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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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Aging with Disability: What Should We Pay Attention to?

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Despite our attention to population aging in recent decades, aging in people with long-term medical disabilities has been overlooked. People living with long-term disabilities have various problems associated with premature aging as their biological age is higher than their chronological age. Given the high prevalence of chronic diseases in people with disabilities, the presence of frailty and geriatric diseases needs to be identified before advanced age. Since the United Nation’s declaration of the Healthy Ageing Decade (2020–2030), worldwide concerns have increased regarding healthy aging policies for older populations. Considering these concerns, we should be aware of the urgent need to establish a healthy aging strategy for people with aging and disability.

People with congenital or acquired disabilities in childhood and early adulthood, such as cerebral palsy, spinal cord injury, and poliomyelitis, experience a variety of problems throughout their lives. As they age, ordinary functional decline due to natural aging is superimposed on pre-existing dysfunction, creating various late effects. “Late effects” is a concept referring to all new health problems deriving from the chronic impairment associated with existing impairment and disability. Chronic pain and dysfunction caused by stiffness and deformity often exacerbate pre-existing disabilities in middle and old age. Degenerative changes in the spine and joints due to abnormal repetitive motions and improper posture occur early in life, leading to functional decline. Secondary disorders related to medical and musculoskeletal complications involved in long-term disability, such as osteoporosis, osteoarthritis, fractures, obesity, and sarcopenia, are major health threats to people with disabilities. Therefore, a continuous systemic response is urgently required.

Age-related functional decline among people with disabilities is a chronic and complex problem that is challenging to manage. Ideally, reversible factors could be identified and addressed appropriately as early as possible; however, the complexity of aging with disabilities makes it difficult for long-term survivors with disabilities to receive appropriate medical care. Regarding individual chief complaints and symptoms, most healthcare professionals provide a piecemeal approach and symptomatic resolution of individual problems. Consequently, these patients often do not receive appropriate care that fits their needs and suits their problems. For example, surgical or nonsurgical treatments offered for secondary musculoskeletal problems are sometimes ineffective or lead to unexpected adverse effects on functional consequences. Thus, the treatment and management of these problems are of concern because they cannot be resolved by fragmented clinical treatment.

How can we improve on these situations? In recent years, we have increasingly recognized the influence of lifestyle, behavioral, and biological risk factors on the initial impairment, which influences the development of secondary or late effects. Successful aging with long-term disabilities has been discussed in a unique context, i.e., a complex construct comprising several interrelating domains including psychological resiliency and adaptation, autonomy, social connectedness, and the availability of appropriate and accessible healthcare. The overarching view of disability entwined with aging is essential. A paradigm shift has emphasized the “life-course perspective.” Indeed, the life experience of people with disabilities must be considered based on this life-course perspective. For example, the median age of the polio survivor population has already exceeded 60 years in Korea. Thus, our focus should now be on the interaction between aging and the effects of longstanding preexisting disabilities. From the life-course perspective of polio survivors, the development of secondary disorders, their aggravation, and limited function in connection with these disorders, all of which are predictable with aging, have become a serious threat to the health of these survivors. Thus, a comprehen-
sive, integrated approach and intervention to overcome and prevent these late effects in people with disabilities have emerged as a new paradigm.

From the perspective of geriatric rehabilitation, it is important not only to provide rehabilitative treatments according to the care needs in the acute and subacute recovery phases but also to detect various late effects or worsening of physical disabilities as early as possible, to implement appropriate interventions, and to monitor the outcome periodically for people with disabilities who are experiencing a functional decline in middle and old age. The primary healthcare system for people with disabilities, which has been implemented as a pilot project for the past 3 years since the Act on Guarantee of Right to Health and Access to Medical Services for People with Disability came into force in Korea in 2017, is expected to play a significant role in the age-related issues of people with disabilities. This is a system in which general healthcare and specific management for their impairment and disability work together to reflect the types and levels of disability, while also considering the clinical features and needs of people with disabilities living in the community. The attention of primary care physicians to the life course of people with severe disabilities and the provision of medical treatment and healthcare management in the community would help to solve problems related to aging with disability and simultaneously improve the primary healthcare system throughout the community, a win-win approach and the starting point of healthy aging for people with disabilities.

However, the currently implemented pilot project for people with disabilities has limitations, such as the absence of a link between general healthcare and disability management and a lack of collaboration with community resources. Meanwhile, in 2018, the Regional Health and Medical Centers for people with disabilities were established as a multidisciplinary workforce, such as physicians, nurses, social workers, and therapists, to serve as a link between community healthcare and social care systems for the medical and healthcare management of people with disabilities living in the community. It is time to prepare a healthy aging strategy for aging with disability by utilizing the multidisciplinary capabilities of the Regional Health and Medical Centers and facilitating communication and collaboration among healthcare and social care providers for people with disabilities.

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CONFLICT OF INTEREST

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INTRODUCTION

Fragility fractures, which occur owing to low-energy trauma such as a fall from a standing height or lower, are a major public health and economic concern worldwide, with an incidence estimated to outnumber those of stroke, heart attack, and breast cancer combined.\(^1,2\) With aging populations, fragility fractures are predicted to become a burden on healthcare systems. Although fragility fractures occur at various sites, including the wrist, humerus, and spine, commonly causing pain and disability and reducing quality of life, hip fractures present the most serious consequences. A recent epidemiological study using a nationwide database revealed that 14% and 21% of women and men, respectively, died within 1 year of hip fractures.\(^3\) Even if they recover, more than six out of ten older adults with hip fractures require assistance to carry out their activities of daily living.\(^4,5\) Therefore, preventing these low-trauma fractures is critical for independent living in older age.

Osteoporosis is a metabolic skeletal disorder characterized by low bone mass and poor bone quality, which result in an increased risk of fragility fractures. The prevalence of osteoporosis increases with age in both men and women in Korea, reaching nearly 70% in women aged > 70 years.\(^3\) Based on the underlying mechanisms of osteoporosis, many effective drugs, such as anti-resorptives or bone-forming agents, have been developed and used in clinical practice to improve bone strength.\(^6\) However, despite these efforts, decreases in the incidence of osteoporosis and resultant fractures have been stagnant, thereby forming the major cause of increased morbidity and mortality in older adults. Given the multifaceted pathogenesis of fragility fractures, a systemic approach to various risk factors besides deteriorated bone health is essential for fracture prevention.

Sarcopenia corresponds to a progressive loss of skeletal muscle mass and function due to an imbalance between protein synthesis and breakdown.\(^7\) Several lines of evidence indicate that sarcopenia is closely associated with higher mortality and adverse health outcomes, such as metabolic and degenerative diseases, disability, comorbidities, and institutionalization in older adults.\(^8-10\) As a result,
this syndrome has received attention globally in the last decade and is now considered a “geriatric giant” in super-aged societies.\(^\text{1}\) In particular, sarcopenia directly enhances fragility fractures by increasing the risk of falling due to aberrant balance and poor physical performance.\(^\text{1,13}\) Consequently, to effectively reduce fragility fractures, not only the metabolism of each bone and muscle but also the mechanisms underlying their interactions should be elucidated. The present review discusses muscle–bone communication, with a focus on the impact of muscles on bone health.

**CLINICAL EVIDENCE SUPPORTING THE HIGHLY INTEGRATED NATURE OF MUSCLES AND BONES**

Skeletal muscles and bones represent the largest tissues in the body of a non-obese person and comprise the musculoskeletal system, the structure of which allows mobility and protects the internal organs.\(^\text{14}\) In the law of the jungle, the coordination between muscles and bones is critical. For example, even if an animal has strong bones, weak muscles make it difficult to avoid predators. Conversely, in cases of weak bones but strong muscles, abrupt muscle-derived stress on the neighboring bones might increase fracture risk. Therefore, muscular and bone changes are likely matched throughout life.

