lifestyle was defined as scores of < 64 for men and < 52 for women according to the Physical Activity Scale for the Elderly (PASE). Functional capacity was measured using the Short Physical Performance Battery (SPPB) scale, and altered physical performance was defined as a score < 8. The Lawton Index measures the ability to perform instrumental activities of daily living (IADL), with scores ≤ 7 and ≤ 4 for women and men, respectively, considered as functional impairment. According to the Functional Reach Test, the risk of falling was determined for those with a score ≤ 20.32 cm.

Measurement of HGS Asymmetry
HGS was assessed using a handheld dynamometer (Baseline Dynamometer, series 120286) and measured in kilograms (kg). The test was administered by a trained interviewer. Two measurements were performed, and the better of the two measurements was used for scoring. The HGS asymmetry ratio was calculated as HGS non-dominant hand/HGS dominant hand, using the highest HGS values. We determined asymmetry according to the 10% rule, in which participants with an HGS ratio < 0.90 (10%) were considered to have dominant asymmetric HGS, whereas those with an HGS ratio > 1.10 (10%) were classified as having non-dominant asymmetric HGS. We considered patients with either dominant or non-dominant HGS asymmetry as having HGS asymmetry.

Statistical Analysis
We used Stata version 16.0 (StataCorp, College Station, TX, USA) for data processing. Descriptive statistics were used to determine the demographic and clinical characteristics of the participants. Categorical variables were presented as frequencies and percentages. We performed the first bivariate analysis using the chi-square test to evaluate the presence of significant differences between HGS asymmetry and categorical variables. The second bivariate analysis evaluated the presence of HGS asymmetry and potential influencing factors, stratified by sex.

Finally, we applied individual Poisson regression models and robust variance to assess the association between each potential influencing factor and HGS asymmetry. Crude prevalence ratios (cPR) and adjusted prevalence ratios (aPR) were calculated for the bivariate and multivariate analyses. In addition, we adjusted these models for age, sex, comorbidities, body mass index, calf circumference, PASE score, SPPB scale score, Lawton Index, and Functional Reach Test score. Polypharmacy was excluded from the multivariate analyses due to multicollinearity with multimorbidity, which was evaluated using the variance inflation factor. All models were presented with their respective 95% confidence intervals (CIs), and p < 0.05 was considered significant.

Ethical Considerations
This study was approved by the Ethics Committee of the Naval
Medical Center, Callao, Peru (No. #54). Information from a secondary database was evaluated using codes for each participant to maintain the confidentiality of all included patients. Also, this study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research.*

**RESULTS**

Our study included a total of 1,468 patients, of whom 863 (58.79%) were male, and 816 (55.59%) were aged 60–79 years. The prevalence of asymmetry was 74.66% (*Table 1*).

In the asymmetry group, 640 (74.16%) patients were male, 1,031 (75.37%) had multimorbidity, and 280 (67.15%) used ≥ 5 drugs. The asymmetric group showed a higher proportion of comorbidities, reduced calf muscle mass, and polypharmacy than the symmetric group did (all *p* < 0.05) (*Table 2*).

The multivariable analyses revealed that HGS asymmetry was independently associated with reduced calf muscle mass (cPR = 1.08; 95% CI, 1.01–1.16), polypharmacy (cPR = 0.86; 95% CI, 0.80–0.93), and multimorbidity (cPR = 1.16; 95% CI, 1.01–1.34). After adjusting for age, sex, multimorbidity, BMI, calf circumference, PASE score, SPPB scale score, Lawton Index and Functional Reach Test score, reduced muscle mass measured by

<table>
<thead>
<tr>
<th>Variable</th>
<th>Symmetry (n = 372)</th>
<th>Asymmetry (n = 1,096)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multimorbidity</td>
<td></td>
<td></td>
<td>&lt; 0.05*</td>
</tr>
<tr>
<td>&lt; 2</td>
<td>35 (35.00)</td>
<td>65 (65.00)</td>
<td></td>
</tr>
<tr>
<td>≥ 2</td>
<td>337 (24.63)</td>
<td>1,031 (75.37)</td>
<td></td>
</tr>
<tr>
<td>Calf circumference (cm)</td>
<td></td>
<td></td>
<td>&lt; 0.05*</td>
</tr>
<tr>
<td>Normal muscle mass</td>
<td>143 (29.24)</td>
<td>346 (70.76)</td>
<td></td>
</tr>
<tr>
<td>Reduced muscle mass</td>
<td>229 (23.39)</td>
<td>750 (76.61)</td>
<td></td>
</tr>
<tr>
<td>Polypharmacy (drugs)</td>
<td></td>
<td></td>
<td>&lt; 0.05*</td>
</tr>
<tr>
<td>0–4</td>
<td>235 (22.36)</td>
<td>816 (77.64)</td>
<td></td>
</tr>
<tr>
<td>≥ 5</td>
<td>137 (32.85)</td>
<td>280 (67.15)</td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td></td>
<td></td>
<td>0.347</td>
</tr>
<tr>
<td>60–79</td>
<td>199 (24.39)</td>
<td>617 (75.61)</td>
<td></td>
</tr>
<tr>
<td>≥ 80</td>
<td>173 (26.53)</td>
<td>479 (73.47)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td>0.599</td>
</tr>
<tr>
<td>Male</td>
<td>223 (25.84)</td>
<td>640 (74.16)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>149 (24.63)</td>
<td>456 (75.37)</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td></td>
<td>0.572</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>304 (25.65)</td>
<td>881 (74.35)</td>
<td></td>
</tr>
<tr>
<td>≥ 30</td>
<td>68 (24.03)</td>
<td>215 (75.97)</td>
<td></td>
</tr>
<tr>
<td>PASE (points)</td>
<td></td>
<td></td>
<td>0.417</td>
</tr>
<tr>
<td>No sedentarism</td>
<td>197 (24.50)</td>
<td>607 (75.50)</td>
<td></td>
</tr>
<tr>
<td>Sedentarism</td>
<td>175 (26.36)</td>
<td>489 (73.64)</td>
<td></td>
</tr>
<tr>
<td>SPPB (points)</td>
<td></td>
<td></td>
<td>0.291</td>
</tr>
<tr>
<td>Unaltered physical performance</td>
<td>220 (24.39)</td>
<td>682 (75.61)</td>
<td></td>
</tr>
<tr>
<td>Altered physical performance</td>
<td>152 (26.86)</td>
<td>414 (73.14)</td>
<td></td>
</tr>
<tr>
<td>Lawton Index (points)</td>
<td></td>
<td></td>
<td>0.257</td>
</tr>
<tr>
<td>No functional impaired</td>
<td>139 (23.76)</td>
<td>446 (76.24)</td>
<td></td>
</tr>
<tr>
<td>Functional impaired</td>
<td>233 (26.39)</td>
<td>650 (73.61)</td>
<td></td>
</tr>
<tr>
<td>Functional Reach test (cm)</td>
<td></td>
<td></td>
<td>0.328</td>
</tr>
<tr>
<td>No fall risk</td>
<td>236 (26.22)</td>
<td>664 (73.78)</td>
<td></td>
</tr>
<tr>
<td>Fall risk</td>
<td>136 (23.94)</td>
<td>1,096 (76.06)</td>
<td></td>
</tr>
</tbody>
</table>

Values are presented as number (%). BMI, body mass index; PASE, Physical Activity Scale for the Elderly; SPPB, Short Physical Performance Battery.

**Table 1. Characteristics of the sample (n=1,468)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td></td>
</tr>
<tr>
<td>60–79</td>
<td>816 (55.59)</td>
</tr>
<tr>
<td>≥ 80</td>
<td>652 (44.41)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>863 (58.79)</td>
</tr>
<tr>
<td>Female</td>
<td>605 (41.21)</td>
</tr>
<tr>
<td>Multimorbidity</td>
<td></td>
</tr>
<tr>
<td>&lt; 2</td>
<td>100 (6.81)</td>
</tr>
<tr>
<td>≥ 2</td>
<td>1,368 (93.19)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
</tr>
<tr>
<td>&lt; 30</td>
<td>1,185 (80.72)</td>
</tr>
<tr>
<td>≥ 30</td>
<td>283 (19.28)</td>
</tr>
<tr>
<td>Hand grip strength</td>
<td></td>
</tr>
<tr>
<td>Symmetry</td>
<td>372 (25.34)</td>
</tr>
<tr>
<td>Asymmetry</td>
<td>1,096 (74.66)</td>
</tr>
<tr>
<td>Calf circumference (cm)</td>
<td></td>
</tr>
<tr>
<td>Normal muscle mass</td>
<td>489 (33.31)</td>
</tr>
<tr>
<td>Reduced muscle mass</td>
<td>979 (66.69)</td>
</tr>
<tr>
<td>Polypharmacy (drugs)</td>
<td></td>
</tr>
<tr>
<td>0–4</td>
<td>1,051 (71.59)</td>
</tr>
<tr>
<td>≥ 5</td>
<td>417 (28.41)</td>
</tr>
<tr>
<td>PASE (points)</td>
<td></td>
</tr>
<tr>
<td>No sedentarism</td>
<td>804 (54.77)</td>
</tr>
<tr>
<td>Sedentarism</td>
<td>664 (45.23)</td>
</tr>
<tr>
<td>SPPB (points)</td>
<td></td>
</tr>
<tr>
<td>Unaltered physical performance</td>
<td>902 (61.44)</td>
</tr>
<tr>
<td>Altered physical performance</td>
<td>566 (38.56)</td>
</tr>
<tr>
<td>Lawton Index (points)</td>
<td></td>
</tr>
<tr>
<td>No functional impaired</td>
<td>585 (39.85)</td>
</tr>
<tr>
<td>Functional impaired</td>
<td>883 (60.15)</td>
</tr>
<tr>
<td>Functional Reach Test (cm)</td>
<td></td>
</tr>
<tr>
<td>No fall risk</td>
<td>900 (61.31)</td>
</tr>
<tr>
<td>Fall risk</td>
<td>568 (38.69)</td>
</tr>
</tbody>
</table>

BMI, body mass index; PASE, Physical Activity Scale for the Elderly; SPPB, Short Physical Performance Battery.

Cutoff values of calf circumference (31 cm), PASE (men 64 points; women 52 points), SPPB (8 points), Lawton index (women 7 points; men 4 points), and Functional reach test (20.32 cm).

*p* < 0.05 using a chi-square test.
calf circumference (aPR = 1.08; 95% CI, 1.01–1.15), fall risk measured by Functional Reach Test (aPR = 1.08; 95% CI, 1.02–1.16), and functional impairment measured by Lawton Index (aPR = 0.92; 95% CI, 0.84–0.99) were associated with HGS asymmetry (Table 3).

In the male group with asymmetry, 601 (75.03%) had multimorbidity, 438 (76.44%) had reduced muscle mass, 163 (64.43%) had polypharmacy, 218 (68.99%) had functional impairment, and 196 (80.00%) were at risk of falling. The male group with asymmetry showed a higher proportion of comorbidities, reduced muscle mass, polypharmacy, and functional impairment than the male group with symmetry did (all p < 0.05). In contrast, the female group with asymmetry showed a higher fall risk than the female group without asymmetry did (p < 0.05) (Table 4). Supplementary Table S1 presents the HGS values in the dominant and non-dominant hands according to the sarcopenic variables (SPPB scale score and calf circumference).

**DISCUSSION**

This cross-sectional study of older Peruvian adults presents three main findings. First, reduced muscle mass, fall risk, and functional impairment were independently associated with HGS asymmetry. Second, the male population with asymmetry showed a higher proportion of reduced muscle mass, multimorbidity, polypharmacy, and functional impairment, compared with those without asymmetry. Third, the female population with asymmetry showed a higher fall risk, compared with those without asymmetry.

In contrast to similar studies, we observed a higher prevalence of HGS asymmetry (51.7%, 45.2%, and 74.6%, respectively). Moreover, in our study, the prevalence of HGS asymmetry was higher in men (74.1%) compared with those reported in similar studies (38.3% and 47.8%). This difference could be explained by the inclusion of a Peruvian military-based population, in which more than half of the study participants were men and 75.1% were considered pre-frail and frail.

Reduced muscle mass is associated with HGS asymmetry. This specific measure is important because a previous study demonstrated that frailty increases as calf muscle mass decreases. As HGS asymmetry improves evaluations of muscle strength as part of the frailty criteria, our findings can lead to further evaluation and suggest that reduced calf muscle mass may be an alternative criterion of frailty. In addition, we observed an association between HGS asymmetry and fall risk. McGrath et al. reported that patients with HGS asymmetry have increased risks of recurrent falls and fractures. Furthermore, Go et al. showed a higher proportion of HGS asymmetry in the group with falls than in the group without falls. This finding is explained by the links among neuromuscular function, physical performance, and the process of development of impairment. Neuromuscular function deficiencies precede poor physical performance and mark disability onset. As individuals progress to advanced stages of the disabling process, their reduced physical performance limits the effectiveness of fall prevention interventions. Low neuromuscular function, measured by indicators, such as HGS and functional asymmetries, could represent disability.

Furthermore, according to the Lawton Index, functional impairment, which measures the ability to perform IADLs, was also associated with HGS asymmetry. Similar to our results, Mahoney et al. reported a greater likelihood of IADL limitations, such as

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**Table 3. Association between potential influencing factors and handgrip strength asymmetry**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Crude model</th>
<th>Adjusted model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>cPR (95% CI)</td>
<td>aPR* (95% CI)</td>
</tr>
<tr>
<td>Calf circumference (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal muscle mass</td>
<td>Ref.</td>
<td>Ref.</td>
</tr>
<tr>
<td>Reduced muscle mass</td>
<td>1.08 (1.01–1.16)</td>
<td>1.08 (1.01–1.15)</td>
</tr>
<tr>
<td>Functional Reach Test (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No falls risk</td>
<td>Ref.</td>
<td>Ref.</td>
</tr>
<tr>
<td>Falls risk</td>
<td>1.03 (0.97–1.10)</td>
<td>1.08 (1.02–1.16)</td>
</tr>
<tr>
<td>Polypharmacy (drugs)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–4</td>
<td>Ref.</td>
<td>-</td>
</tr>
<tr>
<td>≥ 5</td>
<td>0.86 (0.80–0.93)</td>
<td></td>
</tr>
<tr>
<td>Multimorbidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 2</td>
<td>Ref.</td>
<td>-</td>
</tr>
<tr>
<td>≥ 2</td>
<td>1.16 (1.01–1.34)</td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60–79</td>
<td>Ref.</td>
<td>-</td>
</tr>
<tr>
<td>≥ 80</td>
<td>0.97 (0.91–1.03)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>Ref.</td>
<td>-</td>
</tr>
<tr>
<td>Female</td>
<td>1.02 (0.96–1.08)</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 30</td>
<td>Ref.</td>
<td>-</td>
</tr>
<tr>
<td>≥ 30</td>
<td>1.02 (0.95–1.10)</td>
<td></td>
</tr>
<tr>
<td>PASE (points)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No sedentaryism</td>
<td>Ref.</td>
<td>-</td>
</tr>
<tr>
<td>Sedentaryism</td>
<td>0.98 (0.92–1.04)</td>
<td></td>
</tr>
<tr>
<td>SPPB (points)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unaltered physical performance</td>
<td>Ref.</td>
<td>-</td>
</tr>
<tr>
<td>Altered physical performance</td>
<td>0.96 (0.91–1.03)</td>
<td></td>
</tr>
<tr>
<td>Lawton Index (points)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No functional impaired</td>
<td>Ref.</td>
<td>Ref.</td>
</tr>
<tr>
<td>Functional impaired</td>
<td>0.97 (0.91–1.03)</td>
<td>0.92 (0.84–0.99)</td>
</tr>
</tbody>
</table>

BMI, body mass index; PASE, Physical Activity Scale for the Elderly; SPPB, Short Physical Performance Battery; PR, prevalence ratio; CI, confidence interval.

*Adjusted for age, sex, comorbidities, BMI, calf circumference, PASE, SPPB, Lawton Index and the Functional Reach Test.
transfer and toileting in individuals with HGS asymmetry. HGS asymmetry reflects reduced neural and motor system function, indicating a decline in overall neuromuscular function.\textsuperscript{31} This deterioration leads to physical and functional limitations, thereby increasing the impairment of IADLs.\textsuperscript{32}\textsuperscript{33}

Moreover, the link between hand and brain hemisphere dominance suggests that differences in HGS between hands may reflect lower functioning in a specific brain hemisphere.\textsuperscript{32}\textsuperscript{33}

A higher proportion of male patients with HGS asymmetry showed reduced muscle mass compared to females. HGS is a simple and accessible method to assess muscle strength because of its low cost and association with leg strength; moreover, this measure is also associated with sarcopenia as it reflects decreased muscle strength.\textsuperscript{34}\textsuperscript{35}

Men have greater strength and muscle mass than women do; however, this difference decreases with age.\textsuperscript{36} Because the sample in this study was composed of Navy veterans (older adults), their strength decrement was greater than that of the general population.

We observed an independent association between multimorbidity and HGS asymmetry and polypharmacy among men. Men are more likely to have heart disease, stroke, and diabetes compared to women; moreover, most men do not attend regular check-ups, and veterans report more morbidities.\textsuperscript{37}\textsuperscript{38}\textsuperscript{39} Moreover, in chronic kidney disease, muscle strength decreases due to diabetic neuropathy, myopathy in arterial insufficiency, or skeletal muscle impairment.\textsuperscript{40}\textsuperscript{41}\textsuperscript{42}

In addition, older adults with several diseases often consume multiple drugs, some of which can cause neuropathy or myopathy.\textsuperscript{43}\textsuperscript{44}

The sum of the above effects could lead to more adult men presenting with muscular or neurological damage, and therefore, HGS asymmetry. Parker et al.\textsuperscript{45} reported that HGS asymmetry is a predictor of IADL limitations, whereas Mahoney et al.\textsuperscript{22} observed an association between ADL and HGS asymmetry in both sexes. We observed this association only in men, which may be due to the composition of the sample and comorbidities.