Epidemiological studies have revealed that muscle and bone losses frequently occur simultaneously, especially in older individuals. In a nationwide population-based study of Asians aged > 65 years, lower height-adjusted appendicular skeletal muscle was associated with lower bone mineral density (BMD) after considering potential confounders.\(^\text{15}\) Other studies, including a systematic review and meta-analysis, have consistently suggested that middle-aged and older adult men and women with sarcopenia are more likely to have a higher risk of developing osteoporosis than those without sarcopenia.\(^\text{16-19}\) More importantly, skeletal muscles affect not only bone mass but also bone quality and strength. Poor structural parameters of the femoral neck and distal radius, including thinner cortices, reduced cortical area, deteriorated microarchitecture, and lower section modulus, are more common in men with lower muscle mass and weaker handgrip strength.\(^\text{19,20}\) In a representative cohort of the general Korean population aged ≥ 50 years, women with sarcopenia had markedly decreased femoral neck composite strength indices for compression, bending, and impact.\(^\text{21}\) These findings provide clinical evidence of the strong relationship between muscles and bones in aging.

To describe the concurrent development of osteoporosis and sarcopenia, “osteosarcopenia,” a unique geriatric syndrome, was initially proposed by Hirschfeld et al.\(^\text{22}\) Although common hormonal, nutritional, lifestyle, and genetic determinants may explain at least some of the highly integrated nature of muscles and bones,\(^\text{23-26}\) the pathogenesis of osteosarcopenia is multifactorial and remains actively investigated. From the perspective of physicians investigating the musculoskeletal system, the clinical implication of osteosarcopenia is that treatment strategies that target either osteoporosis or sarcopenia separately may not be sufficient for fracture prevention; thus, novel approaches to simultaneously improve both tissues are needed. Several comprehensive reviews on osteosarcopenia have been published recently.\(^\text{27-29}\)

**MUSCLE CHANGES OCCUR FIRST, FOLLOWED BY BONE ALTERATIONS**

Although the crosstalk between muscles and bones is bidirectional, some clinical and preclinical observations indicate the dominant role of muscles over bones in synchronizing the mass and quality of these two tissues. For example, a longitudinal study of 138 boys and girls during pubertal development revealed that the rate of muscle force accrual was the highest a few months before the peak gain in bone strength.\(^\text{30}\) Similarly, other studies including adolescents and young adults showed that lean mass changes preceded alterations in whole-body BMD and bone strength.\(^\text{31,32}\) Antecedent muscle atrophy also affected bone loss in an animal model.\(^\text{33}\) Furthermore, when astronauts return to normal gravity, their muscle loss is recovered six times faster than the bone loss.\(^\text{34}\) Consequently, these data suggest that muscle changes occur first, followed by bone alterations, in the sequence of muscle–bone communication.

**MUSCLE FORCE-GENERATED MECHANICAL SIGNALS TO THE BONE**

The impact of muscles on bones has traditionally been addressed from a mechanical standpoint. The skeletal muscles attach to bones along the motion axis, transforming skeletal segments into a lever system that requires significant muscle force to generate the torque necessary for movement.\(^\text{35}\) The muscle force-generated strain transducing anabolic activity in nearby bones has been theoretically supported by the “mechanostat” theory.\(^\text{36,37}\) Osteocytes, the most mechanosensitive bone cells, respond to fluid shear stress and convert mechanical strain into biochemical signals to recruit osteoclasts or osteoblasts.\(^\text{38,39}\) Therefore, osteocytes are key players in mediating the loading effects on bone strength. The model of bone as a biomechanical tissue is further supported by the results of murine experiments showing the beneficial effects of low-magnitude mechanical stimuli on bone mass and structure.\(^\text{40,41}\)
Patients with spinal cord injury (SCI) are a useful human model to better understand the importance of muscle atrophy in bone health. This devastating condition refers to temporary or permanent spinal cord damage, mainly resulting from trauma, such as sports injuries, falls, or vehicle accidents, and mimics neuroectodermal by surgical procedures to induce deteriorated musculoskeletal phenotypes. Paralyzed patients enter an extreme catabolic state and undergo dramatic contractile and morphological muscular changes below the injury level, leading to a substantial loss of muscle mass, function, and endurance. Osteoporosis is a common consequence of SCI, with bone loss occurring at a rate of 1% per week during the first 6–12 months after SCI, that is, 5–20 times faster than that observed with aging, prolonged bed rest, or microgravity. Interestingly, bone loss is observed mainly in the paralyzed limbs and not in the non-affected areas. Other studies have shown that electrical stimulation of paralyzed muscles markedly reduces deleterious post-SCI bone adaptations and even reverses, at least partially, bone loss after SCI. These human data point to the elimination of internal loading via muscle contractions and regular gravity loading via ground reaction forces as the primary causes of SCI-related weak bone strength.

Consistent with findings showing concomitant muscle atrophy and bone loss in rodent disuse models of hindlimb unloading and botulinum toxin injection, muscle-induced mechanical impulses are the main factors with positive effects on bone metabolism.

BEYOND MECHANICAL: THE ROLE OF MYOKINES ON THE MUSCLE–BONE CROSS-TALK

To describe cytokines or other peptides that are expressed, synthesized, and secreted from the skeletal muscles and exert biological activity in the human body, Pedersen et al. coined the term “myokine,” from the Greek words for “muscle” and “motion.” Recognizing muscles as an endocrine organ marks a watershed moment in our knowledge of how muscles communicate with other organs, such as the liver, brain, and adipose tissues, and establishes the notion of the critical need to maintain muscle health to reduce clinical disorders. With the development of modern technologies, including quantitative mass spectrometry-based proteomics, several secretome analyses have led to the identification of novel muscle-derived factors and various candidates from the supernatants of mouse C2C12 cells, human skeletal muscle cells, and L6 rat myotubes. Determining their biological roles in human health is currently a hot topic in this field.

Because skeletal muscles and bones are in close anatomical proximity, myokines likely biochemically influence bone homeostasis in a paracrine manner, a possibility strongly supported by long-standing observations in humans and rodents. Extensive muscle damage in open fractures is well known to impede fracture healing, with more negative consequences if the muscles are lost rather than crushed. Quantitative peripheral computed tomography, mechanical testing, and histomorphometry analysis in a mouse model indicated that covering open tibial fractures stripped from the periosteum with muscle flaps increased bone regeneration quality and rate compared to those obtained by covering them with similarly vascularized fasciocutaneous tissues. Furthermore, early soft tissue cover with a vascularized muscle flap markedly improved the healing of severe open tibial fractures after trauma in humans. These findings supported the idea that muscle production of local growth factors may induce bone formation, irrespective of physical load, and that biochemical and mechanical stimuli work together for muscle–bone crosstalk.

Several research groups have experimentally demonstrated the direct effect of myokines on bone metabolism. Conditioned media (CM) collected from C2C12 myotubes exerted protective effects against glucocorticoid-induced osteoblast and osteocyte apoptosis through β-catenin activation, and the primary myoblast CM of exercised mice significantly enhanced in vitro osteoblastogenesis. We first demonstrated that myotube CM suppressed in vitro bone resorption by inhibiting osteoclastogenesis and the resorptive activity of individual osteoclasts, whereas the same CM increased osteoblast viability and migration, thereby stimulating calvaria bone formation (Fig. 1). Furthermore, systemic treatment with myotube CM through the tail vein in ovariectomized mice increased bone mass by 30.7% compared to that of the non-CM. Although skeletal muscles can secrete complex factors, including positive or negative regulators, in terms of bone metabolism, our results showed the osteoprotective in vitro and in vivo net effects of various myokines on bone metabolism.

Fig. 1. Myotube-conditioned media (CM) show dual osteoprotective effects of simultaneously stimulating bone formation and inhibiting bone resorption.
The finding that CM from skeletal muscle cells can promote bone formation while inhibiting bone resorption has crucial therapeutic implications in the management of osteoporosis. Although anti-resorptive agents, such as bisphosphonate and denosumab, have been most frequently used to treat osteoporosis worldwide, these drugs also concomitantly suppress bone formation due to a coupling phenomenon, raising questions about their long-term side effects and efficacy. Bone-forming medications such as teriparatide or alendronate have been suggested as alternatives. However, these drugs also sequentially stimulate bone resorption, rendering their anabolic action ineffective after 2 years of use. Therefore, dissociation of bone resorption from bone formation is essential for effective osteoporosis treatment. In this regard, muscle-secreted factors with opposing effects on osteoblasts and osteoclasts might be ideal candidates as potential therapeutic targets against metabolic bone diseases.

**MUSCLE-DERIVED FACTORS INFLUENCING BONE METABOLISM**

Specific myokines affecting bone homeostasis are being continuously discovered. Among these factors, myostatin and irisin have attracted the most attention in muscle–bone interactions. Myostatin, also known as growth differentiation factor 8, is a protein released by myocytes. Its levels are increased in catabolic situations, causing muscle atrophy, such as inflammation, microgravity, and immobilization. Although myostatin has been primarily evaluated as a negative regulator of muscles, increasing data indicate its direct function in bone remodeling. Myostatin strongly accelerates receptor activator of nuclear factor-κB ligand (RANKL)-mediated osteoclastogenesis, whereas osteogenic differentiation of bone marrow-derived mesenchymal stem cells increases in a load-dependent manner in myostatin-deficient mice, resulting in increased bone mass and strength. Consequently, myostatin plays a detrimental role in both bones and muscles. Irisin is a myokine that regulates energy metabolism and is activated by physical activity. In bone metabolism, irisin stimulated in vitro osteoblastogenesis and in vivo bone formation and prevented bone loss in hindlimb-suspended mice, while inhibiting bone resorption by directly suppressing osteoclast differentiation or indirectly downregulating RANKL expression in osteoblasts and osteocytes. Therefore, exercise-induced irisin is a pro-osteoergic factor explaining the parallel muscle and bone changes.

Our group proposed lumican, a small leucine-rich repeat proteoglycan, as a muscle-derived osteoprotective factor. Norheim et al. identified lumican in CM collected from human myotubes based on the results of proteomic analyses using database searches and reported significantly upregulated lumican expression in human skeletal muscles following strength training. These results matched our findings of its strong production and secretion in both cell lysates and the CM of myotubes. Importantly, lumican knockdown markedly reduced the known beneficial effects of myotube CM on the bones, while adding lumican to these CM restored the reduced osteoblast viability caused by lumican silencing. Additional in vitro and animal experiments revealed that lumican not only increased bone formation by stimulating osteoblast viability and differentiation but also suppressed osteoclastogenesis and in vitro bone resorption. These findings indicate that lumican may be a myokine involved in bone anabolism.

β-Aminoisobutyric acid (BAIBA), a metabolite released during muscle contraction, is involved in various metabolic processes such as improved insulin resistance and white adipose tissue browning. BAIBA has also recently demonstrated bone-protective activities such as enhancing osteocyte survival under oxidative stress and reducing bone loss with hindlimb unloading. Brain-derived neurotrophic factors, follistatin, leptin, interleukin (IL)-6, and IL-7 have been suggested as myokines that link muscle activity with skeletal health. In contrast, biochemical muscle–bone communication is a complicated process involving various beneficial or detrimental mediators to preserve musculoskeletal homeostasis. Therefore, in addition to the important roles of individual myokines, future studies should focus on identifying how combinations of these muscle-derived factors precisely regulate bone metabolism, especially in vivo.

**CONCLUSION**

Although muscles and bones have a close relationship throughout life, observations during development and aging and in both human and animal disuse models revealed that the synchronization of tissue mass occurs in such a way that changes in muscle phenotypes precede BMD and bone strength alterations. The present review discussed evidence that mechanical forces, which have been the traditional focus, are not the only mechanisms by which muscle-derived signals may affect bone metabolism and emphasized the significance of skeletal muscles as an endocrine organ that secretes bone-regulatory factors. Consequently, both mechanical and biochemical aspects should be considered to fully understand muscle–bone crosstalk. Moreover, muscle-secreted factors could be ideal therapeutic targets for osteoporosis, with dual effects of increasing bone formation and reducing bone resorption. A particularly intriguing characteristic of myokines is that they
can affect muscle metabolism in an autocrine manner. In addition to myostatin and irisin, which have well-established functions in muscles, apelin rejuvenated behavioral and circadian phenotypes and prevented muscle weakness and poor physical activity in aged mice. These results suggested that muscle-derived factors may be promising pharmacological candidates against osteosarcopenia and can simultaneously control bone and muscle losses beyond those due to osteoporosis (Fig. 2).

The ultimate objective of musculoskeletal research is to prevent fragility fractures and their consequent morbidity and mortality. To achieve this objective, the early detection of high-risk populations who are vulnerable to these low-trauma fractures is critical, in addition to effective treatment for osteoporosis and sarcopenia. In this regard, the levels of muscle-released factors can be easily measured in the blood; thus, myokines, whose actions on bone and/or muscle metabolism have been verified, could be useful as potential circulating biomarkers to predict musculoskeletal health. However, despite tremendous efforts to uncover the pivotal role of myokines in muscle and bone metabolism, human evidence of the clinical applicability of these muscle-derived factors as therapeutic targets and blood-based biomarkers for musculoskeletal diseases is lacking. Future efforts are expected to provide a solution to these limitations, allowing older individuals to live healthy lives through independent daily activities.

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Importance of Sclerostin as Bone-Muscle Mediator Crosstalk

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INTRODUCTION

In recent decades, the aging population has dramatically increased. Loss of bone and muscle mass are common side effects of aging and have become a growing public health problem. Osteoporosis is a skeletal illness that affects bone microarchitecture and strength.1 Sarcopenia, in contrast, is defined as a loss of muscle mass, strength, and/or functional capacity.2 While sarcopenia and osteoporosis frequently co-occur, whether one condition occurs before the other and how the two are connected are unclear.3 Kirk et al.4 defined osteosarcopenia as a subpopulation of older adults with both osteoporosis and sarcopenia. Osteosarcopenia is a syndrome characterized by poor bone density (osteopenia/osteoporosis) and decreased muscle mass, strength, and/or functional capacity (sarcopenia).5 Because loss of bone mass is frequently coupled with a loss of muscle mass, this condition leads to a new paradigm in which bone may affect muscle and vice versa, necessitating additional research into the mechanisms of bone and muscle interaction. Muscle and bone are physically and physiologically linked and interact as a functional unit and both are influenced by aging.6

Loss of bone and muscle mass is a frequent aging condition and has become a growing public health problem. The term “osteosarcopenia” denotes close links between bone and muscle. Mechanical exercise was once thought to be the only mechanism of crosstalk between muscle and bone. Sclerostin is an important player in the process of unloading-induced bone loss and plays an important role in mechanotransduction in the bone. Furthermore, bones and muscles are categorized as endocrine organs because they produce hormone-like substances, resulting in “bone-muscle crosstalk.” Sclerostin, an inhibitor of bone development, has recently been shown to play a role in myogenesis. This review discusses the importance of sclerostin in bone-muscle crosstalk.

Key Words: Aging, SOST protein, Bone, Muscles

They share common mechanical and molecular mechanisms.6,7 The discovery of both bone and muscle as endocrine organs has recently demonstrated that muscle and bone can produce, express, and release cytokines and other peptides with paracrine, autocrine, or endocrine effects.8 The discovery of myokines, including myostatin, which are secreted by muscle, as well as the molecular biology revolution in the previous decade, has prompted in-depth investigations of muscle-bone interactions. Sclerostin is a cysteine knot protein released into the environment. It is part of the gene aberrative in neuroblastoma (DAN) family of proteins, which are proteins that stop bone morphogenetic protein (BMP) and Wingless-related integration site (Wnt) signaling.8 Produced by the sclerostin gene (SOST),9 sclerostin is a powerful inhibitor of bone growth that is produced mostly by osteocytes. Sclerostin was recently discovered in muscle cells in vitro and in muscles from variably aged mice with diverse metabolic and load-bearing capabilities.9 This finding could be the first step toward establishing the role of sclerostin in not only bone formation but also in myogenesis. Although a new paradigm has discovered the significance of sclerostin in bone-muscle crosstalk, the role of sclerostin remains
controversial and the mechanisms are unknown. We discuss the role of sclerostin in bone-muscle crosstalk, as well as potential common pathways in the following sections. This new knowledge is critical for the development of therapeutics for pathophysiological illnesses such as aging-related osteosarcopenia. In addition to targeting pathways that control bone and muscle at a systemic level, manipulating pathways that allow communication between bone and muscle is also important and could lead to new therapeutic targets that prevent, mitigate, or restore bone and muscle degradation.