In contrast, the female population with HGS asymmetry in this study presented a higher risk of falls. McGrath et al.\textsuperscript{26} reported that

| Table 4. Differences between handgrip strength symmetry and asymmetry by sex (n=1,468) |
|-----------------------------------------------|---------------|--------------|----------------|----------------|
| Variable                                      | Male          |               | Female         |               |
|                                               | Symmetry (n = 282) | Asymmetry (n = 581) | p-value | Symmetry (n = 187) | Asymmetry (n = 418) | p-value |
| Multimorbidity (%)                            |               |               |                |                |               |               | 0.304 |
| < 0.05*                                       |                |               |                |                |                |               |
| ≥ 0.05*                                       |                |               |                |                |                |               |
| Calf circumference (cm)                       |               |               |                |                |               |               | 0.229 |
| Normal muscle mass                            | 88 (30.34)    | 202 (69.66)   | 55 (27.64)     | 144 (72.36)   |                |                | 0.161 |
| Reduced muscle mass                           | 135 (23.56)   | 438 (76.44)   | 94 (23.15)     | 312 (76.85)   |                |                |               |
| Polypharmacy (drugs)                          | < 0.05*       |                |                |                |                |               |
| ≥ 0.05*                                       |                |               |                |                |                |               |
| Functional Reach test (cm)                    | 136 (25.19)   | 404 (74.81)   | 100 (27.78)    | 260 (72.22)   |                |                | 0.071 |
| Falls risk                                    | 87 (26.93)    | 236 (73.07)   | 49 (20.00)     | 196 (80.00)   |                |                |               |
| Lawton Index (points)                         | < 0.05*       |                |                |                |                |               |
| No functional impaired                        | 125 (22.85)   | 422 (77.15)   | 14 (36.84)     | 24 (63.16)    |                |                |               |
| Functional impaired                           | 98 (31.01)    | 218 (68.99)   | 135 (23.81)    | 432 (76.19)   |                |                |               |
| BMI (kg/m$^2$)                                |               |               |                |                |               |               | 0.824 |
| < 30                                          |                |               |                |                |                |               |
| ≥ 30                                          |                |               |                |                |                |               |
| Age (y)                                       | 0.379          |                |                |                |                |               |
| ≥ 70                                          |                |               |                |                |                |               |
| ≥ 80                                          |                |               |                |                |                |               |
| PASE (points)                                 | 0.227          |                |                |                |                |               |
| No sedentarism                                 |                |               |                |                |                |               |
| SEDentarism                                    |                |               |                |                |                |               |
| SPPB (points)                                  | 0.912          |                |                |                |                |               |
| Unaltered physical performance                |                |               |                |                |                |               |
| Altered physical performance                  |                |               |                |                |                |               |

Values are presented as number (%).

BMI, body mass index; PASE, Physical Activity Scale for the Elderly; SPPB, Short Physical Performance Battery.

*0.05 using a chi-square test.
for each 0.1 increase in the HGS asymmetry ratio, older adults were 26% more likely to fall in the future, with an increase in these odds as the degree of asymmetry increased. Similar findings were reported by Go et al. \(^{27}\) in an older Korean population, with an odds ratio of 1.89 for falls in a group with HGS asymmetry. In the study by Yang et al. \(^{40}\) in a Taiwanese population, weakness and reduced exercise duration were observed in a fall group, which also included a higher proportion of women. Falls can be attributed not only to musculoskeletal system alterations, as in the case of sarcopenia or osteoarthritis, but also to the complexity of the neuronal component, including functional deficiencies and disparity in the activation in brain hemispheres, which may influence brain networks related to cognitive function, as these effects are associated with limitations in ADLs. \(^{22,31,47-49}\) Therefore, further studies of the relationship between neuroanatomical changes and HGS asymmetry are required.

Our study has some limitations. First, as this was a cross-sectional study, we could not evaluate the causality between HGS asymmetry and associated factors; thus, a follow-up study is required to confirm our results. Second, HGS asymmetry is a new concept and has been analyzed using a previous database. However, as the measurement was performed using a standardized procedure, our results were not affected. Third, we did not exclude patients with neurological diseases or a history of upper-body surgery that could influence HGS asymmetry. Fourth, using a database from 2010 to 2016 may have included a population with access to technology and a different lifestyle, as this was before the coronavirus disease pandemic. Fifth, the external validity was limited because the results were obtained from a single center. Finally, we could not compare HGS and toe grip strength with the potential influencing variables as the latter is also a predictor of functional limitations in older adults. \(^{60}\) Despite these limitations, this is the first Latin American study to assess factors influencing HGS asymmetry in an older adult population.

In summary, the results of this study demonstrated the association of HGS asymmetry with reduced muscle mass, fall risk, and functional impairment in older adults. Furthermore, HGS asymmetry was differentially related to multimorbidity, reduced muscle mass, functional impairment, and polypharmacy only in men. We also observed a significant association with an increased risk of falls among women. Our findings suggest that the evaluation, management, and rehabilitation of older adults should be comprehensive and specific to the damaged organs or limbs. HGS asymmetry should be measured in conjunction with other geriatric assessments to evaluate health outcomes in older adults. Moreover, these findings may inform a more accurate approach for patients, improve health promotion and prevention, and determine specific interventions aimed at preserving muscle strength to curb functional limitations in older adults. These results also reveal the opportunity for interventions beyond biomarkers or yes/no disease diagnosis.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

None.

AUTHOR CONTRIBUTIONS

Conceptualization, AZ, JFP, FMRC; Investigation, AZ, RPV, KCC, RCC, DCM, PGR, WGB; Methodology, AZ, RPV; Formal analysis, AZ, RPV; Data Curation, AZ, RPV, KCC, RCC, DCM, PGR, WGB; Writing–original draft, AZ, RPV, KCC, RCC, DCM, PGR, WGB, JFP, FMRC; Writing–review & editing, AZ, RPV, KCC, RCC, DCM, PGR, WGB, JFP, FMRC; Visualization, AZ, JFP, FMRC; Project administration, AZ, JFP, FMRC; Resources, JFP, FMRC; Supervision, JFP, FMRC.

DATA AVAILABILITY

Data are available at the following link: https://osf.io/df7tn/files/?view_only=.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4235/agmnr.23.0194.

REFERENCES

4. Wang DX, Yao J, Zirek Y, Rejniierse EM, Maier AB. Muscle mass, strength, and physical performance predicting activities of daily
Association of Phase Angle Dynamics with Sarcopenia and Activities of Daily Living in Osteoporotic Fracture Patients

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Background: This study aimed to determine whether changes in phase angle during rehabilitation are associated with clinical outcomes such as activities of daily living (ADL), skeletal muscle mass index (SMI), and strength in patients with osteoporotic fractures. Methods: This retrospective observational study included patients with osteoporotic fractures admitted to convalescent rehabilitation wards. Changes in phase angle were defined as the difference between the phase angle values at discharge and on admission. The primary outcome was the Functional Independence Measure motor (FIM-motor) score at discharge. The secondary outcomes were SMI and handgrip strength at discharge. We used multivariate analysis to adjust for confounding factors and examine the association between changes in the phase angle and outcomes. Results: We analyzed a total of 115 patients (97 women, mean age of 81.0±10.0 years), with a median change in phase angle of 0° during hospitalization. We observed increased phase angles in 49 patients (43%), with a median increase of 0.2°. Multiple regression analysis showed that changes in phase angle were independently associated with FIM-motor score at discharge (β=0.238, p=0.027). Changes in phase angle were not significantly associated with SMI (β=0.059, p=0.599) or handgrip strength (β=-0.032, p=0.773) at discharge. Conclusion: An increased phase angle during rehabilitation was positively associated with ADL improvement in patients with osteoporotic fractures. These findings may help clinicians make informed decisions regarding patient care and treatment strategies for better outcomes.

Key Words: Osteoporotic fractures, Body composition, Prognosis, Rehabilitation

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INTRODUCTION

The phase angle calculated using bioelectrical impedance analysis (BIA) is of interest as a nutritional indicator and a marker of muscle quality. The phase angle is also an indicator of cellular health and reflects cell membrane integrity and cellular function, with a lower value indicating poor cellular function and malnutrition. Cutoff values for phase angle have been reported for diseases including stroke, heart failure, and cancer. As an indicator of muscle quality, the phase angle has demonstrated high accuracy in detecting sarcopenia and cancer, and is correlated with skeletal muscle mass and strength in older hospitalized patients. The usefulness of the phase angle in predicting prognosis has also been demonstrated in rehabilitation research. The admission phase angle is an independent predictor of discharge physical function in patients with stroke in acute-care settings, and discharge physical function and swallowing function in post-acute rehabilitation. In addition, phase angle is independently associated with gait and balance at discharge in patients with hip fractures. Therefore, the phase angle may be useful for predicting rehabilitation outcomes.

However, the phase angle lacks sufficient evidence for clinical application. Few reports have described the impact of changes in...
phase angle on activities of daily living (ADL), skeletal muscle mass, and muscle strength in patients with osteoporotic fractures. Osteoporotic fractures occur frequently in older adults, with an estimated 9 million cases occurring annually worldwide. Furthermore, osteoporotic fractures negatively affect ADL and quality of life. Recently, the phase angle has also been studied in patients with hip fractures and was associated with quality of life and the ability to walk and balance. Moreover, changes in phase angle may be useful for predicting clinical outcomes in different populations. Hence, changes in phase angle may be useful for predicting clinical outcomes in patients with osteoporotic fractures is scarce.

Therefore, we examined whether changes in phase angle during rehabilitation were associated with ADL, muscle mass, and strength in patients with osteoporotic fractures.

MATERIALS AND METHODS

Participants and Setting
This was a single-center, cross-sectional study of patients admitted to a private hospital in Japan with a 116-bed convalescent rehabilitation ward. The study population consisted of patients with osteoporotic fractures admitted to the convalescent rehabilitation ward between August 2017 and July 2022. The presence of osteoporosis was determined from the medical records of all patients with a history of osteoporosis. Osteoporotic fractures were defined as non-traumatic fractures caused by low external forces, such as falls from less than standing height. Patients with contraindications to bioelectrical impedance techniques, such as pacemakers, those with artificial joint insertions (defined as previous artificial joint insertion or those with artificial joint insertion after a recent fracture) that could affect the results of bioelectrical impedance techniques, and those with missing data on the survey items were excluded.

Data Collection
On admission, patient information including age, sex, fracture site (vertebral, hip, pelvic, and other fractures), surgery, onset of admission, Charlson Comorbidity Index (CCI), and total number of medications was collected from medical records. Information collected on admission included Mini-Mental State Examination (MMSE) score, handgrip strength, Food Intake Level Scale (FILS) score, body mass index (BMI), energy intake, Functional Independence Measure (FIM) score on admission, days to body composition measurement, skeletal muscle index (SMI), and phase angle. The length of hospital stay, rehabilitation duration, rehabilitation time, handgrip strength, FIM score, SMI, and phase angle were recorded at discharge. Grip strength was defined as the maximum of two measurements taken twice on each side in the standing or sitting position using a grip strength meter (TKKS001; Takei Scientific Instruments Co. Ltd., Tokyo, Japan). Energy intake was calculated from the intake of staple foods and side dishes, each rated by nurses on a 5-point scale. If nutritional supplements were used, the dietary supplement intake was checked by a dietician and added to the energy intake. The FIM on admission was assessed within 24 hours of admission; whereas, the FIM on discharge was assessed by nurses and care workers on the day before or on the day of discharge. The average daily rehabilitation time was calculated by dividing the total time spent on physiotherapy, occupational therapy, and speech therapy during the hospital stay by the length of stay.

Phase Angle
Body composition assessment included the phase angle and SMI were calculated by BIA using a body composition analyzer (InBody S10; InBody, Tokyo, Japan). This device can be used for patients who are unable to maintain a standing or sitting position, or who are bedridden. The patients were asked to refrain from exercise for one hour before measurement and to lie in a resting position. All measured limbs were positioned in a unified back-lying posture. Body composition was measured within 48 hours of admission and discharge. Phase angle was measured from the resistance (R) and reactance (Xc) of the right hemisphere and was calculated using the following formula:

\[ \text{Phase angle} = \arctangent \left( \frac{\text{Xc}}{\text{R}} \right) \times 180/\pi. \]

In this equation, a 50 kHz resistance and reactance were used. Cutoff values for phase angle have been reported for diseases including stroke, heart failure, and cancer. However, the cutoff values for phase angle in patients with osteoporotic fractures, the subject of this study, have not been reported. Some studies stratified the median phase angle as the cutoff value in participants for whom previous research is lacking. Therefore, we also classified the participants into low and normal baseline phase angle groups using median values. The difference between the phase angles at discharge and on admission was calculated and defined as the change in phase angle during hospitalization (phase angle at discharge – phase angle on admission). The SMI was calculated as limb muscle mass divided by height squared (kg/m²).
Outcome
The primary outcome was the FIM motor score (FIM-motor) at discharge, which is used to quantify the amount of help patients receive with ADL. The FIM-motor consists of 13 motor items and five cognitive items, each scored on a seven-point scale from 1 to 7, with a total score of 18–126. The FIM is a valid and reliable assessment method. The secondary outcomes were SMI and handgrip strength at discharge.

Sample Size Calculation
The standard deviation of the FIM-motor score upon admission for patients with fractures in the convalescent rehabilitation ward was 16. If the true difference between the groups was 14, an estimated minimum of 51 patients in each group was needed to reject the null hypothesis with a power of 0.95 and an error of 0.05.

Statistical Analysis
Continuous variables are expressed as mean ± standard deviation for parametric data and median (interquartile range) for non-parametric data. Nominal variables are expressed as numerical values (%). We performed univariate analysis on the changes in phase angle from admission to discharge, dividing the patients into two groups: increased phase angle and decreased phase angle. Comparisons between the two groups were analyzed using t-test, Mann-Whitney U test, χ² test, or Fisher exact test, depending on the variable type. The following tests were used, depending on the type of variable.

Multiple regression analysis was used to determine whether the changes in phase angle were independently associated with FIM-motor score, handgrip strength, and SMI at discharge. We performed multivariate analysis using three models: all patients, patients with normal phase angles, and patients with low phase angles. The results of multiple regression analysis of the FIM-motor score, handgrip strength, and SMI at discharge for the groups with normal phase angles.

RESULTS
In total, 186 patients with osteoporotic fractures were admitted to our hospital during the study period. Of these, 115 patients were included in the analysis after excluding those with pacemaker implants (n = 9), artificial joint insertions (n = 43), or missing survey item data (n = 19) (Fig. 1).

Table 1 presents the baseline patient characteristics. The mean age of the patients was 81.0 ± 10.0 years, with 18 men and 97 women. The median baseline phase angles were 4.1° and 3.6° in men and women, respectively. When comparing the two groups, patients of both sexes with a low baseline phase angle were older and had lower handgrip strength, BMI, and SMI on admission compared with those with a normal phase angle. These patients also had a higher incidence of sarcopenia. Among women, those with a low baseline phase angle had lower FIM-motor, FIM-cognitive, and MMSE scores on admission compared with those with normal phase angles.

Table 2 shows the results of the univariate analyses of FIM-motor score, handgrip strength, and SMI at discharge for the groups with increased and decreased phase angles during hospitalization according to sex. The median change in the overall phase angle was 0°. In the increased and decreased phase angle groups, the changes were 0.2° and -0.2°, respectively. Univariate analysis of the increased and decreased phase angle groups showed no significant differences in FIM-motor score, handgrip strength, or SMI at discharge.

The results of multiple regression analysis of the FIM-motor score, SMI, and handgrip strength at discharge, adjusted for potential confounders, are shown in Table 3. We performed multivariate

Fig. 1. Flowchart of participant screening, inclusion criteria, and follow-up.
# Table 1. Baseline characteristics of participants