BONE-MUSCLE CROSSTALK BEGINS WITH EARLY DEVELOPMENT AND DIFFERENTIATION

The human musculoskeletal system is a complex organ system composed of bones, muscles, tendons, ligaments, cartilage, joints, and other connective tissues that work together to perform coordinated motor activity. Bone and muscle cells are produced from a common mesenchymal precursor during intrauterine development and undergo organogenesis through carefully regulated gene activation and inactivation so that bone and muscle develop simultaneously. Both tissues attain their maximum mass around the same period and begin to lose mass at around the same age. Numerous studies have reported pleiotropic genes that regulate both bone and muscle, including methyltransferase 21C, AARS1 Lysine (METTL21C), a member of the methyltransferase superfamily, and myocyte enhancer factor 2C (MEF2C). The deletion of both genes in rats affected both bone and muscle densities, indicating that bone and muscle share a similar signaling mechanism.

SCLEROSTIN

Molecular Aspects and Expression

Sclerostin was discovered by researchers of rare hereditary diseases associated with sclerostin. Sclerosteosis is an autosomal recessive illness that manifests in early childhood as increased bone mass, thickening of the bone cortex, gigantism, and facial and head malformations. With increasing age, these clinical signs become more prominent. This disorder is caused by a mutation in SOST, which encodes the protein sclerostin and is located on the long arm of chromosome 17 (17q12-q21). Sclerostosis carriers have a normal phenotype, lower sclerostin levels, higher bone mineral density (BMD), and higher levels of bone production biomarkers.

Sclerostin is a 190-residue glycoprotein member of the DAN/Cerberus protein family that is thought to contain a cysteine knot and a glycoprotein that are secreted mostly by the bone matrix, and cartilage matrix. Sclerostin has two conserved N-linked glycosylation sites and several positively charged lysine and arginine residues, giving it a projected isoelectric point (pI) of 9.5. The structure of sclerostin is characterized by disordered N- and C-terminal arms in the free solution state, as well as three loops formed around the cysteine knot motif. The cysteine knot is at the base of Loops 1 and 3; their tips are linked by a disulfide link, giving the protein a structured core. The opposing side of the cysteine knot, Loop 2, is highly mobile in solution and is a functionally important portion of the protein that binds low-density lipoprotein receptor-related protein (LRP) 5/6 (Fig. 1).

SCLEROSTIN AS A MEDIATOR OF BONE-MUSCLE CROSSTALK VIA MECHANICAL LOADING AND ACTIVITY

Mechanical interaction was once thought to be the only method of muscle-bone communication. For an organism to move, it relies on the movement of its bones, which are related to skeletal muscles. Muscle forces are the source of mechanical stress that results in bone strain. Loss of skeletal muscle mass induces bone loss due to bone unloading, which supports the mechanical link between bone and muscle. Osteosarcopenia is another disorder that demonstrates the close link between bone and muscle. The “mechanostat” theory describes the mechanical interaction between muscle and bone, in which the muscles put mechanical stress on bones and the balance of bone turnover shifts away from

Fig. 1. The molecular structure of sclerostin showing the presence of disulfide bonds, resulting in a 3-loop structure.
bone resorption and toward bone formation.  
Skeleton unloading, which is frequently induced by immobilization, greatly reduces bone growth and mass. Understanding of the process of mechanotransduction has advanced at a breakneck pace. However, for many years, the mechanism by which osteocytes convert loading information into biochemical signals that direct bone formation has remained a mystery. Sclerostin expression may be regulated by mechanical loading in a way that affects osteocyte function. Sclerostin is a crucial regulator of unloading-induced bone loss and plays an important function in mechanotransduction in bone. Sclerostin levels were higher in human studies of bed rest. Some studies reported that increasing mechanical loading reduces osteocyte sclerostin expression, whereas decreased loading, such as from disuse or aging, is linked to increased sclerostin production and bone loss. Sclerostin is a protein that inhibits bone growth. Osteoclast resorption shifts the balance of bone remodeling in favor of osteoclast resorption when there is a lack of mechanical stimulus or disuse. During this mechanotransduction process, the lysosome rapidly degrades sclerostin, allowing new bone production by osteoblasts to occur. In contrast, the molecular processes by which osteocytes sense and transduce loading-related signals into changes in sclerostin expression remain unclear.

**Immobilization, Aging, and Defective Autophagy**

Several aging-related conditions, including aging itself, trigger alterations in autophagy, which could affect bone and muscle. Autophagy is a lysosome-dependent system that regulates cytoplasmic turnover in cells and is an important part of cellular proteostasis. Autophagosomes remove damaged, broken, or unnecessary proteins and organelles by fusion with lysosomes. This maintains a balance between protein formation and breakdown. Autophagy ability decreases with age, in part because lysosomal acidity decreases and fewer autophagy-related proteins are formed. The load-dependent breakdown of sclerostin is controlled by autophagy in bone, which is stimulated by mechanical load. Defects in lysosome function in older adults can affect bone health by preventing the removal of sclerostin, an inhibitor of bone formation.

Muscle, like bone, alters its mass in response to reduced load situations such as bed rest, immobilization, and inactivity. To meet the lower mechanical demand, the myofibrillar content and levels of supporting proteins are reduced, resulting in smaller myofibers and, consequently, muscle mass. Mechanical demand also influences skeletal muscle mass and performance. Outside of the normal homeostatic setpoint, high-intensity resistance training boosts the number of myofibrils and other muscle fiber contractile control mechanisms in the body. When these organelles and proteins are recruited, the cross-sectional area of muscle fibers increases, resulting in greater muscular hypertrophy (morphology) (function). The link between muscle loading and sclerostin expression is not as obvious as in the case of bone-induced mechanical loading. Sclerostin is a mediator that regulates bone-muscle crosstalk.

At the molecular level, osteocytes are believed to use at least two important chemicals, sclerostin and receptor activator of nuclear factor β ligand (RANKL), to control bone response to mechanical loading. Sclerostin, which is encoded by SOST, is only produced postnatally by mature osteocytes. Sclerostin reduces bone formation in vitro and in vivo by inhibiting osteoblast proliferation and differentiation through the canonical Wnt signaling pathway. Sclerostin likely suppresses Wnt-β-catenin signaling by binding to low-density LRPS/6. Furthermore, because its expression increases with mechanical unloading and decreases with loading, sclerostin may be crucial in bone response to mechanical loading. Lin et al. proved that unloading decreased Wnt/β-catenin signaling in WT mice, indicating that it is physiologically responsive to mechanical unloading. Sclerostin and Dkk1 were both responsive to mechanical stimulation, among several Wnt antagonists. Unloading had little effect on Wnt/β-catenin signaling in the absence of sclerostin, suggesting the major role of sclerostin in antagonizing Wnt/β-catenin signaling in the context of mechanotransduction. The increased sclerostin released by osteocytes in response to unloading suppresses Wnt/β-catenin signaling, causing apoptosis and reducing osteoblast activity, resulting in decreased bone production and lower bone mass.

Muscle was initially defined as a secretory organ by Pedersen who used the term “myokines” to describe the substances produced by muscles. Along with the discovery of myokines, the bone can also function as a secretory endocrine organ, producing many substances that regulate both bone and muscle. Muscle metabolites have recently been discovered to modulate bone mass. Sclerostin, which will be addressed further in the section below, is one of several myokines that affect bones.

**ROLE OF SCLEROSTIN AND WNT SIGNALING PATHWAY IN BONE-MUSCLE CROSSTALK AS A PARACRINE ORGAN**

Skeletal muscles and bones were long thought to be mechanically linked in the sense that muscles attach and put stress on bones. In the last decade, however, studies demonstrated that these two tissues work together at a higher level through crosstalk signaling processes that are important for the functioning of both paracrine
and endocrine tissues. Muscle and bone create factors (myokines and osteokines, respectively) that circulate and can operate as endocrine molecules that target distant organs. This field of study is fairly new; future studies are needed to learn more about how this hypothesized paracrine or endocrine crosstalk and biochemical interactions work.

**Sclerostin Expression in Bone and Muscle**

Sclerostin is a glycoprotein produced primarily by the bone and cartilage matrixes. Animal tests have shown that sclerostin can inhibit the formation of new bone. Sclerostin overexpression causes reduced bone mass, bone growth, and bone strength in mice. Sclerostin inhibits osteoblastogenesis and preosteocyte differentiation in osteoblasts, and also causes osteocytes to release RANKL to induce osteoclastogenesis and rapid bone resorption.

Bone remodeling refers to two processes that are constantly involved in bone construction and reconstruction throughout a person’s life. Osteoclasts and osteoblasts are responsible for bone resorption and production, respectively. Both of these cells are firmly connected in a basic multicellular unit (BMU) component, and bone resorption always occurs before bone formation. Sclerostin expression by nascent osteocytes at the start of osteoid mineralization serves as a negative feedback signal to osteoblasts, preventing excessive BMU. Sclerostin maintains quiescence in the cells surrounding the bone during bone remodeling to avoid osteoblast activation and bone growth without first resorbing the bone. Sclerostin inhibits osteoblast proliferation and differentiation during the early and late stages of osteoblast proliferation and differentiation, which is how it inhibits bone production. Sclerostin also promotes osteoblast death and osteocyte RANKL release, both of which are important for osteoclast activity and development. A higher BMD score is associated with more osteocytes. Moreover, sclerostin signaling to osteoblasts as target cells is more paracrine than endocrine.

The action and control of sclerostin in bone are better understood than those in muscles. A few recent studies have suggested the role of sclerostin in muscle mass modulation. The Wnt signaling system is also important in muscle stem cell formation. Kim et al. reported increased lean body mass with age in SOST -/- mice (p = 0.06). However, sclerostin overexpression via an adenovirus in the Bmp and Wnt pathways increased RANKL signaling. These findings are consistent with recognized crosstalk between the Wnt and Bmp pathways, Bmp signaling’s adipogenic effects, and recent findings that Bmp4 enhances adipocyte hypertrophy by increasing fatty acid production while reducing oxidation.

The Wnt/β-catenin pathway is a prominent therapeutic target for osteoporosis. Since sclerostin, a bone-forming inhibitor, is inhibited, many studies have investigated whether muscle cells may also produce this protein. SOST mRNA expression levels were also reported in different tissues, including skeletal muscle, despite being regarded as an osteocyte-specific protein; however, its synthesis in muscle has not been described in detail.
Magaro et al.\textsuperscript{9} studied bone-muscle crosstalk in vitro in osteogenic (2T3) and myogenic (C2C12) cell lines to demonstrate the role of sclerostin. Conditioned media derived from differentiating C2C12 cells considerably affected the functional maturation of osteoblasts.\textsuperscript{9} They also examined SOST/sclerostin protein expression and secretion in C2C12 and C57 muscle cells and found that it is produced at all three levels.\textsuperscript{9} A transient gain-of-function experiment in young mice with growing bones assessed the similarity of muscle sclerostin and osseous sclerostin.\textsuperscript{9} The skeletal system was also negatively affected by muscle-released sclerostin in this study.\textsuperscript{9} The co-administration of muscle and osseous sclerostin showed a similar effect. These findings suggest that muscle sclerostin may function in tandem with bone sclerostin to prevent osteogenesis and subsequent bone growth.\textsuperscript{9}

**Molecular Pathway of Sclerostin in Bone**

The Wnt/\(\beta\)-catenin signaling system plays a key role in osteoblast cell proliferation and development.\textsuperscript{32,41} Wnt is a glycoprotein that binds to the LRP5/6 receptor and Frizzled co-receptor to trigger signaling pathways. Through suppression of glycogen synthase kinase 3 (GSK3) activity using protein complexes with Disheveled (Dsh), Axin, and adenomatous polyposis coli (APC), this receptor complex blocked the phosphorylation of \(\beta\)-catenin.\textsuperscript{9,32} \(\beta\)-catenin accumulates in the cytoplasm and translocates to the nucleus as a result of this protein complex interaction.\textsuperscript{32} \(\beta\)-catenin is a transcriptional coactivator that collaborates with other transcription factors to kick-start gene expression, which leads to cell proliferation and differentiation.\textsuperscript{42} Mutations in the N-terminal chain of the human LRP5 protein decrease its affinity for sclerostin, resulting in an abnormal condition defined by increased bone mass, indicating that sclerostin is involved in bone mass control.\textsuperscript{32,33} Meanwhile, \(\beta\)-catenin activity is necessary for the development of mesenchymal stem cells from osteoblasts. Wnt pathway activation increases family transcription factor 2 (Runx2) expression in mice, whereas \(\beta\)-catenin inactivation results in a decrease in components needed for osteoblast development, such as Runx2 and Osx, and poor osteoblast differentiation. \(\beta\)-catenin also stimulates osteoblastogenesis while inhibiting chondrogenesis.\textsuperscript{33}

Structural studies of sclerostin and LRP5/6 also provided information on how these two proteins interact. Sclerostin has a flexible loop domain surrounded by two cysteine-containing fixed-structure finger domains.\textsuperscript{13,32} Recently, the flexible loop domain was demonstrated to be responsible for its interaction with the LRP6 receptor.\textsuperscript{43,44} Additionally, a sclerostin monoclonal antibody can bind to this location, preventing sclerostin-LRP interaction.\textsuperscript{43} In contrast, LRP5/6 is a transmembrane protein. In its extracellular domain, LRP5/6 has four \(\beta\)-propeller domains separated by four epidermal growth factor (EGF) domains: low-density lipoprotein receptor domain class A (LDLA), a transmembrane domain, and a cytoplasmic domain.\textsuperscript{15} The cytoplasmic domain is required for the recruitment of the GSK3/Dsh/Axin/APC complex, whereas the extracellular domain is antagonistic and is in charge of binding to Wnt protein.\textsuperscript{15} LRP6’s first two propellers (E1E2) are also involved in binding to Wnt and sclerostin ligands, suggesting that sclerostin and Wnt are competitors for binding to LRP6.\textsuperscript{15} Sclerostin inhibition is caused by a conformational shift in the LRP6 domain (Fig. 3).\textsuperscript{15}

**Molecular Pathway of Sclerostin in Muscle**

Although the mechanism by which sclerostin modulates muscle mass is not fully understood, the Wnt signaling system, which is important for mediating sclerostin in bone, is also thought to function in muscles. Wnt signaling is required for embryonic muscle development and adult skeletal muscle homeostasis.\textsuperscript{44} Muscle tissue is a highly flexible and complicated structure. Myogenesis, or muscle development, is the consequence of a well-coordinated network of transcriptional cascades and signaling channels.\textsuperscript{45} Wnt signaling influences the expression of myogenic regulatory factors, which are important transcriptional regulators of myogenic lineage development and differentiation.\textsuperscript{46} Wnt signaling is also critical for the development of the dermomyotome.\textsuperscript{34} Mice lacking both Wnt1 and Wnt3a do not form the medial compartment of the dermomyotome, which is associated with decreased myogenic factor 5 (Myf5) expression via a \(\beta\)-catenin-dependent process.\textsuperscript{34} Additionally, Wnt6-catenin-dependent signaling from the dorsal ectoderm is necessary for somite epithelial structure and dermal myotome development.\textsuperscript{34}