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n = 115)</th>
<th>Men (n = 18)</th>
<th>Women (n = 97)</th>
<th>p-value</th>
<th>Low phase angle on admission, ≤ 4.1 (n = 10)</th>
<th>Normal phase angle on admission, &gt; 4.1 (n = 8)</th>
<th>p-value</th>
<th>Low phase angle on admission, ≤ 3.6 (n = 55)</th>
<th>Normal phase angle on admission, &gt; 3.6 (n = 42)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>81.0 ± 10.0</td>
<td>83.2 ± 11.0</td>
<td>65.0 ± 16.5</td>
<td>0.013*</td>
<td>83.7 ± 8.1</td>
<td>80.0 ± 7.3</td>
<td>0.022*</td>
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<tr>
<td>Sex</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Men</td>
<td>18 (15.7)</td>
<td>-</td>
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<tr>
<td>Women</td>
<td>97 (84.3)</td>
<td>-</td>
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<tr>
<td>Fracture site</td>
<td></td>
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<td></td>
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<tr>
<td>Vertebral compression fracture</td>
<td>47 (40.9)</td>
<td>7 (70)</td>
<td>5 (62.5)</td>
<td>0.397</td>
<td>15 (27.3)</td>
<td>20 (47.6)</td>
<td>0.003**</td>
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</tr>
<tr>
<td>Hip fracture</td>
<td>51 (44.3)</td>
<td>3 (30)</td>
<td>1 (12.5)</td>
<td></td>
<td>35 (63.6)</td>
<td>12 (28.6)</td>
<td></td>
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<tr>
<td>Pelvic fracture</td>
<td>9 (7.8)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
<td>4 (7.3)</td>
<td>5 (11.9)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Other</td>
<td>8 (7)</td>
<td>0 (0)</td>
<td>2 (25)</td>
<td></td>
<td>1 (1.8)</td>
<td>5 (11.9)</td>
<td></td>
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<tr>
<td>Surgery</td>
<td>60 (52.2)</td>
<td>4 (40)</td>
<td>3 (37.5)</td>
<td>1</td>
<td>36 (65.5)</td>
<td>17 (40.5)</td>
<td>0.023*</td>
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</tr>
<tr>
<td>Onset-admission (day)</td>
<td>20 (15–29)</td>
<td>18.5 (12.5–47.5)</td>
<td>21 (9.8–30)</td>
<td>0.592</td>
<td>25 (17–31)</td>
<td>18 (13.5–24.8)</td>
<td>0.025*</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Days to body composition measurement (day)</td>
<td>20 (15–29)</td>
<td>18.5 (12.5–47.5)</td>
<td>21 (9.8–30)</td>
<td>0.592</td>
<td>25 (17–31)</td>
<td>18 (13.5–24.8)</td>
<td>0.018*</td>
<td></td>
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<tr>
<td>FIM-motor on admission</td>
<td>50 (36–64.5)</td>
<td>48.5 (31.3–58.8)</td>
<td>68 (41.3–73)</td>
<td>0.075</td>
<td>46 (31–59)</td>
<td>58.5 (46.3–71.5)</td>
<td>0.001**</td>
<td></td>
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</tr>
<tr>
<td>FIM-cognitive on admission</td>
<td>34 (27–35)</td>
<td>35 (33.5–35)</td>
<td>34 (29.5–35)</td>
<td>0.329</td>
<td>32 (24–35)</td>
<td>35 (31–35)</td>
<td>0.012*</td>
<td></td>
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<tr>
<td>MMSE on admission</td>
<td>26 (21–30)</td>
<td>24 (23–26)</td>
<td>29 (26–30)</td>
<td>0.064</td>
<td>23 (19–28)</td>
<td>29 (23.3–30)</td>
<td>&lt; 0.001***</td>
<td></td>
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<tr>
<td>CCI</td>
<td>1 (0–2)</td>
<td>2 (1–2)</td>
<td>1 (0–1.3)</td>
<td>0.129</td>
<td>1 (0–2)</td>
<td>0 (0–2)</td>
<td>0.104</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Handgrip strength on admission (kg)</td>
<td>15 (11.4–18.7)</td>
<td>18 (15–23.9)</td>
<td>34.3 (25–36.4)</td>
<td>0.009**</td>
<td>12 (8.8–15)</td>
<td>16 (14.4–19)</td>
<td>&lt; 0.001***</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FILS on admission</td>
<td>10 (8–10)</td>
<td>9 (7–10)</td>
<td>10 (10–10)</td>
<td>0.070</td>
<td>10 (7–10)</td>
<td>10 (10–10)</td>
<td>0.001**</td>
<td></td>
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</tr>
<tr>
<td>BMI on admission (kg/m²)</td>
<td>21.7 (18.8–23.8)</td>
<td>22.1 (19–23.2)</td>
<td>25.8 (24.3–26)</td>
<td>0.021*</td>
<td>19.9 (17.1–22.1)</td>
<td>22.8 (21.5–24)</td>
<td>&lt; 0.001***</td>
<td></td>
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</tr>
<tr>
<td>SMI on admission (kg/m²)</td>
<td>5.1 (4.2–5.8)</td>
<td>5.9 (5.5–6.2)</td>
<td>7.7 (7.1–7.9)</td>
<td>0.002**</td>
<td>4.2 (3.6–5.1)</td>
<td>5.4 (4.9–6)</td>
<td>&lt; 0.001***</td>
<td></td>
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</tr>
<tr>
<td>Sarcopenia</td>
<td>86 (74.8)</td>
<td>9 (90)</td>
<td>2 (25)</td>
<td>0.013*</td>
<td>49 (89.1)</td>
<td>26 (61.9)</td>
<td>0.003**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of hospital stay (day)</td>
<td>78 (58.5–86)</td>
<td>85.5 (79.8–87.8)</td>
<td>59 (41.3–75.8)</td>
<td>0.050</td>
<td>79 (67–87)</td>
<td>69 (54.3–85)</td>
<td>0.125</td>
<td></td>
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</tr>
<tr>
<td>Duration of rehabilitation time (min/day)</td>
<td>77 (57.5–85)</td>
<td>84.5 (78.8–86.8)</td>
<td>58 (40.3–74.8)</td>
<td>0.050</td>
<td>78 (66–86)</td>
<td>68 (53.3–84)</td>
<td>0.125</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rehabilitation energy intake (kcal/kg/day)</td>
<td>1,400 (1,000–1,500)</td>
<td>1,454 (1,374–1,600)</td>
<td>1,600 (1,232–1,650)</td>
<td>0.857</td>
<td>1,400 (1,147–1,400)</td>
<td>1,400 (1,211.3–1,500)</td>
<td>0.056</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of total medications</td>
<td>8 (6–11)</td>
<td>10.5 (7.5–12.8)</td>
<td>10 (6.8–14.5)</td>
<td>0.929</td>
<td>8 (6–11)</td>
<td>8 (6–10.8)</td>
<td>0.841</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phase angle on admission</td>
<td>3.6 (3.1–4.1)</td>
<td>3.7 (3.1–4)</td>
<td>5.3 (4.5–5.5)</td>
<td>&lt; 0.001***</td>
<td>3.1 (2.8–3.5)</td>
<td>4 (3.8–4.4)</td>
<td>&lt; 0.001***</td>
<td></td>
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</tr>
</tbody>
</table>

Values are presented as mean ± standard deviation or number (%) or median (interquartile range). FIM, Functional Independence Measure; MMSE, Mini Mental State Examination; CCI, Charlson Comorbidity Index; FILS, Food Intake Level Scale; BMI, body mass index; SMI, skeletal muscle mass index.

*p < 0.05, **p < 0.01, ***p < 0.001. 
analysis using three models according to the baseline phase angle values. Model 1 included all patients, model 2 included patients with low baseline phase angle values, and model 3 included patients with normal baseline phase angle values. We observed no multicollinearity between variables in any model. In model 1, changes in phase angle during hospitalization were independently and positively associated with discharge FIM-motor score ($\beta = 0.238$, $p = 0.027$). Changes in phase angle during hospitalization were not significantly associated with SMI ($\beta = 0.059$, $p = 0.599$) or handgrip strength ($\beta = 0.032$, $p = 0.773$). Model 2 was similar to model 1, with changes in phase angle during hospitalization showing an independent and positive association with FIM-motor score at discharge ($\beta = 0.398$, $p = 0.006$) and not with SMI ($\beta = 0.100$, $p = 0.519$) or handgrip strength ($\beta = 0.047$, $p = 0.763$). In model 3, changes in phase angle during hospitalization were not significantly associated with FIM-motor score ($\beta = 0.189$, $p = 0.328$), SMI ($\beta = 0.190$, $p = 0.326$), or handgrip strength ($\beta = 0.006$, $p = 0.972$) at discharge (Table 4).

The results of changing the outcome to “change in FIM,” “change in SMI,” and “change in handgrip strength” are shown in Supplementary Table S1. The results of the multiple regression analysis adjusted for potential confounders showed that in model 1, changes in phase angle during hospitalization were not significantly associated with changes in FIM-motor score ($\beta = 0.179$, $p = 0.114$), SMI ($\beta = 0.150$, $p = 0.169$) or handgrip strength ($\beta = -0.027$, $p = 0.804$) at discharge. In model 2, changes in phase angle during hospitalization were not significantly associated with changes in FIM-motor score ($\beta = 0.302$, $p = 0.05$), SMI ($\beta = 0.035$, $p = 0.822$), or handgrip strength ($\beta = 0.043$, $p = 0.779$) at discharge. In model 3, changes in phase angle during hospitalization were not significantly associated with changes in FIM-motor score ($\beta = 0.065$, $p = 0.730$), SMI ($\beta = 0.171$, $p = 0.358$), or handgrip strength ($\beta = 0.243$, $p = 0.208$) at discharge. Therefore, the original data are of high clinical value and this is the conclusion of the present study.

**DISCUSSION**

This study investigated the association between changes in phase angle during rehabilitation and outcomes including ADL, skeletal muscle mass, and muscle strength at discharge in patients with osteoporotic fractures. Three notable clinical findings were observed: first, changes in phase angle were independently and positively associated with improvements in ADL. This association was stronger in patients with a lower baseline phase angle than in those without. Second, changes in phase angle were not statistically associated with increases in SMI or handgrip strength. Third, 43% of the patients had an increased phase angle during hospitalization, with a median increase of 0.2°. The three results are discussed below.

Changes in phase angle were positively associated with improvements in ADL in patients with osteoporotic fractures. This association was stronger in patients with lower baseline phase angles. Because the phase angle reflects nutritional status and muscle quality, it is reasonable to assume that an increased angle is closely associated with improved nutritional status and muscle quality. Furthermore, our findings support those of previous studies showing that improved nutritional status may lead to greater improvement in ADL in patients receiving rehabilitation, especially those with hip fracture. Improvements in sarcopenia during hospitalization are reportedly independently and positively associated with improvements in ADL. However, poor muscle quality is associated with worse ADL. In addition, the association between increased phase angle and improved ADL in this study was stronger in patients with a lower phase angle at admission. A low phase angle is associated with poor cellular health and increased morbidity, suggesting that it may indicate the overall patient health status. Therefore, patients with a lower baseline phase angle may experience greater improvements in physical function and health status compared with patients with a normal baseline phase angle receiving comprehensive interventions such as early rehabilitation.
Table 3. Univariate analyses of outcomes between increase phase angle and decrease phase angle groups in women

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n = 97)</th>
<th>Increase phase angle group (n = 39)</th>
<th>Decrease phase angle group (n = 56)</th>
<th>p-value</th>
<th>Increase phase angle group (n = 26)</th>
<th>Decrease phase angle group (n = 29)</th>
<th>p-value</th>
<th>Increase phase angle group (n = 13)</th>
<th>Decrease phase angle group (n = 29)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIM-motor at discharge</td>
<td>84.0 (67.5–88.5)</td>
<td>83.5 (74.3–87.8)</td>
<td>0.754</td>
<td>77.5 (65.0–85.5)</td>
<td>80.0 (68.0–84.0)</td>
<td>0.980</td>
<td>88.0 (87.0–90.0)</td>
<td>87.0 (83.0–89.0)</td>
<td>0.106</td>
<td></td>
</tr>
<tr>
<td>SMI at discharge (kg/m²)</td>
<td>5.1 (4.3–5.6)</td>
<td>5.1 (4.3–5.5)</td>
<td>0.941</td>
<td>4.6 (4.0–5.3)</td>
<td>4.3 (3.9–5.3)</td>
<td>0.643</td>
<td>5.6 (5.2–5.9)</td>
<td>5.4 (5.1–5.7)</td>
<td>0.390</td>
<td></td>
</tr>
<tr>
<td>Handgrip strength at discharge (kg)</td>
<td>15.0 (11.5–17.5)</td>
<td>15.0 (12.0–18.0)</td>
<td>0.848</td>
<td>12.8 (11.0–15.4)</td>
<td>13.5 (9.0–17.0)</td>
<td>0.946</td>
<td>17.0 (16.0–20.0)</td>
<td>16.5 (14.0–19.5)</td>
<td>0.333</td>
<td></td>
</tr>
</tbody>
</table>

Values are presented as median (interquartile range).
FIM, Functional Independence Measure; SMI, skeletal muscle mass index.

Table 4. Multiple linear regression analysis of patient outcomes for changes in phase angle

<table>
<thead>
<tr>
<th>Variable</th>
<th>FIM-motor at discharge</th>
<th>SMI at discharge</th>
<th>Handgrip strength at discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>β</strong></td>
<td>B (95% CI)</td>
<td>B (95% CI)</td>
<td>B (95% CI)</td>
</tr>
<tr>
<td><strong>Model 1</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Changes in phase angle</td>
<td>0.238</td>
<td>9.755 (1.076 to 18.434)</td>
<td>0.027*</td>
</tr>
<tr>
<td>Propensity score</td>
<td>-0.433</td>
<td>-28.078 (-41.804 to -14.353)</td>
<td>&lt; 0.001***</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Changes in phase angle</td>
<td>0.398</td>
<td>20.703 (5.901 to 35.505)</td>
<td>0.006**</td>
</tr>
<tr>
<td>Propensity score</td>
<td>-0.529</td>
<td>-31.436 (-48.333 to -14.538)</td>
<td>&lt; 0.001**</td>
</tr>
<tr>
<td><strong>Model 3</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Changes in phase angle</td>
<td>0.189</td>
<td>5.487 (-5.684 to 16.660)</td>
<td>0.328</td>
</tr>
<tr>
<td>Propensity score</td>
<td>-0.104</td>
<td>-3.564 (-16.702 to 9.572)</td>
<td>0.587</td>
</tr>
</tbody>
</table>

Model 1 indicates total patients; Model 2, patients with low phase angle on admission; Model 3, patients with normal phase angle on admission. Propensity score were calculated for the following variables: age, sex, fracture site, surgery, onset-admission, FIM-motor on admission, FIM-cognitive on admission, MMSE on admission, CCI, handgrip strength on admission, FILS on admission, BMI on admission, SMI on admission, energy intake at admission, total number of medications, and phase angle at admission.

FIM, Functional Independence Measure; MMSE, Mini-Mental State Examination; CCI, Charlson Comorbidity Index; FILS, Food Intake Level Scale; BMI, body mass index; SMI, skeletal muscle mass index; CI, confidence interval.
*p<0.05, **p<0.01, ***p<0.001.

The phase angle is more sensitive to changes than skeletal muscle mass. The present study is novel and clinically significant. The phase angle is more sensitive to changes than skeletal muscle mass. Therefore, further high-quality studies are required to verify this association.

In this study, 43% of patients experienced an increase in phase angle during rehabilitation, with a median increase of 0.2°. Few studies have examined changes in phase angle over time; thus, the present study is novel and clinically significant. The phase angle is more sensitive to changes than skeletal muscle mass.

### Discussion

Nutritional status, oral health, and polypharmacy assessment and management. Furthermore, owing to the ceiling effect of the phase angle scores, patients with a lower baseline phase angle may demonstrate more pronounced improvements in phase angle over the study period than those without. This suggests that phase angle may be an important indicator for early screening and intervention in patients with osteoporotic fractures, especially in those with a low phase angle. These findings suggest that the therapeutic effects of nutrition and exercise are more likely to be reflected in changes in skeletal muscle mass or handgrip strength. The possible explanations for this finding include the fact that changes in skeletal muscle mass and handgrip strength were not the primary outcomes of this study and that the study design and adjustment for confounders in the multivariate analysis were designed based on the primary outcome. Thus, although this association was not statistically significant, this does not mean no association was present. Indeed, recent research has shown a positive association between changes in phase angle and increases in muscle mass and strength in post-stroke patients. Therefore, further high-quality studies are required to verify this association.
in older adults. Resistance training has been incorporated into the rehabilitation programs for patients with fractures to prevent bone loss, reduce fall risk, and prevent or improve sarcopenia. Additionally, systematic reviews and meta-analyses have shown that nutritional interventions for patients with cancer can change their phase angles. These findings suggest that rehabilitation, including resistance training, nutritional management, or their combination, may have a greater potential to improve the phase angle. Therefore, to maximize improvement of patient outcomes, careful observation of the phase angle and its trends, rather than routine and conventional treatment, may help facilitate high-quality treatment, including personalized nutrition and exercise, in a multidisciplinary manner.

This study has several limitations, the first of which is its single-center design, which limits its generalizability. Future multicenter studies are needed to confirm these findings. Second, as a cross-sectional study, it was not possible to obtain detailed information regarding the influences of preoperative ADL, presence or absence of pain, type of rehabilitation provided during hospitalization, and changes in energy intake on the results. Further high-quality prospective studies adjusting for these confounders are warranted.

In conclusion, changes in phase angle during rehabilitation were independently and positively associated with improvements in ADL in patients with osteoporotic fractures. Furthermore, this association was stronger in patients with a low baseline phase angle compared with patients without. Therefore, changes in phase angle are a useful indicator of functional outcomes in patients with osteoporotic fractures and may be used to improve discharge outcomes.

ACKNOWLEDGMENTS
We express our deepest gratitude to the participants and organizations that collaborated on this study.

CONFLICT OF INTEREST
The researchers claim no conflicts of interest.

FUNDING
None.

AUTHOR CONTRIBUTIONS
Conceptualization, YI, YY; Data curation, YI, YY; Investigation, YI, YY; Methodology, YI, YY; Supervision, YY; Writing–original draft, YI; Writing–review & editing, YI, YY, FN, AM, HW.

SUPPLEMENTARY MATERIALS
Supplementary materials can be found via https://doi.org/10.4235/agmr.23.0212.

REFERENCES


Effects of Different Extubation Strategies on Atelectasis in Older Adults after Major Abdominal Surgery: A Prospective Randomized Controlled Trial

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Department of Anesthesiology and Critical Care, All India Institute of Medical Sciences, Jodhpur, India

Background: Older patients are particularly vulnerable to age-related respiratory changes. This prospective randomized controlled trial studied the effects of high and low fractions of inspired oxygen (FiO₂) with the recruitment maneuver (RM) during extubation on lung atelectasis postoperatively in older patients undergoing major abdominal surgery. Methods: We randomized a total of 126 patients aged >60 years who underwent both elective and emergency major abdominal surgeries and met the inclusion criteria into three groups (H, HR, and LR) using computer-generated block randomization. Group H received high FiO₂ (1), Group HR received high FiO₂ (1) with RM followed by a positive end-expiratory pressure of 5 cm H₂O, and Group LR received low FiO₂ (0.4) with RM followed by a positive end-expiratory pressure of 5 cm H₂O 10 minutes before extubation. Oxygenation and atelectasis were measured using the arterial partial pressure of oxygen (PaO₂)/FiO₂ ratios and lung ultrasound score. Postoperative pulmonary complications were recorded up to 24 hours postoperatively. Results: The mean PaO₂/FiO₂ at 30 minutes post-extubation was significantly higher in Groups LR and HR compared to that in Group H (390.71 ± 29.55, 381.97 ± 24.97, and 355.37 ± 31.70; p<0.001). In the immediate postoperative period, the median lung ultrasound score was higher in Group H than that in Groups LR and HR (6 [5–7], 3 [3–5], and 3.5 [2.25–4.75]; p<0.001). The incidence of oxygen desaturation and oxygen requirements was higher in Group H during the postoperative period. Conclusion: The RM before extubation is beneficial in reducing atelectasis and postoperative pulmonary complications, irrespective of the FiO₂ concentration used in older adults undergoing major abdominal surgeries. (Trial registration number: Reference No. CTRI/2022/04/042115; date of CTRI registration 25/02/2022; and date of enrolment of the first research participant 05/05/2022)

Key Words: Atelectasis, Airway extubation, Elderly, Frail older adults, Surgery

INTRODUCTION

Older patients have altered respiratory physiology owing to age-related changes and decreased physical activity, leading to decreased physical and pulmonary reserves. In this population, the lungs undergo changes with respect to respiratory mechanics, gas exchange, and immune function. Decreased immunity, upper airway tone, and ineffective cough reflexes increase the risk of postoperative pulmonary complications (PPCs). At the molecular level, alterations in collagen levels lead to alveolar duct dilation and the loss of lung recoil, decreased tidal volume, forced expiratory volume in 1 second, and decreased forced vital capacity, along with increased residual volume and respiratory rate. These patients are at increased risk of developing postoperative lung complications after major abdominal surgeries under general anesthesia, as anesthetic drugs can cause decreased respiratory muscle tone and abolish the sigh reflex. Open upper abdominal surgeries impact ventilation, as they can affect diaphragm function and cause reduced motility, thereby decreasing ventilation in dependent zones and atelectasis. During major laparoscopic abdominal surgeries, the creation of a
pneumoperitoneum causes decreased compliance. Additionally, positioning during surgery, such as in the Trendelenburg position, with increased intra-abdominal pressure due to artificial pneumoperitoneum, exacerbates the problem by causing lung base atelectasis. Intraoperatively, this problem leads to decreased oxygenation, which can be overcome by using a high fraction of inspired oxygen; however, this in turn can lead to absorption atelectasis. Absorption atelectasis occurs due to the rapid movement of oxygen into the capillaries, which is not compensated for by the diffusion of gases back from the capillaries into the alveoli at the same rate.