The Wnt family of human proteins consists of 19 members: Wnt1, Wnt2, Wnt2b (Wnt13), Wnt3, Wnt3a, Wnt4, Wnt5a, Wnt5b, Wnt6, Wnt7a, Wnt7b, Wnt8a, Wnt8b, Wnt9a (Wnt14), Wnt9b (Wnt14b), Wnt10a, Wnt10b, Wnt11, and Wnt16.\textsuperscript{45} These genes encode cysteine-rich secreted glycoproteins.\textsuperscript{33} Wnts can connect with important autocrine regulators and/or participate in paracrine modification by adhering to nearby cell membrane receptors.\textsuperscript{46} Wnt3a and Wnt4 are hypothesized to be greatly involved in bone-muscle interaction.\textsuperscript{46} These two proteins can also be separated into two categories based on their functions: Wnt3a is involved in the canonical signaling pathway, whereas Wnt4 activates both canonical and noncanonical signaling pathways.\textsuperscript{46} A strict balance between signaling pathways and their precise activation is required for successful skeletal muscle regeneration, with a temporal switch from Notch to canonical Wnt signaling required
for proper differentiation. Notch signaling is blocked by canonical Wnt signaling, allowing myogenic commitment and differentiation to proceed (Fig. 4).

**Sclerostin as inhibitor of Wnt3a signaling in muscle**

Wnt3a, which is found in the extracellular matrix of various cell types, is expressed in C2C12 myoblast cells and 2T3 osteoblasts and occurs at relatively high levels in both human (16.9 ± 2.4 ng/mL) and mouse (0.225–3.74 ng/mL) serum, suggesting a potential role of Wnt3a in bone-muscle crosstalk. Sclerostin inhibited Wnt3a-mediated crosstalk between MLO-Y4 osteocytes and muscle cells (C2C12) by modulating the Wnt/β-catenin pathway. Sclerostin inhibited the capacity of 10% MLO-Y4 CM and 10 ng/mL WNT3a to differentiate C2C12 cells. The combination of CM and WNT3a did not slow the acceleration of C2C12 cell differentiation by sclerostin. These findings indicate that the Wnt/β-catenin signaling pathway is involved in the MLO-Y4 CM and WNT3a promotion of C2C12 cell development. When WNT3a and sclerostin competed for binding to LRP5 and LRP6, they diminished sclerostin’s inhibitory effect on the Wnt/β-catenin signaling pathway. Canonical Wnt signaling causes satellite cell development in adult skeletal muscles, mostly through the Wnt3a ligand. Rudolf et al. reported that the disruption or stimulation of β-catenin in adult satellite cells affected regeneration, highlighting the importance of balanced canonical Wnt signaling for skeletal muscle regeneration. Wnt3a also activated MyoD and myogenin, which are essential myogenic regulatory proteins (Fig. 5).

**Sclerostin as inhibitor of the Wnt4 canonical signaling pathway in muscle**

The Wnt4 pathway is also involved in the action of sclerostin in muscle. Myoblast differentiation consists of two primary steps: irreversible cell cycle exit and subsequent myogenic factor expression and activation. Myf5 and MyoD are expressed early in myogenesis. Myogenin and MRF4 are activated as cells proceed toward a differentiated phenotype and work together to form an irreversible commitment to final differentiation. Myf5 levels are elevated in the G0 phase of cell differentiation. Borello et al. previously demonstrated that the canonical Wnt/β-catenin signaling pathway regulates Myf5 expression directly during somitogenesis. Wnt4 overexpression induced Myf5 expression, while Wnt4 silencing suppressed Myf5 expression during myoblast and satellite cell differentiation, implying a role for the ca-

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Fig. 3. Activation (right): Wnt protein binds to the LRPS/6 receptor and the Frizzled co-receptor to activate signalling pathways. With the help of protein complexes with Disheveled (Dsh), Axin, and Adenomatous Polyposis coli, this receptor complex inhibits the phosphorylation of β-catenin (APC) causing β-catenin accumulation in the cytoplasm and translocated to the nucleus. Inactivation pathway (left): sclerostin will inhibit Wnt signalling pathway causing dissociation of LRP 5/6 complex and frizzled receptor. LRP, lipoprotein receptor-related protein; GSK3, glycogen synthase kinase 3; APC, adenomatous polyposis coli; Dsh, disheveled.
Fig. 4. Activation of Wnt signaling during muscle regeneration. (A) In quiescent satellite cells, Wnt signaling (blue line) is inactive; (B, C) Canonical Wnt signaling suppresses the Notch pathway, leading the satellite cell to switch from proliferation to differentiation. (D) Wnt signaling induces myogenic gene expression via Barx2 activation, stimulates Follistatin, inhibits myostatin, and translocates the negative regulator Setdb1 into the cytoplasm, promoting myoblast development and fusion. (E) Finally, Wnt activity returns to low levels. Overall, Wnt/β-catenin signaling must be regulated in a timely manner for muscle regeneration to occur.  

Fig. 5. Mechanism of sclerostin as inhibitor of Wnt3a signaling in muscle via Wnt/β-catenin signaling pathway.  

Sclerostin may have a role in bone-muscle crosstalk via the canonical pathway (Wnt/β-catenin signaling). Sclerostin was revealed to inhibit Wnt3a-mediated crosstalk, resulting in reduction of the Wnt/β-catenin signaling pathway and inhibition of satellite cell development. Wnt3a also induces MyoD and Myogenin, both of them are required for myogenesis. Myf5, myogenic factor 5; LRP, lipoprotein receptor-related protein; GSK3, glycogen synthase kinase 3; APC, adenomatous polyposis coli; Dsh, disheveled; TCF/LEF, T-cell factor/lymphoid enhancer factor.
nonical pathway in Wnt4’s myogenic characteristics. Wnt4 was initially described as a noncanonical Wnt, it is also involved in the activation of the canonical Wnt/β-catenin signaling pathway. Wnt4 hypertrophic activity in C2C12 and satellite cells was linked to Tcf/LEF promoter activation, demonstrating the involvement of Wnt/β-catenin signaling in myogenesis regulation.

Myostatin may also be involved in the Wnt4 pathway. Myostatin acts via Smad2 and Smad3 receptor-associated proteins. Phosphorylated Smad2 and Smad3 form a heterodimeric complex with the common mediator Smad4. These activated Smad proteins act as the primary intracellular mediators of myostatin signaling by translocating into the nucleus and activating target gene transcription via interactions with DNA and other nuclear factors. Takata et al. reported that Wnt4 had no effect on Smad2 phosphorylation in differentiated C2C12 myoblasts but suppressed myostatin-induced Smad2 phosphorylation. Wnt4 induced myogenesis by inhibiting myostatin. Wnt4-mediated suppression of the myostatin pathway may be related to decreased myostatin expression and/or decreased myostatin/Smad transduction. However, myostatin did not decrease Tcf/LEF activity caused by Wnt4 overexpression in proliferating and differentiated C2C12 myoblasts. Thus, myostatin did not affect the Wnt4/β-catenin signaling pathway (Fig. 6).

CONCLUSION

Numerous investigations have confirmed the existence of bone-muscle communication. Mechanical and endocrine relationships explain how these two organs communicate. Sclerostin is a novel myokine and osteokine that increases bone metabolism via mechanical loading. Physical activity and mechanical loading reduce sclerostin levels, which prevent future bone and muscle loss. Aging causes changes in autophagy, which could affect bones and muscles.