A high fraction of inspired oxygen is routinely administered during extubation. However, this may aggravate existing atelectasis and increase the risk of postoperative lung complications in older patients. The recruitment maneuver (RM) involves the use of positive inspiratory airway pressure to recruit collapsed alveoli to increase available alveolar units participating in gas exchange, decrease intrapulmonary shunts, increase lung compliance, and improve oxygenation. Ning et al. reported that RM is safe in older patients and significantly improves oxygenation after major surgeries. Several studies have compared the effects of high and low fractions of inspired oxygen (FiO₂) in different age groups and non-abdominal surgeries; however, few studies have compared high and low FiO₂ with RM followed by the application of positive end-expiratory pressure (PEEP) in older patients undergoing abdominal surgery.

In this study, we hypothesized that a low FiO₂ (0.4) during extubation with RM would decrease the incidence of lung atelectasis postoperatively in older patients undergoing major abdominal surgeries as compared to a high FiO₂ (1) with or without RM.

**MATERIALS AND METHODS**

After obtaining institutional ethics committee approval (No. AIIMS/IEC/2021/3738) on August 31, 2021, and registering the trial in the Clinical Trials Registry-India (CTRI; Reference No. CTRI/2022/04/042115, date of registration April 25, 2022), written informed consent was obtained from all patients who fulfilled the inclusion criteria. We conducted this study at a single academic tertiary care hospital between April 2022 and April 2023, adhering to the applicable Consolidated Standards of Reporting Trials (CONSORT) guidelines. This study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.

This study included patients aged ≥ 60 years who underwent elective and emergency major abdominal surgery. Major abdominal surgery included procedures lasting over 2 hours or with anticipated blood loss exceeding 500 mL. We excluded patients with body mass index > 30 kg/m², severe cardiopulmonary disease, hemodynamic instability, and cerebrovascular disease.

We randomly allocated the patients at a ratio of 1:1:1 into three treatment groups—H: high FiO₂ (1) alone; HR: high FiO₂, RM, and PEEP; and LR: low FiO₂ (0.4), RM, and PEEP—based on computer-generated block randomization. The use of sealed, opaque envelopes allowed the concealment of allocations handed to the respective treating anesthesiologist. All patients fasted overnight and received oral alprazolam (0.25 mg) the night before surgery. In the operating theater, the patients were monitored using a three-lead electrocardiogram, non-invasive blood pressure measurement, and pulse oximetry. Electrodes for Bispectral Index and a train-of-four monitoring were attached (Drager Primus Anesthesia Device Monitor; Drager Medical Systems Inc., Denver, MA, USA). A standard anesthesia protocol was followed for all patients. After 3 minutes of pre-oxygenation with 100% oxygen, general anesthesia was induced with fentanyl (2 µg/kg), propofol (2–3 mg/kg), and atracurium (0.5 mg/kg). Anesthesia was maintained using isoflurane, 40% oxygen in the air, and atracurium boluses. The lungs were ventilated using volume-controlled ventilation with a tidal volume of 6–8 mL/kg ideal body weight, a respiratory rate of 12–14 breaths/min, and a PEEP of 5 cm H₂O. The tidal volume and respiratory rates were adjusted to maintain an end-tidal carbon dioxide concentration of 35–40 mmHg and an oxygen saturation of 95%–100%. In laparoscopic surgery, CO₂ was insufflated into the peritoneal cavity until the intra-abdominal pressure reached 12 mmHg. During surgery, all patients received 5–8 mL/kg/hr Ring-er’s lactate. An epidural catheter was inserted before induction in all patients, and 0.2% ropivacaine with fentanyl (2 µg/mL) was administered at a rate of 5 mL/hr and continued postoperatively. Fentanyl (1 µg/kg) was administered intraoperatively for analgesia when required at the discretion of the treating anesthesiologists. Postoperatively, all patients received a 0.2% ropivacaine infusion through an epidural catheter for postoperative analgesia. Paracetamol (1 g) was administered intravenously as a rescue analgesic for breakthrough pain to maintain a visual analog score < 4.

Ten minutes before extubation, FiO₂ in Group H was increased to 1 (control group). Group LR patients received RM with 40 cm H₂O for 40 seconds, followed by PEEP (5 cm H₂O) and low FiO₂ (0.4). Group HR patients received RM with 40 cm H₂O for 40 seconds, followed by PEEP (5 cm H₂O) and high FiO₂ (1) (Fig. 1).

At the end of surgery, the neuromuscular block was reversed with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg). The trachea was extubated when the patient was fully awake without applying any positive pressure. Arterial blood gas samples were obtained at baseline before anesthesia induction (T1), 10 minutes
after anesthesia induction (T2), 30 minutes after extubation (T3), and 6 hours postoperatively (T4). Lung ultrasonography (USG) was performed preoperatively, 30 minutes after extubation, and 24 hours after surgery. Lung ultrasound (LUS) imaging was performed by two trained anesthesiologists with > 3 years of experience in lung USG using a 5–9 MHz linear probe (M-Turbo; Sonosite, Bothell, WA, USA). Both anesthesiologists performing the USG and the patients were blinded to the allotment. The modified lung ultrasound score (LUSS) system suggested by Monatesses et al.12 was used for assessment. The thorax was divided into 12 quadrants: the anterior, lateral, and posterior zones (separated by the anterior and posterior axillary lines), each divided into the upper and lower portions of the right and left lungs. The aeration loss was assessed by calculating the LUSS. Each of the 12 quadrants was assigned a score of 0–3 according to a grading system. The LUSS (0–36) was then calculated by adding the 12 individual quadrant scores, with higher scores indicating more severe aeration loss. Scoring was defined as follows: 0, normal lung with sliding pleura and equidistant A lines parallel to the smooth pleural line; 1, moderate aeration loss and no less than three scattered B lines derived from the pleural line; 2, severe aeration loss and an irregular pleural line with coalescent B lines; and 3, complete aeration loss and a tissue-like pattern or subpleural consolidation.

The treating anesthesiologists collected demographic and anthropometric data preoperatively. pH, PaO2, PaCO2, PCO2, HCO3−, and lactate values were obtained using arterial blood gas (ABG) analysis at the specified time points. Other relevant data, including the ventilatory setting and surgical position, were obtained from anesthesia charts. We measured the primary outcomes in terms of postoperative oxygenation and atelectasis using the ABG and LUSS. The LUSS was recorded at specified time points by the anesthesiologists performing the USG. We recorded the secondary outcomes in terms of postoperative desaturation, oxygen requirement, pneumonia, and intensive care unit (ICU) admission during the hospital stay.

**Statistical Analysis**

As reported by Kim et al.13 the LUSS in the high FiO2 group was 12.5 ± 1.73. To estimate a 10% decrease in the low FiO2 group, we calculated a sample size of 44 per group at a 95% confidence interval, 80% power (adjusted for three groups), and 10% contingency for dropouts. The data were entered into MS Excel and analyzed using IBM SPSS Statistics for Windows, version 20.0 (IBM, Armonk, NY, USA). We assessed the normality of the data using the Kolmogorov–Smirnov test. Continuous parametric data were reported as means and standard deviations, while non-parametric data were reported as medians. Categorical data are reported as percentages. We compared categorical data between two or more groups using the chi-square test and continuous data between more than two groups using one-way analysis of variance (ANOVA). We applied post-hoc Tukey’s test to assess the statistical significance of differences between the two groups.

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**Fig. 1.** Methodology. Group H, high FiO2 (1) alone; Group HR, high FiO2, recruitment maneuver (RM), and positive end-expiratory pressure (PEEP); and Group LR, low FiO2 (0.4), RM, and PEEP; ABG, arterial blood gas; LUSS, lung ultrasound score.

---

<table>
<thead>
<tr>
<th>Pre-induction</th>
<th>Induction &amp; preoxygenation</th>
<th>Maintenance</th>
<th>Emergence and extubation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Group H</strong></td>
<td>FiO2 -0.21</td>
<td>FiO2 -1</td>
<td>FiO2 -0.4+PEEP 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FiO2 -1</td>
<td>FiO2 -0.4+PEEP 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FiO2 -1</td>
<td>FiO2 -0.4+PEEP 5</td>
</tr>
<tr>
<td><strong>Group HR</strong></td>
<td>FiO2 -0.21</td>
<td>FiO2 -1</td>
<td>FiO2 -0.4+PEEP 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FiO2 -1</td>
<td>FiO2 -0.4+PEEP 5</td>
</tr>
<tr>
<td><strong>Group LR</strong></td>
<td>FiO2 -0.21</td>
<td>FiO2 -1</td>
<td>FiO2 -0.4+PEEP 5</td>
</tr>
</tbody>
</table>

**Timeline**

A- Baseline ABG  
B- 10 minutes post-induction ABG  
C- 30 minutes post-extubation ABG  
D- 6 hours post-operative ABG  
E- Pre-op LUSS  
F- Post-extubation LUSS  
G- 24 hours post-operative LUSS

* Supplemental oxygen given only if SpO2 < 92% on room air or if desaturating.
continuous data across a one-time interval was performed using a paired t-test, and a comparison across multiple time intervals was performed using a repeated-measures ANOVA. Statistical significance was set to p < 0.05.

RESULTS

We assessed a total of 132 patients for eligibility for inclusion in this study. Among these, six patients were excluded from the analysis because they were not extubated and were transferred to the ICU. Thus, we analyzed 126 patients (Fig. 2). The baseline characteristics are summarized in Table 1. The baseline patient characteristics were comparable across the three groups.

Regarding the primary outcome, the PaO$_2$/FiO$_2$ decreased in all groups from baseline until 6 hours postoperatively. The PaO$_2$/FiO$_2$ differed significantly between Group H and Groups LR and HR 30 minutes after extubation and 6 hours after the procedure, with higher ratios in Groups LR and HR (Table 2, Fig. 3), with no statistically significant difference between Groups LR and HR.

In the postoperative period, the median LUSS was highest in Group H (median 6, interquartile range [IQR] 5–7) and differed significantly from the median LUSS values observed in Groups LR and HR (median 3, IQR 3–5 and median 3.5, IQR 2.25–4.75, respectively; p < 0.001). We observed similar trends at 24 hours postoperatively, with a significantly higher difference in median LUSS in Group H (median 4, IQR 3.25–5.75) compared with Groups LR and HR (median 3, IQR 2–4 and median 3, IQR 2–3).

### Table 1. Characteristics of patient and surgery (n=126)

<table>
<thead>
<tr>
<th></th>
<th>Group H (n = 41)</th>
<th>Group HR (n = 43)</th>
<th>Group LR (n = 42)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>69.02 ± 7.71</td>
<td>69.9 ± 8.7</td>
<td>66.22 ± 6.03</td>
<td>0.061</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td>0.969</td>
</tr>
<tr>
<td>Male</td>
<td>24 (58.53)</td>
<td>26 (60.46)</td>
<td>25 (59.52)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>17 (41.46)</td>
<td>17 (39.53)</td>
<td>17 (40.47)</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>63.4 ± 9.91</td>
<td>61.5 ± 10.13</td>
<td>61.29 ± 11.03</td>
<td>0.577</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>23.49 ± 3.02</td>
<td>22.82 ± 3.29</td>
<td>22.78 ± 3.20</td>
<td>0.512</td>
</tr>
<tr>
<td>Smoking</td>
<td>8 (19.51)</td>
<td>8 (18.60)</td>
<td>6 (14.28)</td>
<td>0.804</td>
</tr>
<tr>
<td>ASA I</td>
<td>20 (48.78)</td>
<td>27 (62.79)</td>
<td>22 (52.38)</td>
<td>0.322</td>
</tr>
<tr>
<td>ASA II</td>
<td>21 (51.21)</td>
<td>16 (37.20)</td>
<td>20 (47.61)</td>
<td></td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
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<tr>
<td>Diabetes mellitus</td>
<td>8 (19.51)</td>
<td>6 (13.95)</td>
<td>5 (11.90)</td>
<td>0.650</td>
</tr>
<tr>
<td>Hypertension</td>
<td>11 (26.82)</td>
<td>10 (23.25)</td>
<td>11 (26.19)</td>
<td>0.960</td>
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<td>Hypothyroidism</td>
<td>4 (9.75)</td>
<td>0 (0)</td>
<td>2 (4.76)</td>
<td>0.123</td>
</tr>
<tr>
<td>Parkinson’s</td>
<td>1 (2.43)</td>
<td>0 (0)</td>
<td>1 (2.38)</td>
<td>0.602</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>1 (2.43)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0.365</td>
</tr>
<tr>
<td>None</td>
<td>20 (48.78)</td>
<td>30 (69.76)</td>
<td>25 (59.52)</td>
<td>0.099</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>273.78 ± 78.49</td>
<td>304.28 ± 86.9</td>
<td>297.79 ± 88.14</td>
<td>0.229</td>
</tr>
<tr>
<td>Type of surgery administered</td>
<td></td>
<td></td>
<td></td>
<td>0.214</td>
</tr>
<tr>
<td>Open</td>
<td>21 (51.2)</td>
<td>29 (69.04)</td>
<td>28 (65.1)</td>
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<tr>
<td>Laparoscopic</td>
<td>20 (48.7)</td>
<td>13 (30.9)</td>
<td>15 (34.8)</td>
<td></td>
</tr>
</tbody>
</table>

Values are presented as mean ± standard deviation or number (%).

Group H, high FiO$_2$ (1) alone; Group HR, high FiO$_2$, recruitment maneuver (RM), and positive end-expiratory pressure (PEEP); Group LR, low FiO$_2$ (0.4), RM, and PEEP; ICU, intensive care unit.

Fig. 2. Consort diagram. Group H, high FiO$_2$ (1) alone; Group HR, high FiO$_2$, recruitment maneuver (RM), and positive end-expiratory pressure (PEEP); Group LR, low FiO$_2$ (0.4), RM, and PEEP; ICU, intensive care unit.

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Regarding the secondary outcome, we observed desaturation in 8 (19.5%) patients in Group H postoperatively, compared with 3 (6.97%) patients in Group LR and 1 (2.38%) patient in Group HR (p < 0.05). Similarly, significantly more patients in Group H (29.26%) required oxygen support postoperatively because of oxygen desaturation compared with Groups LR (9.3%) and HR (7.14%) (p < 0.05) (Table 4, Fig. 5). Postoperative pneumonia was observed in only one patient (from Group H).

Of the 132 patients that were recruited, six required postoperative ICU admission (three in Group H, one in Group LR, and two in Group HR). These patients were hemodynamically unstable and, therefore, no intervention was performed; hence, they were excluded from the analysis. The ICU requirements did not differ significantly among the three groups.

The mean PaO$_2$/FiO$_2$, and median LUSS did not differ significantly between cases undergoing open and laparoscopic procedures administered to the individual groups. The distribution of cases did not differ significantly according to the surgical position among the three groups.

**DISCUSSION**

Our study shows that older patients undergoing major abdominal surgery benefit from RM followed by PEEP, regardless of the FiO$_2$ used during extubation. Patients who underwent RM experienced less atelectasis, better oxygenation, and fewer PPCs than those who did not undergo RM.

Older patients are more prone to atelectasis due to age-related changes in respiratory mechanics, gas exchange, and immunity. In such patients, general anesthesia with neuromuscular blockade and abdominal surgeries affects respiratory functions and increases the risk of PPCs. Reducing atelectasis decreases the incidence of desaturation and reduces postoperative oxygen requirements.

We exposed Groups H and HR to a FiO$_2$ of 1 and Group LR to a FiO$_2$ of 0.4 for 10 minutes before extubation. RM was performed respectively; p < 0.001) (Table 3, Fig. 4).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group</th>
<th>Baseline</th>
<th>10 minutes after induction</th>
<th>30 minutes after extubation</th>
<th>6 hours postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaO$_2$/FiO$_2$</td>
<td>Group H</td>
<td>400.27 ± 23.16</td>
<td>383.03 ± 50.45</td>
<td>355.37 ± 31.7</td>
<td>359.06 ± 29.97</td>
</tr>
<tr>
<td></td>
<td>Group LR</td>
<td>409.86 ± 28.35</td>
<td>403.79 ± 41.75</td>
<td>381.97 ± 24.97</td>
<td>382.93 ± 24.56</td>
</tr>
<tr>
<td></td>
<td>Group HR</td>
<td>410.53 ± 21.16</td>
<td>406.12 ± 48.85</td>
<td>390.71 ± 29.55</td>
<td>387.41 ± 34.84</td>
</tr>
<tr>
<td>p-value (inter)</td>
<td></td>
<td>0.106</td>
<td>0.053</td>
<td>&lt; 0.001*</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Post-hoc (p-value)</td>
<td>H vs. LR</td>
<td>0.175</td>
<td>0.112</td>
<td>&lt; 0.001*</td>
<td>0.001*</td>
</tr>
<tr>
<td></td>
<td>H vs. HR</td>
<td>0.140</td>
<td>0.070</td>
<td>&lt; 0.001*</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td></td>
<td>LR vs. HR</td>
<td>0.991</td>
<td>0.972</td>
<td>0.346</td>
<td>0.774</td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation.

Group H, high FiO$_2$ (1) alone; Group HR, high FiO$_2$, recruitment maneuver (RM), and positive end-expiratory pressure (PEEP); Group LR, low FiO$_2$ (0.4), RM, and PEEP.