According to a new paradigm, muscle and bone can function as paracrine organs, secreting chemicals to modulate their action. Sclerostin also plays a significant role in bone and muscle crosstalk by activating the Wnt/β-catenin signaling pathway, which acts as a powerful inhibitor. Wnt3a and Wnt4 also play a critical role in myogenesis in muscles. Some studies have shown that Wnt4 interacts with the myostatin pathway to regulate muscle hypertrophy. Further research is required to fully elucidate the processes underlying sclerostin regulation of bone-muscle communication to develop innovative methods to prevent the development of osteoporosis and sarcopenia (Fig. 7).

Fig. 6. Mechanism of sclerostin as inhibitor of Wnt4 signaling in muscle via Wnt/β-catenin signaling pathway and Wnt4’s effect to myostatin.

(Left and center) Wnt4 bone and muscle crosstalk occurs via the Wnt/β-catenin signaling pathway, which inhibit by sclerostin. Wnt4 overexpression increased Myf5 expression, which is necessary for myogenesis. (Right) Myostatin is also thought to be involved in the Wnt4 pathway. Wnt4 induces myogenesis by inhibiting myostatin thus preventing muscle wasting and cachexia. Myf5, myogenic factor 5; LRP, lipoprotein receptor-related protein; GSK3, glycogen synthase kinase 3; APC, adenomatous polyposis coli; Dsh, disheveled; TCF/LEF, T-cell factor/lymphoid enhancer factor.
Fig. 7. Summary of sclerostin role in bone and muscle crosstalk. Crosstalk between bones and muscles is mediated not just by mechanical loads and activity, but also as a paracrine organ. Sclerostin is a key regulator of unloading-induced bone loss and is involved in bone mechano-transduction. Sclerostin levels will be reduced as a result of increased activity and mechanical loading. Sclerostin is a Wnt antagonist that responds to mechanical stimulation. Mechanical loading reduces sclerostin levels, which activates Wnt/β signaling. A meanwaging will result in alterations in autophagy, which will have an impact on bone and muscle. Meanwhile, a new paradigm has emerged, claiming that bone and muscle can function as an endocrine organ, secreting sclerostin, which can function as both myokines and osteokine. Reduced sclerostin levels in the bone lower osteoclast and RANKL stimulation, resulting in increased bone growth and osteoblast. On the other hand, two key wnt families play important roles in muscle: Wnt3 which acts via the canonical pathway and Wnt4 which acts via both the canonical and non-canonical pathways. Wnt3 and Wnt4 activation leads to myogenesis. Sclerostin is an effective inhibitor of both.

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CONFLICT OF INTEREST
The researchers claim no conflicts of interest.

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Fear of falling is a geriatric condition that must be understood from both a clinical perspective and from the environment in which older adults live. This review aimed to describe the scientific evidence reported in the last 5 years regarding the fear of falling in older adults and its relationship with environmental factors. The relationships between fear of falling and environmental factors are mainly evidenced in the built environment. Older adults with a fear of falling are described as perceiving the built environment as dangerous when they do not meet the requirements of safety, accessibility, and comfort; they also report the importance of living in communities with controlled crime levels and available social support for older adults to improve their insecurity and feelings of vulnerability.

Key Words: Fear of falling, Environment, Aged, Healthy aging

INTRODUCTION

Fear of falling is a geriatric condition that has been described as both a cause and a consequence of falls.\(^1\) This condition is defined as the loss of confidence to avoid falls while performing relatively non-hazardous daily activities so that the person avoids performing them despite having the capabilities to do so.\(^2,3\) The prevalence of fear of falling ranges between 3% and 85% and varies among populations, partly due to the diversity of methods used for its measurement.\(^4\) As fear progresses, the person restricts the performance of activities inside and outside the home, increasing the likelihood of further mobility restriction,\(^5\) which contributes to a cycle of inactivity and deconditioning, with a loss of postural control, in addition to functional limitation, mobility disability,\(^7\) increased risk of falls,\(^8\) and, ultimately, institutionalization.\(^9\) Fear of falling involves physical, cognitive,\(^10\) and psychological components,\(^10,11\) which do not necessarily overlap; its predictors have been well studied from the individual aspect, with the physical and functional components being the most investigated. A loss of postural control,\(^12-14\) functional impairment,\(^15\) mobility disability,\(^16,17\) visual and hearing impairments,\(^18\) and a history of falls\(^3\) are predictors of fear of falling. Regarding the cognitive component, the fear of falling is associated with decreased executive functions, decreased memory, verbal fluency,\(^19\) and increased time to perform dual tasks.\(^20\) Concerning the psychological component, depression is a predictor of fear of falling,\(^11,23\) and emotion regulation, fear of falling, and fear-related avoidance behavior are correlated.\(^23\) Other conditions that predict fear of falling are age,\(^16\) being female,\(^16,17\) poor self-perception of health,\(^16,23\) and polypharmacy.\(^21\)

Regarding the environment, most studies have evaluated the influence of the built environment as a variable that influences mobility and disability in older adults, in which the aesthetics of the built environment and the combination of land use and access are predictors of increased physical activity in this population.\(^23\) Likewise, a combination of neighborhood attributes is significantly related to physical activity. Residential density,\(^24\) commercial destinations, transit stops, and sidewalks are associated with increased compliance with physical activity guidelines, while neighborhoods that are highly walkable but unsafe and with few recreational facilities show higher compliance with total physical activity guide-
In contrast, older adults living in neighborhoods with low socioeconomic conditions, residential instability, and negative street characteristics show a higher prevalence of physical disability and difficulty in leaving the home. Some studies have also identified characteristics that negatively affect the mobility and physical activity of older adults from the perspective of the environment. However, few studies have reported on the relationship between fear of falling and the environment, a necessary topic as this geriatric condition directly affects mobility.

This review focuses on the relationship between the fear of falling and the environment in which older adults live. It is important to identify whether the characteristics of the environment contribute to the presence or progression of fear of falling, as occurring with physical activity or the presence of a disability. Assessment of the fear of falling should be approached not only from a clinical perspective but also from other sectors that accompany and guarantee the preservation and improvement of health in groups of older adults. Moreover, the development of intersectoral interventions requires the identification of the environmental attributes that most influence the fear of falling.

According to the World Health Organization (WHO), healthy aging involves creating environments and opportunities that enable people to be and do what they value throughout their lives. Therefore, a better understanding of how people interact with their environment and to what extent the environment hinders or enables their functional capacity is required. In this sense, the healthy aging model argues that the adaptation of older adults to their environment requires understanding and interventions related to geriatric conditions from the following five areas or factors: the built environment; people and their relationships; attitudes and values; health and social policies; the systems that support them and the services they provide.

In this context, the objective of this review is to describe the scientific evidence in the last 5 years regarding older adults with a fear of falling and the relationship of this condition with environmental factors according to the model of healthy aging.

**LITERATURE SEARCH**

We conducted a review based on the parameters of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. We searched the Scopus, Web of Science, and PubMed databases. The search in the Web of Science and PubMed used the keyword “fear of falling” initially, with refinement using Boolean (AND) and specific descriptors such as “environment, build environment, family relations, social relations, attitudes, health policy, public policy, health services, factors a scoping review intervention.” We conducted this search between January and April 2021.

The inclusion criteria were quantitative and qualitative studies of any design and scope focused on environmental components (housing, neighborhood, and city) and fear of falling in older people and manuscripts published in English between 2016 and 2021. We excluded articles that described the environment and fear of falling as independent covariates and those that only mentioned them as related aspects without measurement.

We identified a total of 143 articles. A reviewer assessed these studies to eliminate duplicates and select those eligible for analysis. After 21 duplicate records were eliminated, there were 126 articles for screening based on the titles and abstracts, of which 99 were eliminated because the variables of interest did not meet the inclusion criteria. Subsequently, full-text analysis was performed on the remaining 27 articles and 10 were excluded because the variables of interest in the present review were independent covariates or aspects related to the topic but without measurement. Finally, we included 17 articles in the analysis. Fig. 1 illustrates the study selection.