*p<0.05.
Table 3. Comparison of median LUSS between the three groups (n=126)

<table>
<thead>
<tr>
<th></th>
<th>Group H</th>
<th>Group LR</th>
<th>Group HR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preoperative</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior region</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0.167</td>
</tr>
<tr>
<td>Lateral region</td>
<td>1 (1–0)</td>
<td>0 (1–0)</td>
<td>1 (1–0)</td>
<td>0.357</td>
</tr>
<tr>
<td>Posterior region</td>
<td>1.5 (2–1)</td>
<td>1 (2–0.25)</td>
<td>1 (2–0)</td>
<td>0.305</td>
</tr>
<tr>
<td>Total</td>
<td>2 (2–3)</td>
<td>2 (1–3)</td>
<td>2 (1–3)</td>
<td>0.177</td>
</tr>
<tr>
<td><strong>30 minutes postoperative</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior region</td>
<td>0 (1–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0.019*</td>
</tr>
<tr>
<td>Lateral region</td>
<td>2 (3–2)</td>
<td>1.5 (2–1)</td>
<td>1 (2–0.5)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Posterior region</td>
<td>3 (4–2.5)</td>
<td>2 (4–2)</td>
<td>2 (3–2)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Total</td>
<td>6 (5–7)</td>
<td>3 (3–5)</td>
<td>3.5 (2.25–4.75)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td><strong>24 hours postoperative</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior region</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0.560</td>
</tr>
<tr>
<td>Lateral region</td>
<td>1 (2–1)</td>
<td>1 (1–0)</td>
<td>0 (1–0)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Posterior region</td>
<td>2 (3–2)</td>
<td>2 (2–1)</td>
<td>2 (2–1)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Total</td>
<td>4 (3.25–5.75)</td>
<td>3 (2–4)</td>
<td>3 (2–3)</td>
<td>&lt; 0.001*</td>
</tr>
</tbody>
</table>

Values are presented as median (interquartile range).

Group H, high FiO₂ (1) alone; Group HR, high FiO₂, recruitment maneuver (RM), and positive end-expiratory pressure (PEEP); Group LR, low FiO₂ (0.4), RM, and PEEP; LUSS, lung ultrasound score.

*p<0.05.

Fig. 4. Comparison of median LUSS between the three groups.

Group H, high FiO₂ (1) alone; Group HR, high FiO₂, recruitment maneuver (RM), and positive end-expiratory pressure (PEEP); and Group LR, low FiO₂ (0.4), RM, and PEEP; LUSS, lung ultrasound score.

Table 4. Comparison of PPCs between the three groups (n=126)

<table>
<thead>
<tr>
<th>PPCs</th>
<th>Group H (n = 41)</th>
<th>Group LR (n = 43)</th>
<th>Group HR (n = 42)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desaturation</td>
<td>8 (19.51)</td>
<td>3 (6.97)</td>
<td>1 (2.38)</td>
<td>0.023*</td>
</tr>
<tr>
<td>Oxygen requirement</td>
<td>12 (29.26)</td>
<td>4 (9.30)</td>
<td>3 (7.14)</td>
<td>0.008*</td>
</tr>
<tr>
<td>Postoperative pneumonia</td>
<td>1 (2.43)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0.352</td>
</tr>
</tbody>
</table>

Values are presented as number (%).

Group H, high FiO₂ (1) alone; Group HR, high FiO₂, recruitment maneuver (RM), and positive end-expiratory pressure (PEEP); Group LR, low FiO₂ (0.4), RM, and PEEP; PPC, postoperative pulmonary complication.

*p<0.05.

Fig. 5. Distribution of cases according to complications experienced in the three groups. Group H, high FiO₂ (1) alone; Group HR, high FiO₂, recruitment maneuver (RM), and positive end-expiratory pressure (PEEP); and Group LR, low FiO₂ (0.4), RM, and PEEP.

simultaneously in Groups HR and LR, while Group H did not receive any RM. All three groups received a PEEP of 5 cm H₂O subsequently. Atelectasis was measured in terms of LUSS and oxygenation in terms of PaO₂ and PaO₂/FiO₂.

PaO₂ and PaO₂/FiO₂ at 30 minutes post-extubation and 6 hours postoperatively were significantly higher in Groups HR and LR compared to Group H. Although statistically significant, this difference was not clinically relevant in patients with a normal cardiopulmonary system, as the PaO₂ and PaO₂/FiO₂ values obtained in our results do not warrant the use of supplemental oxygen in Group H; however, these could have grave consequences in patients with a reduced cardiopulmonary reserve, in whom the level
of decrease in \(\text{PaO}_2\) and \(\text{PaO}_2/\text{FiO}_2\) may be higher and could have clinical implications.

The median LUSS increased in all groups in the immediate postoperative period and 24 hours postoperatively, with a statistically significant increase in Group H \((p < 0.001)\) compared to Groups HR and LR. These findings suggest that the RM may be the reason for better alveolar aeration and that the different \(\text{FiO}_2\) values did not significantly increase atelectasis as long as the values were paired with an RM before extubation and continuous PEEP were applied. RM applied before extubation potentially reversed the atelectasis caused by abdominal surgery and general anesthesia, and this effect was maintained by sustained PEEP.

A study by Beniot et al. \(^{10}\) in patients undergoing non-abdominal surgery concluded that the use of high \(\text{FiO}_2\) \((1)\) at the end of surgery caused more postoperative atelectasis regardless of whether a vital capacity maneuver was performed at the end of surgery, and a low \(\text{FiO}_2\) \((0.4)\) completely prevented postoperative atelectasis formation. That study included two groups that were exposed to high \(\text{FiO}_2\) \((1)\) for a long duration before extubation, as the patients were extubated in the anesthesia room rather than the operating room. In contrast, we extubated all patients in the operating room, and they were not exposed to 100% oxygen for prolonged periods, which may explain the similar LUSS values in the HR and LR groups in our study. The previous study included a small group of patients \((n = 10)\), non-abdominal surgeries, and a single computed tomography (CT) slice to reduce radiation exposure. \(^{10}\) In another study, Ostberg et al. \(^{15}\) investigated the effect of PEEP on emergence pre-oxygenation with high \(\text{FiO}_2\) \((1)\) before extubation. Their results showed no significant increase in atelectasis from the baseline with the use of high \(\text{FiO}_2\) at extubation. They included patients who underwent daycare, non-abdominal surgeries, and single-slice CT. These results cannot be extrapolated to patients undergoing abdominal surgery who have a higher risk of pulmonary complications. Similarly, another study evaluated the effect of low \(\text{FiO}_2\) \((0.3)\) at extubation on postoperative atelectasis. The researchers reported no benefit regarding postoperative atelectasis in using low \(\text{FiO}_2\) \((0.3)\) as compared to high \(\text{FiO}_2\) \((1)\). They concluded that the use of intraoperative PEEP resulted in minor atelectasis at emergence and that decreased \(\text{FiO}_2\) did not provide an added benefit. Their study included patients undergoing daycare orthopedic surgery who benefitted from the use of intraoperative PEEP without requiring RM. \(^{15}\) We suggest that RM is needed to reverse atelectasis caused by open abdominal and laparoscopic surgeries.

Our secondary outcome was measured in terms of PPCs, which included desaturation, postoperative oxygen requirement, ICU requirement, and pneumonia. The incidence of desaturation and oxygen requirements was higher in Group H than in Groups HR and LR. PPCs, in terms of ICU requirements and pneumonia, were comparable among all three groups, with only one patient from Group H being diagnosed with pneumonia. We excluded patients requiring postoperative mechanical ventilation or ICU admission from the analysis. A meta-analysis by Pei et al. \(^3\) suggested that RM is beneficial for decreasing the incidence of PPCs and improving postoperative oxygenation and lung mechanics. Our results were consistent with their findings.

Our study included both open and laparoscopic abdominal surgeries in both elective and emergency settings and compared the advantages of different extubation strategies in an older patient population that might benefit most from these various strategies. Subgroup analysis between open and laparoscopic surgeries did not reveal any statistically significant differences in terms of \(\text{PaO}_2\), \(\text{PaO}_2/\text{FiO}_2\), or LUSS. This can be explained by the fact that recruitment was performed after desufflation, 10 minutes before extubation. Through this study, we emphasize the importance of preventing atelectasis in older patients using RM followed by PEEP, irrespective of \(\text{FiO}_2\). This ultimately improves respiratory function and aids in early recovery.

**Limitations**

This single-center study included 132 patients. We used the LUS to calculate atelectasis; however, because ultrasound findings are subjective, errors in LUS interpretation were possible. Although the LUS was performed by experienced anesthesiologists, it is not the gold standard. Additionally, we did not include patients with preexisting pulmonary conditions; hence, the results cannot be extrapolated to that subgroup. Finally, PEEP was not titrated post-RM, and we applied a universal minimal PEEP of 5 cm of H\(_2\)O to all patients.

**Conclusion**

The results of this study which included only older adult patients undergoing major abdominal surgeries, suggested that the use of the RM before extubation with an \(\text{FiO}_2\) of 1 or 0.4 compared to an \(\text{FiO}_2\) of 1 without RM resulted in improved postoperative oxygenation, reduced atelectasis as assessed by LUSS, and reduced postoperative pulmonary complications. In conclusion, RM before extubation was more beneficial in reducing atelectasis and postoperative pulmonary complications, regardless of the \(\text{FiO}_2\) concentration.

**ACKNOWLEDGMENTS**

**CONFLICT OF INTEREST**

The researchers claim no conflicts of interest.
FUNDING
None.

AUTHOR CONTRIBUTIONS
Conceptualization, PB, TMM; Data curation, RMK; Investigation, RMK, TNM; Supervision, PB; Writing–original draft, RMK; Writing–review & editing, SC, RK.

REFERENCES

Knee extensor muscle strength is crucial for older adults because it significantly affects various aspects of physical well-being, mobility, and overall quality of life. Studies on the relationship between knee extensor strength and health in older adults have consistently demonstrated the importance of maintaining or improving knee extensor strength as individuals age. Decreased knee extensor muscle strength is frequently linked to restrictions in activities of daily living (ADLs) in older adults. Adequate knee extensor strength is indispensable for ADLs such as standing up from a seat, ascending stairs, and walking, all of which are pivotal for maintaining function. Decreased knee extensor strength is associated with an increased risk of falls in older adults. Falls can have severe consequences, including fractures and a decline in overall well-being. Therefore, maintaining knee extensor strength can mitigate these risks.

Assessing knee extensor muscle strength is vital for evaluating lower limb function and monitoring changes over time. This is particularly important in clinical and research settings. Several methods have been developed to measure the knee extensor strength. Isokinetic dynamometry is considered the gold standard because it provides a controlled environment and allows for constant angular velocity throughout the range of motion. Researchers and clinicians have applied isokinetic testing to measure the peak torque, work, and power of the knee extensors. Hand-held dynamometers are also commonly used in clinical settings to assess muscle strength, including that of the knee extensors. These portable and cost-effective devices are particularly useful for assessing muscle strength in older adults and individuals with mobil-
Table 1. Subject demographic data and anthropometric characteristics variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>All (n = 110)</th>
<th>Men (n = 52)</th>
<th>Women (n = 58)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>67.79 ± 6.26</td>
<td>65.92 ± 4.64</td>
<td>67.47 ± 6.05</td>
</tr>
<tr>
<td>Mass (kg)</td>
<td>57.30 ± 8.12</td>
<td>60.01 ± 6.65</td>
<td>54.87 ± 8.59</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>157.33 ± 8.42</td>
<td>163.00 ± 6.71</td>
<td>152.25 ± 6.29</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.18 ± 3.12</td>
<td>22.65 ± 2.82</td>
<td>23.63 ± 3.33</td>
</tr>
<tr>
<td>Thigh circumference (cm)</td>
<td>47.25 ± 4.21</td>
<td>48.27 ± 4.77</td>
<td>46.34 ± 3.41</td>
</tr>
<tr>
<td>MVIC of knee extensor muscles strength (kg)</td>
<td>27.50 ± 7.60</td>
<td>32.85 ± 5.70</td>
<td>22.70 ± 5.64</td>
</tr>
<tr>
<td>Time to complete MST in 5 repetitions (s)</td>
<td>6.13 ± 2.37</td>
<td>5.51 ± 1.67</td>
<td>6.71 ± 2.75</td>
</tr>
<tr>
<td>Time to complete MST in 10 repetitions (s)</td>
<td>11.88 ± 4.65</td>
<td>9.89 ± 2.48</td>
<td>13.65 ± 5.40</td>
</tr>
<tr>
<td>Single-leg standing balance test with eye open (s)</td>
<td>30.88 ± 31.02</td>
<td>39.36 ± 36.68</td>
<td>23.28 ± 22.63</td>
</tr>
<tr>
<td>Single-leg standing balance test with eye closed (s)</td>
<td>4.54 ± 3.01</td>
<td>4.75 ± 3.47</td>
<td>4.35 ± 2.55</td>
</tr>
</tbody>
</table>

Values are presented as mean ± standard deviation.

BMI, body mass index; MVIC, maximum voluntary isometric contraction; MST, Modified Squat Test.
pendently without using walking aids are listed in Table 1. The exclusion criteria were musculoskeletal issues in the lower extremities (e.g., osteoarthritis or rheumatoid arthritis); bone fractures or dislocations and underlying causes; surgical history; neurological disorders affecting balance and muscle strength (e.g., stroke, spinal cord diseases, or Parkinson's disease); and communication, vision, or hearing impairments.

Research Protocol
The participants were provided with a comprehensive explanation of the study objectives and data collection procedures. Before commencing participation, the participants were required to provide informed consent by signing a consent form. Demographic data and anthropometric characteristics including sex, age, body weight, height, and thigh circumference were collected from each participant. Before the official commencement of the trial, the participants were allotted 5 min to practice the prescribed movements and ensure their comfort and familiarity with these. The assessment included measurement of the maximum voluntary isometric contraction (MVIC) of the knee extensor muscle, followed by 5 and 10 repetitions each of MST, and a single-leg standing balance test. A minimum of 5 minutes of rest was provided between each assessment to ensure optimal performance and recovery. The following sequences and methods were applied for the variable measurements.

MVIC of the knee extensor muscle
We evaluated the MVIC of the knee extensor muscle with the participants seated on an N-K table with their knees flexed at 60°. To accommodate individual leg lengths, the N-K table was adjusted accordingly. Safety measures were implemented by using a secure belt to stabilize the trunk and upper legs. For the assessment, a push-pull dynamometer (Baseline analog hydraulic push-pull dynamometer; Fabrication Enterprises Inc., White Plains, NY, USA) was affixed to the N-K table leg, employing a strap oriented perpendicular to the vertical axis and situated 1 cm above the lateral malleolus, as depicted in Fig. 1. The participants were given precise instructions to extend their knees to the fullest extent possible against the push-pull dynamometer while maintaining contraction for 4 seconds. This testing protocol entailed three rounds of assessment, with a 2-minute rest period between each round to ensure participants' readiness and consistent performance. We recorded the maximum force (in kg) exerted during these trials.

Modified squat test
All participants were provided with explicit instructions to assume a prescribed stance, with both feet firmly planted on the floor and spaced shoulder-width apart, and with the hands on the chest. The researchers emphasized maintaining an upright posture with the back and knees in straight form. Subsequently, the participants were directed to flex their knees to 60°, which was accurately measured using a universal goniometer. Subsequently, the researcher adjusted the chair height to ensure contact between the participant's buttocks and the chair seat. The core of the assessment revolved around the participants' ability to perform squats using both feet simultaneously, with the primary objective of touching their buttocks to a cushioned seat. This squatting and standing sequence was executed in sets of 5 and 10 repetitions, respectively, with the participants striving to complete each repetition with agility and safety (Fig. 2). To ensure a comprehensive evaluation, the test consisted of three distinct trials, each separated by a 2-minute rest interval to allow the participants to recuperate. We recorded the time required by the participants to successfully complete both 5 and 10 repetitions.

Single-leg standing balance test
The single-leg standing balance test commenced with the participants in standing position, with both feet on the ground and their gaze directed straight ahead. Subsequently, the researcher instructed the participants to transfer their weight onto their dominant leg.
while crossing their arms over their chests. The non-dominant knee was flexed to 90° and a timer was activated to record how long the participants could maintain their balance. The test was conducted three times with a 2-minute break between each trial. In this study, we administered two variations of the single-leg standing balance test: one with the eyes open (SSEO) and the other with the eyes closed (SSEC).

Statistical Analyses
We collected the participants' demographic information and used descriptive statistics to express the means and standard deviations. The Shapiro–Wilks test was used to assess the distributions of the variables. We used Pearson product-moment correlation coefficient statistics to investigate the relationships among the following factors: the MVIC of the knee extensor muscle, subjects' demographic data (sex, age, weight, height, body mass index [BMI], and thigh circumference), and the time taken to complete both 5 and 10 repetitions of the MST. To delve further into the predictive aspects, we performed stepwise multiple linear regression analysis to construct a predictive equation for knee extensor strength that incorporated demographic data and the time required to complete the MST. The model selection criteria included the highest adjusted $R^2$ value while minimizing variance inflation. We included independent variable coefficients in each prediction model based on their significance within the model. All statistical analyses were conducted using IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, NY, USA) with the significance threshold set at $p < 0.05$.

RESULTS
This study included 110 older adults (52 men and 58 women; average age, 67.79 ± 6.26 years). The participants' mean weight, height, and BMI were 57.30 ± 8.12 kg, 157.33 ± 8.42 cm, and 23.18 ± 3.12 kg/m$^2$, respectively. The average thigh circumference was 47.25 ± 4.21 cm. The average strength of the knee extensor muscles, as measured by MVIC, was 27.50 ± 7.60 kg. The participants required an average of 6.13 ± 2.37 seconds and 11.88 ± 4.65 seconds to complete 5 and 10 repetitions of the MST, respectively. The average duration of the single-leg standing balance test were 30.88 ± 31.02 seconds for SSEO and 4.54 ± 3.01 seconds for SSEC (Table 1).

Knee extensor muscle strength was associated with various demographic characteristics of the participants, including sex, age, weight, height, and thigh circumference. These associations exhibited varying degrees of correlation, ranging from low to moderate ($r = 0.299–0.670, p < 0.005$). We also observed significant negative correlations between knee extensor muscle strength and the time required to complete the two different MST repetitions. Specifically, we observed a moderate negative correlation with the time taken for 5 repetitions ($r = -0.492, p < 0.001$) and a strong negative correlation with the time taken for 10 repetitions ($r = -0.722, p < 0.001$). Furthermore, knee extensor muscle strength was moderately positively correlated with SSEO ($r = 0.550, p < 0.001$) and SSEC ($r = 0.419, p < 0.005$). The detailed correlation findings are presented in Table 2 and Fig. 3.

Based on the results of the comprehensive multiple regression analysis of the strength of the knee extensor muscles, five factor models were identified (Table 3). In Model 1, the only significant factor affecting knee extensor muscle strength was the time required to complete 10 repetitions of the MST. Conversely, the contributing factors in Models 2–5 included sex, SSEO, age, and thigh circumference. Among the five models, Model 5 exhibited the strongest correlation ($r = 0.888, p < 0.05$) and the highest coefficient of determination ($R^2 = 0.778$). This indicates that the combined influence of the time taken to complete 10 repetitions of the MST, sex, SSEO, age, and thigh circumference accounted for 77.8% of the variation in knee extensor muscle strength. The standard error of the estimate was approximately 3.58 kg. Subsequently, we formulated an equation to predict knee extensor muscle
In this study, the stronger correlation between MST and knee extensor strength for 10 repetitions than for 5 repetitions can be attributed to several factors. Muscle fatigue can accumulate with increasing MST repetitions. The accumulated fatigue affects individuals differently depending on their knee extensor strength. Individuals with stronger knee extensors may experience less fatigue and maintain a better form throughout the 10 repetitions, resulting in a stronger correlation with overall muscle strength. Stronger knee extensors have a higher threshold for engagement, allowing them to sustain a greater force output for longer periods before experiencing significant fatigue. This enables individuals with greater knee extensor strength to perform additional repetitions before muscle failure or exhaustion occur. The 5 repetitions of the MST, which involve rising from a seated position five times consecutively, may be relatively easier for some individuals, especially those with moderate to high knee extensor strength. Therefore, the test may not fully challenge their strength and they may complete it with relative ease, unlike the five-time STS. Thus, 5 repetitions of the MST may not effectively differentiate between knee extensor strengths, whereas weaker knee extensor muscles may lead to difficulties and reduced stability. Thus, the MST can be used to assess the strength and functionality of the knee extensor muscles for daily tasks and mobility.

In the present study, we observed a moderate association between decreased knee muscle strength and thigh circumference. Therefore, the regular assessment of demographic and anthropometric profiles is important to prevent a decline in muscle strength and reduce fall risk.

The relationship between the MST and knee extensor muscle strength in older adults is important for studying physical function and mobility. We observed a moderate-to-strong association between knee extensor strength and the time taken to complete both 5 and 10 repetitions of the MST. MST reflects knee extensor strength because it involves movements that rely on the strength of these muscles. During the test, individuals squat and stand from a seated position, which requires knee joint extension. The knee extensor muscles straighten the knee and lift body weight against gravity. The relationship between MST and knee extensor strength lies in the biomechanics of squatting and standing. When moving from a seated to a standing position or lowering into a squat, the knee joint moves from a flexed to an extended position. This requires the quadriceps muscles to contract and straighten the knee joint. The knee extensor muscles must generate the necessary force to support and lift the body during the descent into a squat and ascent to a standing position, respectively. Adequate muscle strength is necessary to control these descent and ascent phases and ensure stability of the knee joint. The ability to perform the MST effectively indicates sufficient knee extensor muscle strength, whereas weaker knee extensor muscles may lead to difficulties and reduced stability.

**DISCUSSION**

Knee muscle strength is important for independence and quality of life in older adults. Thus, geriatric healthcare should include strategies to assess and improve knee muscle strength. This study aimed to identify a functional test for predicting knee muscle strength in older adults. Our results revealed an association between participant characteristics and knee muscle strength. Men generally have stronger knee muscles than women, which can be influenced by hormones, activity levels, and aging. Although both men and women experience a decline in knee muscle strength with age, women may experience a more pronounced decline after menopause. Regular resistance training can help reduce sex differences in muscle strength. Weak knee muscles in women can affect daily activities and the overall quality of life. Anthropometric data such as body measurements can predict knee muscle mass in older adults. Reduced muscle mass, which is often associated with aging, contributes to decreased knee muscle strength. Anthropometric measurements can identify individuals at risk for muscle weakness and mobility problems. In the present study, we observed a moderate association between decreased knee muscle strength and thigh circumference. Therefore, the regular assessment of demographic and anthropometric profiles is important to prevent a decline in muscle strength and reduce fall risk.

The relationship between the MST and knee extensor muscle strength in older adults is important for studying physical function and mobility. We observed a moderate-to-strong association between knee extensor strength and the time taken to complete both 5 and 10 repetitions of the MST. MST reflects knee extensor strength because it involves movements that rely on the strength of these muscles. During the test, individuals squat and stand from a seated position, which requires knee joint extension. The knee extensor muscles straighten the knee and lift body weight against gravity. The relationship between MST and knee extensor strength lies in the biomechanics of squatting and standing. When moving from a seated to a standing position or lowering into a squat, the knee joint moves from a flexed to an extended position. This requires the quadriceps muscles to contract and straighten the knee joint. The knee extensor muscles must generate the necessary force to support and lift the body during the descent into a squat and ascent to a standing position, respectively. Adequate muscle strength is necessary to control these descent and ascent phases and ensure stability of the knee joint. The ability to perform the MST effectively indicates sufficient knee extensor muscle strength, whereas weaker knee extensor muscles may lead to difficulties and reduced stability. Thus, the MST can be used to assess the strength and functionality of the knee extensor muscles for daily tasks and mobility.

In this study, the stronger correlation between MST and knee extensor strength for 10 repetitions than for 5 repetitions can be attributed to several factors. Muscle fatigue can accumulate with increasing MST repetitions. This accumulated fatigue affects individuals differently depending on their knee extensor strength. Individuals with stronger knee extensors may experience less fatigue and maintain a better form throughout the 10 repetitions, resulting in a stronger correlation with overall muscle strength. Stronger knee extensors have a higher threshold for engagement, allowing them to sustain a greater force output for longer periods before experiencing significant fatigue. This enables individuals with greater knee extensor strength to perform additional repetitions before muscle failure or exhaustion occur. The 5 repetitions of the MST, which involve rising from a seated position five times consecutively, may be relatively easier for some individuals, especially those with moderate to high knee extensor strength. Therefore, the test may not fully challenge their strength and they may complete it with relative ease, unlike the five-time STS. Thus, 5 repetitions of the MST may not effectively differentiate between...
Fig. 3. Scatter plot graphs illustrating the relationship between the knee extensor strength variable and participants’ demographic information, single-leg standing balance, and MST performance. (A) Age. (B) Thigh circumference. (C) Time to complete MST in 5 repetitions. (D) Time to complete MST in 10 repetitions. (E) Single-leg standing balance test with eye open. (F) Single-leg standing balance test with eye closed. MVIC, maximum voluntary isometric contraction; MST, Modified Squat Test.

individuals with varying levels of knee extensor strength, leading to a potential ceiling effect. Therefore, an increased number of repetitions allows better differentiation between individuals with varying levels of strength, making it more sensitive for identifying differences in muscle strength. Additionally, maintaining balance during the MST is crucial for preventing falls and loss of stability. Knee extensor strength plays a role in balance by controlling movement and preventing the knee from buckling or collapsing during
Table 3. Model of regression analysis for knee extensor muscles strength with different predictive variables

<table>
<thead>
<tr>
<th>Included variables</th>
<th>β</th>
<th>p-value</th>
<th>r</th>
<th>Adjusted R²</th>
<th>SEE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>41.491</td>
<td>&lt; 0.001**</td>
<td>0.722</td>
<td>0.516</td>
<td>5.284</td>
</tr>
<tr>
<td>Time to complete MST in 10 repetitions</td>
<td>-1.178</td>
<td>&lt; 0.001**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>34.714</td>
<td>&lt; 0.001**</td>
<td>0.831</td>
<td>0.685</td>
<td>4.261</td>
</tr>
<tr>
<td>Time to complete MST in 10 repetitions</td>
<td>-0.880</td>
<td>&lt; 0.001**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>6.840</td>
<td>&lt; 0.001**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>31.189</td>
<td>&lt; 0.001**</td>
<td>0.868</td>
<td>0.747</td>
<td>3.822</td>
</tr>
<tr>
<td>Time to complete MST in 10 repetitions</td>
<td>-0.735</td>
<td>&lt; 0.001**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>6.310</td>
<td>&lt; 0.001**</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>SSEO</td>
<td>0.067</td>
<td>&lt; 0.001**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>47.207</td>
<td>&lt; 0.001**</td>
<td>0.882</td>
<td>0.770</td>
<td>3.643</td>
</tr>
<tr>
<td>Time to complete MST in 10 repetitions</td>
<td>-0.554</td>
<td>&lt; 0.001**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>6.314</td>
<td>&lt; 0.001**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSEO</td>
<td>0.051</td>
<td>&lt; 0.001**</td>
<td></td>
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</tr>
<tr>
<td>Age</td>
<td>-0.261</td>
<td>0.001*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 5</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Constant</td>
<td>36.779</td>
<td>&lt; 0.001**</td>
<td>0.888</td>
<td>0.778</td>
<td>3.581</td>
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<tr>
<td>Time to complete MST in 10 repetitions</td>
<td>-0.537</td>
<td>&lt; 0.001**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>6.156</td>
<td>&lt; 0.001**</td>
<td></td>
<td></td>
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<tr>
<td>SSEO</td>
<td>0.046</td>
<td>0.001*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-0.241</td>
<td>0.002*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thigh circumference</td>
<td>0.192</td>
<td>0.033*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MST, Modified Squat Test; SSEO, single-leg standing balance test with eye open; SSE, standard error of estimation.
Sex was coded as a binary variable, with female=0 and male=1.
*p<0.005, **p<0.001.

This explanation is consistent with the outcomes of our study, which demonstrated a moderate association between knee extensor strength and performance in the single-leg standing test.

The combined model indicated that multiple factors significantly influenced knee extensor muscle strength. We analyzed various factors, including the time taken to complete 10 repetitions of the MST, sex, whether the single-leg standing balance test was performed as SSEO, age, and thigh circumference. These factors were selected because they could potentially contribute to knee extensor muscle strength. These factors collectively explained 77.8% of the observed variation in knee extensor muscle strength. This high percentage suggests that the model effectively captured and explained a significant portion of the variance in knee extensor muscle strength. The time required to complete 10 repetitions of the MST was a crucial factor in the model. Individuals who can quickly perform squatting and rising tasks tend to have stronger knee extensor muscles. Sex was also a significant factor, indicating sex-related differences in knee extensor muscle strength. This aligns with previous research reporting sex disparities in muscle strength, with men typically exhibiting greater strength than women. The inclusion of SSEO as a factor suggests that balance, as assessed using the single-leg standing test, plays a role in knee extensor muscle strength. Age of the participant was also considered, highlighting the well-established association between aging and declining muscle strength. Thigh circumference was another important factor, indicating that the muscle size and mass in the thigh region directly affect knee extensor strength. This is consistent with the understanding that greater muscle mass generally contributes to increased muscle strength. Furthermore, during the multiple regression analysis, when investigating the reverse relationship with the MST as the dependent variable and muscle strength as the independent variable, muscle strength, in conjunction with age as a covariate, impacted physical function performance in older adults by approximately 56%. This finding suggests a bidirectional influence between these variables, further implying that the MST can serve as an indicator of muscle strength.

The substantial variations explained by this model have both clinical and practical implications, suggesting that healthcare professionals and practitioners should consider these factors when...
assessing knee extensor muscle strength in clinical settings. Strategies to improve knee extensor strength may include targeted exercises to enhance muscle endurance, balance training, and strength-building interventions that can be tailored to sex, age, and individual characteristics. We also present a predictive equation for knee extensor strength, which is a valuable outcome of this study. The equation is as follows: knee extensor strength (kg) = 36.78 – 0.24 (age) + 0.616 (sex) + 0.19 (thigh circumference) + 0.05 (SSEO) – 0.54 (time required to complete 10 MST repetitions). This equation allows the estimation of an individual’s knee extensor strength based on certain variables. The equation also includes an associated margin of error (± 5.51 kg) to account for variability in the prediction.

Although our study provides valuable insights, it has several limitations. First, the measurement of knee extensor muscle strength using a push-pull dynamometer may not be the most accurate method, unlike the isokinetic dynamometer, which is considered the gold standard. Although the push-pull dynamometer is widely used because of its accessibility and accuracy in assessing the maximum force produced by isometric muscle contraction, future research should investigate the relationship between MST performance and knee muscle strength measured using the gold standard isokinetic dynamometer. Another limitation of our study is the lack of a separate analysis of women and men. However, this limitation was mitigated by the relatively equal proportions of women and men in our sample. Although we included sex as a cofactor in predicting knee extensor muscle strength, future studies should conduct separate analyses to derive sex-specific prediction equations for a more comprehensive analysis.

The results of this study emphasize the multifactorial nature of knee extensor muscle strength and highlight the combined influence of various factors, including MST performance, sex, balance, age, and thigh circumference, in explaining a significant proportion of the variation in knee extensor strength. These findings underscore the importance of comprehensive assessments and tailored interventions to address and optimize knee extensor muscle strength for different populations, particularly in the context of aging and functional capacity.

ACKNOWLEDGMENTS

We thank all the participants who volunteered to participate in this study.

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

None.

AUTHOR CONTRIBUTIONS

Conceptualization, WT, NS; Methodology, WT, NS, PM, SK; Software, WT; Formal analysis, WT, NS; Data curation, WT, NS; Investigation, WT, SK; Writing—original draft, WT, NS, PM; Writing—review and editing, WT, NS, PM, SK; Visualization, WT, NS; Supervision, WT.

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Overlap between Osteosarcopenia and Frailty and their Association with Poor Health Conditions: The Bushehr Elderly Health Program

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Background: The aim of this study was to investigate the association of osteosarcopenia with frailty and poor health conditions among older Iranian adults. Methods: This cross-sectional study analyzed data from the Bushehr Elderly Health Program. Osteosarcopenia was defined as the presence of osteopenia/osteoporosis and sarcopenia, while the Fried criteria were used to assess frailty. We assessed the history of falls and health-related quality of life (HRQoL), including physical and mental component summaries (PCS and MCS, respectively), history of fractures, activities of daily living (ADL), and instrumental activities of daily living (IADL), as indicators of poor health conditions. Results: This study included a total of 2,371 older adults. The prevalence rates of osteosarcopenia-only, frailty-only, and osteosarcopenia with frailty were 17.4%, 3%, and 4.8%, respectively. The prevalence of a history of falls, poor ADL, and poor IADL was significantly higher in the frailty-only and osteosarcopenia with frailty groups. Osteosarcopenia with frailty was significantly associated with a history of falls (adjusted odds ratio [adjOR]=1.94; 95% confidence interval [CI], 1.20–3.15), poor ADL (adjOR=2.85; 95% CI, 1.81–4.50), and poor IADL (adjOR=5.09; 95% CI, 2.85–9.11). However, the frailty-only group also showed an association with falls and poor ADL and IADL. Only osteosarcopenia was associated with an increased OR for fracture. Frailty had the greatest effect on the MCS and PCS scores, whereas osteosarcopenia with frailty had a moderate impact. Conclusion: Osteosarcopenia with frailty significantly increased the odds of falls, poor ADL, poor IADL, and lower HRQoL compared with the robust group. Combined osteosarcopenia and frailty were not associated with poor health. These findings indicate the importance of diagnosing osteosarcopenia and frailty as separate entities to provide appropriate interventions and treatment.

Key Words: Osteosarcopenia, Frailty, Quality of life, Accidental Falls, Fractures, Bone, Disability Evaluation

INTRODUCTION

Aging leads to changes in body mass composition and can increase the risk of chronic diseases such as osteoporosis and sarcopenia. These diseases share common mechanisms, risk factors, and adverse outcomes. The coexistence of both conditions, known as osteosarcopenia, can occur in many older adults. Moreover, the risks of falls, fractures, and mortality are higher than those associated with either disease alone. Therefore, the concomitant occurrence of sarcopenia and osteoporosis may have additive effects on ad-
verse outcomes.2) Frailty is another increasingly prevalent aging syndrome characterized by the inability of body systems to maintain homeostasis3) in response to stressors such as pain or psychologically stressful incidents.5) Frailty often manifests as the deterioration of cognitive function, muscle, nervous system, and cardiopulmonary reserve.5)

These two geriatric syndromes, osteosarcopenia and frailty, are musculoskeletal conditions causing devastating morbidity and mortality in older adults.6) The prevalence of osteosarcopenia varies from 11% to 30% among community-dwelling older adults.7) In addition, the prevalence of frailty increases with age, independent of the tools used to assess this condition, ranging from 4% to 59% in older adults.9) Moreover, both disorders are commonly associated with adverse outcomes.8,11)

Factors such as inflammation, hormonal imbalance, and malnutrition lead to musculoskeletal aging and frailty syndrome.12) Additionally, many older adults have coexistence of some geriatric syndromes. Identifying the link between osteosarcopenia and frailty may inform the implementation of effective interventions to prevent and control chronic diseases, improve quality of life, and reduce disability and death among older adults.

Therefore, the present study aimed to determine the overlap between osteosarcopenia and frailty and its association with poor health conditions in older adults.

MATERIALS AND METHODS

Study Population

This cross-sectional study included 2,426 older adults in the second stage of the Bushehr Elderly Health (BEH) Program, a population-based prospective cohort study. This program aims to assess the incidence of non-communicable diseases and their risk factors among men and women aged > 60 years. The participants were selected for phase one based on multi-stage randomized sampling in Bushehr, Iran.13)

The prevalence of cardiovascular risk factors was investigated in 3,000 older people in the first phase of the BEH Program. The second stage of the first phase of the study was conducted 2.5 years later on eligible people from the first stage, and examined cognitive and musculoskeletal disorders.14) The study included older adults ≥ 60 years of age of both sexes with sufficient physical and mental ability to participate. The exclusion criterion was the absence of a residence in Bushehr.

The Research Ethics Committee of Bushehr University of Medical Sciences and the Endocrinology & Metabolic Metabolism Research Institute approved this study (IR.TUMS.EMRI.REC. I 394.0036). All participants provided written informed consent. Also, this study complied the ethical guidelines for authorship and publishing in the Annals of Geriatric Medicine and Research.15)

Measurements

Trained personnel interviewed the participants privately and face-to-face using valid questionnaires. Initially, information on sociodemographic characteristics, lifestyle factors, general health, medical history, mental and functional health, and medication use was collected.14) Height and weight were measured with a fixed stadiometer and digital scale, respectively, with shoes removed and the participants wearing lightweight clothing. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m²). Waist circumference (WC) was recorded midway between the iliac crest and the lowest rib with the participants in a standing position. After 15 minutes in a sitting position, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured on the right arm, with the average of the two measurements considered the participant’s blood pressure. Daily dietary intake was assessed using a 24-hour dietary recall questionnaire. Physical activity levels were assessed using the Physical Activity questionnaire described by Aadahl and Jorgensen.16)

Body composition was measured using dual X-ray absorptiometry (DXA Discovery Wi; Hologic Inc., Waltham, MA, USA). The bone mineral density of the lumbar spine (L1–4) and total hip were measured in the correct position. The appendicular skeletal muscle mass index (ASM) for each participant was derived as the sum of the upper and lower limb muscle masses, and the skeletal muscle mass index (SMI) was calculated as ASM/height² (kg/m²). Muscle strength was measured based on handgrip strength using a digital dynamometer. The measurement was performed three times for each hand, and the maximum grip strength was calculated by taking the average of the highest measurements from both hands. The usual walking speed (m/s) on a 4.57-m course was used as an objective measure of physical performance.

Blood samples were collected from each participant for biochemical analyses after overnight fasting. Details of the measurements of fasting plasma glucose (FPG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG) levels in this population have been reported elsewhere.14)

Definitions of Terms

The coexistence of osteopenia/osteoarthritis and sarcopenia was defined as osteosarcopenia. Participants with a T-score > -2.5 standard deviation (SD) and < -1.0 SD of the average value of normal young adults in either the femoral neck, lumbar spine or total hip densitometry were defined as having osteopenia while those with
a T-score ≤ -2.5 SD were defined as having osteoporosis.\textsuperscript{17} Sarco-
penia was defined according to the European Working Group on Sarcopenia in Older People (EWGSOP-2) guidelines as follows: low handgrip strength, slow gait speed, and low SMI.\textsuperscript{16} The muscle
strength cutoff was < 26 kg for men and < 18 kg for women. Furthermore, the cutoff for low physical function was difficulty in
normal walking at a speed of < 0.8 m/s for both sexes.\textsuperscript{19} A low
SMI was defined as < 7.0 kg/m\textsuperscript{2} for men and 5.4 kg/m\textsuperscript{2} for
women based on Iranian cutoff values.\textsuperscript{20} Frailty was determined based
on the criteria defined by Fried et al.,\textsuperscript{21} with ≥ 3 of the following
components present: unintended weight loss, exhaustion, low muscle
strength, slow gait speed, and low physical activity. In this study, we classified the participants into four groups: robust (with-
out osteosarcopenia and frailty), osteosarcopenia-only, frailty-only,
and osteosarcopenia with frailty.

We defined diabetes mellitus as current FPG ≥ 126 mg/dL, gly-
cated hemoglobin (HbA1c) ≥ 6.5, the participant’s self-report of
diabetes mellitus based on a doctor’s diagnosis, or current use of
anti-diabetic drugs.\textsuperscript{22} Hypertension was defined as current SBP
≥ 140 mmHg or DBP ≥ 90 mmHg, the participant’s self-report of
hypertension based on a doctor’s diagnosis, or the current use of
anti-hypertension drugs.\textsuperscript{23} Smoking refers to the current use of
cigarettes or waterpipes. High WC was defined as a WC > 102 cm
in men and > 88 cm in women. Low HDL-C was defined as
HDL-C < 40 mg/dL in men and < 50 mg/dL in women. High
LDL-C was defined as LDL-C ≥ 110 mg/dL and high serum TG
as serum TG ≥ 150 mg/dL.\textsuperscript{24}

**Outcomes**

A history of falling was defined as a self-reported unintentional fall
on the ground in the previous year.\textsuperscript{25} History of fracture was de-
defined as a self-reported fracture after 45 years of age.\textsuperscript{26}

Health-related quality of life (HRQoL) was assessed using a
translated and validated Persian version of the 12-item Short-Form
Health Survey (SF-12). The SF-12 is a self-reported generic
HRQoL measure consisting of 12 questions that can be scored to
provide a physical component summary (PCS) score and a mental
component summary (MCS) score. The PCS subscale measures
physical problems, pain, and self-rated health, while the MCS sub-
scale measures daily functioning related to psychological issues
and vitality. The subscale scores range from 0 to 100, with higher
scores indicating a greater HRQoL.\textsuperscript{27}

The degree of disability was measured using two questionnaires:
activities of daily living (ADL) and instrumental activities of daily
living (IADL), which have previously been validated and transla-
ted in Iran.\textsuperscript{28} Participants with total ADL scores < 95 were consid-
ered to have poor ADL, while those with total IADL scores ≤ 7

were considered to be dependent.\textsuperscript{29,30}

**Statistical Analysis**

The data are presented as mean ± SD and as percentages for con-
tinuous and categorical variables, respectively. To compare the data
between groups (robust, osteosarcopenia-only, frailty-only, and os-
teosarcopenia with frailty), we applied analysis of variance and
Pearson chi-square test to continuous variables and categorical
data, respectively. We used logistic regression analysis to assess the
associations between poor health conditions (falls, history of frac-
ture, poor ADL, and poor IADL) and osteosarcopenia-frailty
groups. In addition, we used multivariate linear regression to test
for osteosarcopenia and frailty status on the MCS and PCS of the
HRQoL.

All multivariate analyses included variables with p < 0.2; the final
significance level for multivariate analyses was p < 0.05. All tests
were two-sided, we defined p < 0.05 as statistically significant. We
performed the statistical analyses using Stata 16 software
(StataCorp, College Station, TX, USA).

**RESULTS**

After excluding participants with missing values for osteosarcop-e
nia or frailty (n = 55), the analysis included 2,371 older adults. The
prevalence rates of osteosarcopenia-only, frailty-only, and osteosar-
copenia with frailty were 17.4% (n = 413), 3% (n = 71), and 4.8%
(n = 114), respectively. Table 1 illustrates the baseline characteristics
of the participants according to their osteosarcopenia and frail-
ty statuses. Participants with osteosarcopenia and frailty were older
and had lower BMI and energy and protein intakes than those in
the other groups (p < 0.001). Furthermore, this and the frailty-on-
ly group had lower levels of physical activity than the other groups.
In addition, the frailty scores were significantly higher in both the
frailty-only and osteosarcopenia with frailty groups than in the ro-
bust group (p < 0.001).

Fig. 1 shows the prevalence of poor health among the four groups
according to the osteosarcopenia and frailty statuses. The preva-
ience of a history of falls, poor ADL, and poor IADL was signifi-
cantly higher in both the frailty-only and osteosarcopenia with frail-
ty groups than in the robust group (p < 0.001). However, the preva-
ience of fractures in each of the groups was the same and was higher
than that in the robust group. In addition, the scores of the HRQoL
components differed significantly between the groups. The MCS
(50.00 ± 13.32 vs. 59.30 ± 9.16; p < 0.001) and PCS (39.19 ± 8.80
vs. 53.43 ± 8.40; p < 0.001) scores in the frailty-only group were
lower compared with the robust group (data not shown).

The odds ratios for poor health conditions in the osteosarcope-
Table 1. Demographic and clinical characteristics of the study participants

<table>
<thead>
<tr>
<th></th>
<th>Robust (n = 1,773)</th>
<th>Osteosarcopenia only (n = 413)</th>
<th>Frailty only (n = 71)</th>
<th>Osteosarcopenia with frailty (n = 114)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, male</td>
<td>892 (50.3)</td>
<td>189 (45.8)</td>
<td>24 (33.8)</td>
<td>50 (43.9)</td>
<td>0.014</td>
</tr>
<tr>
<td>Age (y)</td>
<td>67.87 ± 5.15</td>
<td>72.14 ± 6.85</td>
<td>74.75 ± 8.76</td>
<td>77.16 ± 7.78</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Education (y)</td>
<td>5.85 ± 5.11</td>
<td>3.73 ± 4.43</td>
<td>3.01 ± 4.44</td>
<td>2.86 ± 3.84</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Current smoking (%)</td>
<td>357 (20.2)</td>
<td>103 (24.9)</td>
<td>16 (22.5)</td>
<td>21 (18.4)</td>
<td>0.159</td>
</tr>
<tr>
<td>Physical activity (%)</td>
<td>476 (26.8)</td>
<td>67 (16.2)</td>
<td>3 (4.2)</td>
<td>5 (4.4)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Protein intake (gr)</td>
<td>56.93 ± 23.94</td>
<td>51.81 ± 23.88</td>
<td>48.78 ± 20.39</td>
<td>45.68 ± 22.25</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Energy intake (kcal)</td>
<td>1,637.14 ± 581.82</td>
<td>1,517.47 ± 567.26</td>
<td>1,448.23 ± 549.42</td>
<td>1,337.77 ± 553.93</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.53 ± 4.62</td>
<td>24.04 ± 3.10</td>
<td>27.58 ± 5.77</td>
<td>23.37 ± 3.46</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>High TG (%)</td>
<td>602 (34.0)</td>
<td>110 (26.6)</td>
<td>19 (26.8)</td>
<td>21 (18.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>High HDL-C (%)</td>
<td>517 (29.2)</td>
<td>126 (30.5)</td>
<td>18 (25.4)</td>
<td>40 (35.4)</td>
<td>0.431</td>
</tr>
<tr>
<td>Low HDL-C (%)</td>
<td>867 (48.9)</td>
<td>185 (44.8)</td>
<td>36 (50.7)</td>
<td>59 (52.2)</td>
<td>0.371</td>
</tr>
<tr>
<td>High WC (%)</td>
<td>1,111 (62.7)</td>
<td>167 (40.4)</td>
<td>47 (66.2)</td>
<td>40 (35.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>1,306 (73.7)</td>
<td>282 (68.3)</td>
<td>55 (77.5)</td>
<td>85 (74.6)</td>
<td>0.114</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>567 (32.0)</td>
<td>141 (34.1)</td>
<td>28 (39.4)</td>
<td>32 (28.3)</td>
<td>0.367</td>
</tr>
<tr>
<td>Frailty scores</td>
<td>0 (0–1)</td>
<td>1 (0–2)</td>
<td>3 (3–4)</td>
<td>3 (3–4)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Values are presented as number (%) or mean ± standard deviation or median (interquartile range).

BMI, body mass index; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; WC, waist circumference.

Fig. 1. Prevalence of poor health conditions in osteosarcopenia_frailty status. ADL, activities of daily living; IADL, instrumental activities of daily living.

demia-only, frailty-only, and osteosarcopenia with frailty groups among older adults are shown in Table 2.

Osteosarcopenia with frailty was significantly associated with a history of falls (adjusted odds ratio [adjOR] = 1.94; 95% confidence interval [CI], 1.20–3.15), poor ADL (adjOR = 2.85; 95% CI, 1.81–4.50), and poor IADL (adjOR = 5.09; 95% CI, 2.85–9.11) in the crude and full models. However, frailty-only was associated with a history of falls and poor ADL and IADL in the crude and adjusted models. Regarding the association between a history of fracture and osteosarcopenia and frailty status, only the osteosarcopenia-only group showed an increased OR of fracture in the crude and full models (adjOR = 1.48; 95% CI, 1.10–1.98).

Regarding the quality of life, frailty-only showed the greatest effect on MCS and PCS scores (β = -9.62 [95% CI, -12.19 to -7.05] and β = -10.68 [95% CI, -12.74 to -8.62], respectively), while osteosarcopenia with frailty had a moderate impact on MCS and PCS scores (β = - 5.25 [95% CI, -7.48 to -3.02] and β = -7.99 [95% CI, -9.74 to -6.16], respectively).

DISCUSSION

The results of this study demonstrated the overlap of osteosarcop-
Table 2. Association osteosarcopenia-frailty status with poor health conditions

<table>
<thead>
<tr>
<th></th>
<th>Crude model</th>
<th>Full model1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>History of falls</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robust Osteosarcopenia only</td>
<td>1.14 (0.87, 1.51)</td>
<td>1.18 (0.87, 1.60)</td>
</tr>
<tr>
<td>Frailty only</td>
<td>1.88 (1.10, 3.23)</td>
<td>1.80 (1.03, 3.16)</td>
</tr>
<tr>
<td>Osteosarcopenia with frailty</td>
<td>1.76 (1.13, 2.73)</td>
<td>1.94 (1.20, 3.15)</td>
</tr>
<tr>
<td><strong>History of fracture</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robust Osteosarcopenia only</td>
<td>1.38 (1.08, 1.76)</td>
<td>1.48 (1.10, 1.98)</td>
</tr>
<tr>
<td>Frailty only</td>
<td>1.44 (0.85, 2.45)</td>
<td>1.43 (0.80, 2.56)</td>
</tr>
<tr>
<td>Osteosarcopenia with frailty</td>
<td>1.44 (0.94, 2.20)</td>
<td>1.38 (0.83, 2.31)</td>
</tr>
<tr>
<td><strong>Poor ADL</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robust Osteosarcopenia only</td>
<td>1.03 (0.79, 1.35)</td>
<td>0.75 (0.55, 1.02)</td>
</tr>
<tr>
<td>Frailty only</td>
<td>6.48 (3.95, 10.63)</td>
<td>3.78 (2.17, 6.58)</td>
</tr>
<tr>
<td>Osteosarcopenia with frailty</td>
<td>4.69 (3.18, 6.93)</td>
<td>2.85 (1.81, 4.50)</td>
</tr>
<tr>
<td><strong>Poor IADL</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robust Osteosarcopenia only</td>
<td>1.84 (1.46, 2.32)</td>
<td>1.16 (0.87-1.55)</td>
</tr>
<tr>
<td>Frailty only</td>
<td>9.38 (5.36, 16.42)</td>
<td>4.84 (2.58, 9.10)</td>
</tr>
<tr>
<td>Osteosarcopenia with frailty</td>
<td>11.56 (7.20, 18.56)</td>
<td>5.09 (2.85, 9.11)</td>
</tr>
<tr>
<td><strong>MCS score of QoL</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robust Osteosarcopenia only</td>
<td>0.35 (-0.71, -1.40)</td>
<td>-0.54 (-1.80, -0.73)</td>
</tr>
<tr>
<td>Frailty only</td>
<td>-9.03 (-11.37, -6.70)</td>
<td>-9.62 (-12.19, -7.05)</td>
</tr>
<tr>
<td>Osteosarcopenia with frailty</td>
<td>-2.44 (-4.30, -0.59)</td>
<td>-5.25 (-7.48, -3.02)</td>
</tr>
<tr>
<td><strong>PCS score of QoL</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robust Osteosarcopenia only</td>
<td>-0.99 (-1.90, -0.08)</td>
<td>0.57 (-0.44, -1.59)</td>
</tr>
<tr>
<td>Frailty only</td>
<td>-14.25 (-16.26, -12.23)</td>
<td>-10.68 (-12.74, -8.62)</td>
</tr>
<tr>
<td>Osteosarcopenia with frailty</td>
<td>-11.08 (-12.67, -9.48)</td>
<td>-7.99 (-9.74, -6.16)</td>
</tr>
</tbody>
</table>

Values are presented as adjusted odds ratio (95% confidence interval) in multivariate logistic regression or linear regression analyses. Bold font indicates statistical significance.

ADL, activity of daily living; IADL, instrumental activity of daily living; QoL, quality of life; MCS, mental component summary; PCS, physical component summary.

1In full model, the outcome variables of each health condition: history of falls (age, sex, smoking, education, high waist circumference, diabetes, physical activity), history of fracture (age, sex, education, high waist circumference, diabetes, protein intake, energy intake, Ca/VitD supplement), poor ADL (age, sex, smoking, education, high waist circumference, diabetes, physical activity, hypertension, protein intake, energy intake), poor IADL (age, sex, smoking, education, high waist circumference, diabetes, physical activity, hypertension, protein intake, energy intake, Ca/VitD supplement), MCS (age, sex, smoking, education, high waist circumference, diabetes, physical activity, protein intake, energy intake, Ca/VitD supplement), and PCS (age, sex, smoking, education, high waist circumference, diabetes, physical activity, protein intake, energy intake, Ca/VitD supplement).

Osteosarcopenia with frailty and its association with poor health conditions in a population of community-dwelling older adults in Bushehr, Iran. Our findings revealed that the prevalence of coexisting osteosarcopenia with frailty was 4.8%, while the prevalence of frailty-only and osteosarcopenia was 3% and 17.4%, respectively.

Osteosarcopenia and frailty are closely associated with common factors such as lifestyle behaviors, nutritional status, genetic predisposition, hormones, and biological pathways. The dysregulation of the growth hormone (GH)/insulin-like growth factor 1 (IGF-1) pathway plays an essential role in the pathogenesis of osteoporosis, sarcopenia, and frailty. In addition, our data showed poorer energy and protein intake among patients with osteosarcopenia and frailty compared with those with osteosarcopenia or frailty alone. These findings are consistent with those of previous studies that revealed that nutrition mediates the relationship between osteosarcopenia and frailty.

Little is known about the natural histories of frailty and osteosarcopenia. The overlap between frailty and sarcopenia was discussed in the EWGSOP consensus, which showed that most frail participants had sarcopenia as a parameter of osteosarcopenia and vice versa. Our findings revealed a low coexistence of osteosarcopenia and frailty compared to osteosarcopenia only (4.8% vs. 17.4%). The different definitions and methodologies of osteosarcopenia and frailty used across studies make it difficult to compare results. Muscle strength is included in the definitions of both disorders. However, the cutoff points of this parameter differ between osteosarcopenia and frailty definitions. In addition to muscle function, other components of frailty are independent of the musculoskeletal system. In our study, this discrepancy can be explained by the fact that the mean age of our study population was 69.3 years.
and relatively few participants in this age range showed frailty; in contrast, musculoskeletal diseases were observed more frequently. Moreover, our population comprised community-dwelling older adults; thus, people in care settings who were more likely to have frailty were not included. In addition, while people with osteoporosis were included in the definition of osteosarcopenia, those with prefrailty were not considered.

Frailty and osteosarcopenia are potential risk factors for poor health conditions, such as functional decline, disability, poor quality of life, and mortality.17,38 In this study, we assessed the risk of adverse outcomes in patients with combined osteosarcopenia and frailty compared with those with osteosarcopenia alone, frailty alone, or neither. Unintentional falls are a major health problem in older people and impose high health-related costs and morbidity.19 Osteosarcopenia is strongly associated with falls and fractures.40 Osteoporosis and sarcopenia interact through biomarkers such as osteokines, myokines, and adipokines. However, frailty increases the risk of falls and fractures in older people.41

Declines in gonadal hormone, vitamin D, GH, and IGF-1 levels and elevations in pro-inflammatory cytokine levels and malnutrition may be important markers for the association between frailty and adverse outcomes. Our data showed that frailty alone and osteosarcopenia with frailty were associated with falls, with ORs of 1.80 and 1.94, respectively, compared with the robust group. In addition, the OR of fracture increased in patients with osteosarcopenia alone compared with the other groups. Osteoporosis is a risk factor for fractures, while sarcopenia is a risk factor for falls.12,43 However, as most people who experience a fracture do not have a body mineral density (BMD) reaching the threshold for osteoporosis,40 increased attention is needed in people with BMD less than -1 SD (osteopenia). Our reanalysis of the association between osteosarcopenia and health-related outcomes based on the definition of osteoporosis showed similar results using only osteoporosis to define osteosarcopenia, thus demonstrating that osteopenia/osteoporosis along with sarcopenia are risk factors for poor health conditions (Supplementary Table S1).

Therefore, muscle mass and function, which are used to define frailty, may be important predictors of falls. Other frailty parameters such as weight loss, exhaustion, and low activity are also important factors for falls. Therefore, in our study, frailty alone was more important than osteosarcopenia in terms of fall risk. In contrast, low bone mass (osteoporosis) plays a critical role in fractures, and frailty is not an essential risk factor compared with osteosarcopenia.

We evaluated functional disability using the Barthel and Lawton scales for ADL and IADL, respectively. The results of the crude and adjusted models suggested a significant association between frailty and ADL disability in this population. This association was stronger in the frail-only group than that in the osteosarcopenia with frailty group. In addition, osteosarcopenia with frailty and, to a lesser degree, frailty alone were powerful and independent predictors of developing dependence in IADL (osteosarcopenia with frailty, adjOR = 5.09; frailty-only, adjOR = 4.84). These results confirm that frailty is associated with a higher risk of disability than osteosarcopenia in our population. This is consistent with the results of previous studies showing that frailty is associated with functional disability.45,46 However, while some studies have shown an association between osteosarcopenia and disability,47,48 in our study, osteosarcopenia was only associated with IADL and not with ADL. Both osteosarcopenia and frailty are associated with disability; however, our results showed that the role of frailty was more prominent and significant when these two disorders were combined.

Our findings revealed significantly lower physical and mental HRQoL in the frail-only and osteosarcopenia with frailty groups than in the robust group. Previous studies have shown that low muscle strength and physical performance are related to reductions in both components of HRQoL.49 Both factors were lower in the osteosarcopenia and frailty groups in the present study. In addition, exhaustion, as a component of frailty, through psychological and immunological mechanisms such as increased cytokine production, contributes to low HRQoL.50 Thus, our results showed that frailty had a greater role in reducing HRQoL and that frailty should be diagnosed at an early stage in older people.

This population-based study with a large sample size revealed an overlap between osteosarcopenia and frailty in older adults. To our knowledge, this is the first study to demonstrate the effect of the coexistence of two important geriatric syndromes on poor health conditions in Iran. However, this study has some limitations. While our study results showed a cross-sectional association between osteosarcopenia and frailty in poor health conditions, we could not make causal inferences, and further longitudinal studies are needed. Additionally, disability was measured using two self-reported scales based on limitations in ADL and IADL. The main disadvantage of self-reported questionnaires is the possibility of invalid answers. In the BEH study, we attempted to ask sensitive and important questions to the participants’ companions and minimize information bias. In addition, the fracture data were based on history and self-reports and not on radiographic views. These points should be considered when interpreting the results of this study.

In conclusion, the results of this study demonstrated that older adults with osteosarcopenia with frailty and frailty alone were associated with significantly increased falls, poor ADL, poor IADL, and lower physical and mental HRQoL compared with robust old-
er adults. The limited overlap of osteosarcopenia and frailty in our population suggests that combined assessments have no additional odds of detecting poor health conditions. Osteosarcopenia affects only the musculoskeletal system, whereas frailty is a multifactorial and complex disorder. Thus, frailty has a higher incidence of functional disorders than osteosarcopenia, and the odds of skeletal disorders such as fractures are higher in individuals with osteosarcopenia alone. Our findings highlight the importance of early diagnosis and intervention strategies for osteosarcopenia and frailty as separate entities. Comprehensive clinical guidelines are recommended for use in primary healthcare or community-based health promotion settings to facilitate early identification and lifestyle interventions. Routine screening for osteosarcopenia and frailty is recommended in all people aged ≥ 60 years. In addition, raising awareness among health and social care professionals, healthcare policymakers, and older adults regarding geriatric disorders may help in diagnosing and treating individuals with osteosarcopenia or frailty and decrease the risk of their developing poor health conditions.

ACKNOWLEDGMENTS

We thank the personnel of the Persian Gulf Tropical Medicine Research Center and the study participants.

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

None.

AUTHOR CONTRIBUTIONS

Conceptualization, GS, RH; Data curation, AO; Investigation, NF; Methodology, SMB, FS; Project administration, IN; Supervision, BL; Writing–original draft, ASA; Writing–review & editing, NZB. All authors read and approved the final manuscript.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4235/agmr.23.0220.

REFERENCES


INTRODUCTION

Bisphosphonates have been used as key treatments for osteoporosis for over two decades. In the United States, alendronate, ibandronate, risedronate, and zoledronate are approved for the prevention and treatment of postmenopausal osteoporosis (PMO). Several studies have demonstrated the effectiveness of these medications as antiresorptive agents, which reduce fracture risk by 40%–70%.1

Intravenous bisphosphonates show improved patient compliance compared with oral therapy. However, intravenous bisphosphonates have a greater probability of adverse effects, including post-infusion pyrexia, flu-like symptoms, hypocalcemia, mandibular osteonecrosis, and nephrotoxicity, than oral agents.

Bisphosphonates can induce several types of nephrotoxicity. The mechanism by which bisphosphonates induce nephrotoxicity is unknown, but pathological findings suggest certain tendencies. Many reports of pamidronate-associated glomerular diseases, such as focal segmental glomerulosclerosis and zoledronate-associated acute tubular necrosis, appear in the literature.

Unlike pamidronate and zoledronate, recent clinical studies have indicated that intravenous ibandronate does not cause significant kidney damage and is well-tolerated, even in patients with underlying kidney disease.2 Thus, reports of ibandronate-associated nephrotoxicity are limited.

Herein, we describe a case with podocyte disease accompanied by azotemia following the intravenous administration of ibandronate.

CASE REPORT

An 88-year-old woman was referred to the emergency room be-
cause of generalized edema that had developed one month previously. She had been diagnosed with osteoporosis approximately 20 years before. Twenty months earlier, she received a quarterly intravenous administration of ibandronate (3 mg). The last treatment had been administered 2 weeks before. One month before admission, she noticed edema in both lower extremities that had gradually worsened. At the time of admission, she had gained 7 kg.

After the diagnosis of PMO, calcium and vitamin D were administered for the first 10 years. Subsequently, she took oral ibandronate once monthly for 3 years and continued calcium and vitamin D without ibandronate for 5 years. Finally, the patient had received intravenous ibandronate for 20 months before hospitalization.

The patient had no diagnosis of diseases other than hyperlipidemia and osteoporosis. She had been taking statins, calcium, and vitamin D as oral medications, but no new medications had been recently added. The patient had no family history of renal disease. A physical examination revealed generalized grade 4 edema in both lower extremities. The initial blood pressure and urine volume were 146/81 mmHg and 1,800 mL/day, respectively.

Laboratory tests revealed proteinuria with a urine protein/creatinine ratio (uPCR) of 32 and hypoalbuminemia (1.9 g/dL). The serum creatinine level was elevated (1.8 mg/dL) compared to baseline (0.8 mg/dL). Other serum findings (electrolytes, liver function tests, uric acid, glucose, and complete blood count) were within normal ranges. Serological evaluations for human immunodeficiency virus, hepatitis B virus, hepatitis C virus, antibodies to nuclear antigens, rheumatoid factor, and antineutrophil cytoplasmic antibodies (anti-PR3 and anti-MPO) were all negative. Serum complement (C3 and C4), protein electrophoresis, and immunofixation results were within the normal ranges. Thyroid function test results were normal, and we observed no evidence of cardiogenic problems; the pro-brain natriuretic peptide and troponin levels were within the normal range, and chest radiography showed no cardiomegaly. Additionally, renal ultrasonography showed no abnormal findings. We diagnosed the patient with nephrotic syndrome based on the test results.

A renal biopsy was performed to determine the pathological type. Light microscopy revealed mild mesangial hypercellularity and segmental amorphous collagen deposition in the glomeruli (Fig. 1A). The tubules showed marked focal atrophy and interstitial fibrosis (Fig. 1B). The immunofluorescence findings were unremarkable. Electron microscopy revealed diffuse effacement of the foot processes and no electron-dense deposits (Fig. 1C), consistent with podocyte disease favoring focal segmental glomerulosclerosis (FSGS).

Diuretic therapy was initiated to treat the edema. We administered angiotensin receptor blockers and tacrolimus, with adjustment of the tacrolimus dosage according to the target serum level (5–10 ng/mL). Steroids were not administered due to the severe osteoporosis.

A physical examination performed three months later revealed that the edema had resolved. The laboratory findings had improved (uPCR 2, serum albumin 3.5 g/dL, serum creatinine 0.97 mg/dL). Six months later, proteinuria and serum albumin levels had improved to near-normal levels (uPCR 0.64, serum albumin 4.28 g/dL).

Written informed consents were obtained.

**DISCUSSION**

Many drugs and chemicals can cause structural damage to the glomerulus, thereby increasing its permeability to large molecules. This condition often manifests as proteinuria or nephrotic syndrome. Hence, if common causes of proteinuria, and nephrotic syndrome, such as hypertension, diabetes, infection, and autoimmune disease, are excluded, the drug history must be checked. In

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**Fig. 1.** Renal biopsy was consistent with podocyte disease favoring focal segmental glomerulosclerosis. (A) The light microscopy (periodic acid-Schiff staining, x400) showed a normal size of glomerulus, mild mesangial hypercellularity, and segmental amorphous collagenous deposition in glomerulus. (B) Tubules revealed focal marked atrophy, interstitial fibrosis. (C) Electron microscopy showed diffuse effacement of foot processes and no electron-dense deposit.
this case, various etiologies were considered to be the cause of nephrotic syndrome. However, these were excluded through examination; therefore, the use of ibandronate was the most likely cause.

Compared to pamidronate and zoledronate, ibandronate is more protein-bound and has a significantly shorter renal tissue half-life, which might explain the rarity of ibandronate-associated nephrotoxicity. Several studies have demonstrated the renal safety of ibandronate. For example, a study involving > 3,000 patients with PMO who received 2–12 mg of intravenous ibandronate annually observed no adverse renal effects or renal failure, demonstrating a favorable renal safety profile. In this analysis, the mean decline of estimated glomerular filtration in patients exposed to 12 mg of intravenous ibandronate (-0.72 mL/min) was similar to that of patients treated with 2.5 mg of oral ibandronate (-0.28 mL/min).

Despite the renal safety of ibandronate, one case of nephrotoxicity associated with its oral form has been reported. Jia et al. reported a case of FSGS in a patient with breast cancer after long-term oral ibandronate treatment (50 mg once daily for 29 months). In this case, the patient had normal serum creatinine levels but exhibited clinical features of nephrotic syndrome, including edema, heavy proteinuria, and hypoalbuminemia. A renal biopsy revealed collapsing FSGS with significant podocyte injury. When reviewing cases of nephrotoxicity associated with other bisphosphonates, pamidronate primarily targets podocytes, whereas zoledronate primarily affects the tubular epithelium. However, a few cases have reported the opposite pattern. Contrary to these cases of bisphosphonate nephropathies, our patient showed simultaneous podocyte disease and tubule damage.

Inhibitors of the renin-angiotensin-aldosterone system, steroids, and immunosuppressants are commonly used to treat focal segmental glomerulosclerosis. Older adult patients are often hesitant to initiate immunosuppressive treatment. Severe infection is a major side effect of immunosuppressive treatment and contributes to increased mortality, especially in patients of advanced age. In this case, we administered an immunosuppressant (tacrolimus), considering the patient’s underlying disease and level of functional ability. Consequently, proteinuria and renal function improved. The patient remains alive without any treatment-related side effects.

We reported a relatively rare case of nephrotic syndrome associated with ibandronate treatment. Proteinuria and renal function can be reversed with immunosuppressive treatment if the syndrome is diagnosed early and ibandronate use is discontinued. We recommend monitoring proteinuria and renal function for the early detection of nephrotoxicity in patients treated with ibandronate. In older adult patients, the procedural risk of renal biopsy is not significantly high, and treatment outcomes can be anticipated. Therefore, even in older patients, renal biopsy may be necessary, and immunosuppressive treatment can be started considering the level of physical activity and underlying disease.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

None.

AUTHOR CONTRIBUTION

Conceptualization, BK; Data curation, YRC, HSL; Funding acquisition, YRC; Investigation, YRC, BK; Methodology, BK; Project administration, YRC; Supervision, BK; Writing–original draft, YRC, BK; Writing–review & editing, BK, YRC, DYL, SHL, JSJ.

REFERENCES

Survey of Awareness of Terminology Related to Functional Impairment and Muscle Health among Rehabilitation Healthcare Staff

Kota Hori, Yoshihiro Yoshimura
Department of Physical Medicine and Rehabilitation, Kumamoto Rehabilitation Hospital, Kumamoto, Japan

Older adults undergoing rehabilitation are often complicated by functional and nutritional impairments.\(^1\)\(^3\) Research has highlighted the importance of nutritional rehabilitation in addressing frailty, malnutrition, and sarcopenia in this population. Combining rehabilitation and nutritional care can significantly improve physical function, activities of daily living, and overall quality of life in older adults.\(^3\) Therefore, effectively addressing nutritional and functional impairments is key for successful rehabilitation in this population.

However, although several terms are used to describe functional impairment, they are not widely recognized by healthcare providers and may not be recognized when they occur.\(^1\) Therefore, we conducted a survey to determine the awareness of the terms used to describe functional impairments among staff working in convalescent wards.

We surveyed the staff of a hospital convalescent ward. The survey used Google Forms (Google LLC, Mountain View, CA, USA), which preserved the anonymity of the respondents, and contained questions to investigate staff awareness of terms related to different areas of dysfunction, including post-intensive care syndrome (PICS), locomotive syndrome, sarcopenia, frailty, disuse syndrome, and cachexia as terms related to functional impairment. PICS is mainly discussed in the acute phase, while disuse syndrome and cachexia are often discussed after the acute phase. Locomotive syndrome, sarcopenia, and frailty are well-known terms to describe changes in health status. Although all these terms involve the acute to the chronic phases, we included them in this study because of their different central phases. The respondents were asked whether they were familiar with each term, choosing from a 5-point scale of "Well known," "Known," "Can't say either," "Don't know," or "Not at all familiar." Although the survey items collected personal information, all items were controlled by response ID and did not contain identifiable personal information.

This study was approved by the Institutional Review Board of Kumamoto Rehabilitation Hospital (Approval No. 2023-13). Informed consent was obtained from all the study participants.

The 196 valid responses included those from 7 physicians, 56 nurses, 62 physical therapists, 34 occupational therapists, 14 speech therapists, and 23 allied health professionals. The awareness of sarcopenia, frailty, locomotive syndrome, and disuse syndrome was 83.8%, 76.1%, 70.6%, and 94.9%, respectively. In contrast, 28.9% and 9.6% of the respondents recognized cachexia and PICS, respectively (Fig. 1). Physicians had higher recognition rates for all terms, while physical therapists tended to have higher-than-average rates for all terms except PICS.

The survey results revealed high levels of awareness of locomotive syndrome, sarcopenia, frailty, and disuse syndrome but low levels of awareness of cachexia and PICS. Regarding the high levels of awareness of locomotive syndrome, sarcopenia, frailty, and disuse syndrome, our convalescence wards treat patients with many orthopedic and neurovascular diseases, and the fields of orthopedics and rehabilitation are directly linked. These terms are widely used in these fields, indicating a high level of recognition in directly related fields. Comorbidities, such as locomotive syndrome, sarcopenia, frailty, and disuse syndrome, have also been studied, highlighting their prevalence and interrelationships. Thus, the recognition of these terms in the orthopedic and rehabilitation fields is high.

The low level of cachexia recognition in this study may be because our convalescent wards have few opportunities to see chronically ill patients who meet the diagnosis of cachexia and have little experience in dealing with them. However, such patients may be overlooked due to a lack of staff awareness. Conversely, convalescent wards often accept patients who have completed intensive care. To the best of our knowledge, as no other reports have been described in the English literature, it is difficult to determine the actual situation regarding the degree of recognition of PICS outside the intensive care unit (ICU). The results of the present study...
suggest an extremely low awareness of PICS outside the ICU, and that awareness and collaboration must be addressed. Although physicians and physical therapists tended to have a higher level of awareness of the term dysfunction, understanding the causes of dysfunction and opportunities for direct intervention may have influenced this level of awareness. Further evaluation of professional awareness is warranted.

Ensuring that functional impairment is recognized and linked to support, requires increasing recognition and the coordination of terms with low recognition.

However, this survey was conducted in a single medical facility and cannot be considered fully representative of the situation in convalescent homes nationwide. The response rate was approximately 70%, and respondents with greater interest in dysfunction may have been more likely to respond.

We observed variations in the recognition of dysfunctional terms among staff working in convalescent wards, with high recognition of terms in directly related domains and low recognition in less related domains. Collaboration across domains required the broader dissemination of terminology rather than their use in limited domains.

ACKNOWLEDGMENTS

CONFlict OF INTEREst
The researchers claim no conflicts of interest.

FUNDING
None.

Fig. 1. Recognition of terms indicating functional impairment: (A) sarcopenia, (B) frailty, (C) locomotive syndrome, (D) disuse syndrome, (E) cachexia, and (F) post-intensive care syndrome (PICS).
AUTHOR CONTRIBUTIONS
Conceptualization, KH, YY; Data curation, KH, YY; Writing—original draft, KH; Writing—review & editing, KH, YY.

REFERENCES

Courses and Conferences

Upcoming academic events in 2024 of the Korean Geriatrics Society are as follows:
We would like to invite members of the Korean Geriatric Society and anyone who are interested.

[The 44th Geriatric Medicine Review Course]
August 11, 2023
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August 27, 2023
Auditorium, National Medical Center, 245, Eulji-ro, Jung-gu, Seoul, Republic of Korea
For more information, please contact kgskorea1968@gmail.com

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<table>
<thead>
<tr>
<th>Type of article</th>
<th>Abstract (word)</th>
<th>Text (word)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Reference</th>
<th>Table &amp; figure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original article</td>
<td>Structured&lt;sup&gt;b&lt;/sup&gt;, 250</td>
<td>3,500</td>
<td>50</td>
<td>7</td>
</tr>
<tr>
<td>Review</td>
<td>150</td>
<td>6,000</td>
<td>unlimited</td>
<td>7</td>
</tr>
<tr>
<td>Case report</td>
<td>150</td>
<td>1,500</td>
<td>20</td>
<td>7</td>
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<tr>
<td>Editorial</td>
<td>No</td>
<td>1,200</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>Letter to the editor</td>
<td>No</td>
<td>1,200</td>
<td>15</td>
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