**Data Extraction**

For the analyses, we extracted data on sample size, sociodemo-
graphic characteristics (age and sex), study type (cross-sectional, longitudinal, or experimental), and environmental dimensions from the perspectives of healthy aging (the built environment; people and their relationships; attitudes and values; health and social policies; and the systems that support them and the services they provide). 27, 28, 30

RESULTS

Study Characteristics
The 17 studies included in the analysis had a total sample of 2,901 participants; the average participant age was 72 ± 6 years, 59.9% of whom were female and 40.1% were male. Among the included studies, 58.8% (n = 10) were cross-sectional, 11.8% (n = 2) were clinical trials (CTs) (one explanatory and one pragmatic CT), 5.9% (n = 1) were longitudinal studies, and 23.5% (n = 4) were qualitative studies. The characteristics of the quantitative studies and their measurements and interventions with respect to the environment are presented in Tables 1 and 2. The characteristics of the qualitative studies and identified topics are listed in Table 3.

Study Quality
The results of the present review showed that most of the studies were cross-sectional; thus, the level of evidence was low. However, explanatory multivariate analysis predominated in eight of the studies, which performed linear and logistic regressions. The single longitudinal study used latent class analysis, while the two CTs reported results based on per-protocol and intention-to-treat analyses. Only two studies reported correlational findings. All studies used valid outcome measures and the analyses were adjusted for key sociodemographic and clinical variables.

RELATIONSHIPS BETWEEN FEAR OF FALLING AND THE ENVIRONMENT

The results showed that most of the studies assessed or provided interventions for factors related to the “built environment,” namely, the home, neighborhood, and city. A smaller number of studies described the fear of falling and the perception of social support and safety; their results showed an approach to factors related to “people and their relationships.” Likewise, studies also mentioned “attitudes” regarding concern about falling among older adults. No specific results were identified with respect to the other factors mentioned in the healthy aging model.

Fear of Falling and Factors Related to the Built Living Environment

Only one pragmatic CT demonstrated the results of a modification of the living environment. The authors assessed the effectiveness of nighttime automated LED lighting on the path from the bedroom to the bathroom 31 in reducing the fear of falling and improving sleep in older adults. Intention-to-treat analysis showed a significantly decreased nighttime fear of falling, from a score of 5.5 ± 3.0 to 3.8 ± 3.2 (on a 1–10-point scale) at the end of the study (z = -3.31, p = 0.001, r = 0.30). Per-protocol analysis yielded similar results, with a decrease from 5.6 ± 3.1 at baseline to 4.0 ± 3.4 at final assessment (z = -2.41, p = 0.016, r = 0.26). Additionally, the mean scores on the Falls Efficacy Scale International (FES-I) scale

Table 1. Clinical trials included in the analysis

<table>
<thead>
<tr>
<th>Study (yr)</th>
<th>Number of participants</th>
<th>Average age (y)</th>
<th>Sex</th>
<th>Sample source</th>
<th>Study type</th>
<th>Environmental intervention carried out</th>
</tr>
</thead>
<tbody>
<tr>
<td>Son et al. 31 (2020)</td>
<td>32</td>
<td>75.5</td>
<td>Female (50%)</td>
<td>Elderly with mild dementia who attended a dementia center in K-town, Korea</td>
<td>EC</td>
<td>Intervention based on white noise therapeutics. A white noise walking program was applied for the experimental group (n = 16), and a walking program only for the control group (n = 16). Frequency two times/week, duration 4 weeks. Primary outcome variables: walking time (joining a chair, walking 3 m, turning, and sitting down again), level of anxiety and fear of falling.</td>
</tr>
<tr>
<td>Tholking et al. 31 (2020)</td>
<td>64</td>
<td>80.8</td>
<td>Female (66%)</td>
<td>Community elderly (Netherlands)</td>
<td>Pragmatic clinical trials with pre and posttest</td>
<td>Intervention to improve night lighting through an automated LED guide light (Gight) installed inside the house, in the path from the bedroom to the bathroom. Use of this strategy for 6 months. Primary outcome variables: rate of night falls and fear of falling.</td>
</tr>
</tbody>
</table>

EC, explanatory clinical trial.
Table 2. Cross-sectional and longitudinal studies included in the analysis

<table>
<thead>
<tr>
<th>Study (yr)</th>
<th>Number of participants</th>
<th>Average age (y)</th>
<th>Sex</th>
<th>Sample source</th>
<th>Study type</th>
<th>Measurements conducted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smith et al. (2016)</td>
<td>1,188</td>
<td>78.7</td>
<td>Female (71%) Male (29%)</td>
<td>Vulnerable community-dwelling elderly receiving long-term home care (Detroit).</td>
<td>Longitudinal (15 months)</td>
<td>Barriers at the entrance of the residence: unstable front porch, broken steps. Accessibility for mobility in the neighborhood. Use of Google Street View images in Google Earth to identify sidewalks on both sides of the street, continuous sidewalks, smooth/flat/unbroken sidewalks, free of obstacles, wide enough for two people to pass comfortably, and public transportation stop on the street. Use of commercial, business, institutional or recreational land within the residential block.</td>
</tr>
<tr>
<td>Harada et al. (2017)</td>
<td>238</td>
<td>69.5</td>
<td>Female (45%) Male (55%)</td>
<td>Frail elderly community members in a suburban residential area of Japan.</td>
<td>Cross-sectional</td>
<td>Neighborhood environment: Abbreviated Neighborhood Environment Walkability Scale instrument with 8 subscales: residential density, land use diversity, land use accessibility, street connectivity, walking and cycling facilities, aesthetics, traffic safety and security, and security against crime.</td>
</tr>
<tr>
<td>Auais et al. (2017)</td>
<td>1,841</td>
<td>69.5</td>
<td>Female (51.9%) Male (48.1%)</td>
<td>Community elders from five international cities: Kingston, Saint-Hyacinthe, Tirana, Manizales, and Natal.</td>
<td>Cross-sectional</td>
<td>Living space mobility in five different cities. Living Space Assessment (LSA) instrument.</td>
</tr>
<tr>
<td>Mortazavi et al. (2018)</td>
<td>450</td>
<td>70.4</td>
<td>Female (51.9%) Male (48.1%)</td>
<td>Elderly people in the rural and urban community of Bojnurd (Iran).</td>
<td>Cross-sectional</td>
<td>Instrument: Home Safety Checklist.</td>
</tr>
<tr>
<td>Darvishpoor Kakhki et al. (2018)</td>
<td>301</td>
<td>68.6</td>
<td>Female (54.8%) Male (45.2%)</td>
<td>Elderly with hypertension admitted to one of the hospitals of Shahid Beheshti University of Medical Sciences.</td>
<td>Cross-sectional</td>
<td>Activities reported on the FES-I scale. Presence of hazards in the environment.</td>
</tr>
<tr>
<td>Lee et al. (2018)</td>
<td>394</td>
<td>65.4</td>
<td>Female (55.9%) Male (44.1%)</td>
<td>Middle-aged adults belonging to an integrated health system in four cities: Killeen, Temple, College Station, and Bryan (United States).</td>
<td>Cross-sectional</td>
<td>Neighborhood environment assessed across 4 domains: - traffic safety (traffic speed, traffic volume and distracted drivers) - crime safety (strangers, drunk people and crime rates) - physical environments (light condition, drainage ditches, sidewalk condition and street maintenance) - social environments (people walking and biking, social support)</td>
</tr>
<tr>
<td>Lee et al. (2018)</td>
<td>7,730</td>
<td>72.5</td>
<td>Female (59.2%) Male (40.8%)</td>
<td>Community elders from 16 cities and provinces in Korea.</td>
<td>Cross-sectional</td>
<td>Discomfort with neighborhood environment: home entrance/hallway, stairs, bathroom, bedroom, living room, doorways, kitchen/dining room, other or no space, getting on and off buses (subway), up and down stairs/slopes, lack of transportation, roads too bumpy to travel, transit services without consideration for older adults, hazards from too much traffic, or no discomfort when going out. Accessibility to neighborhood facilities: amount of time to access markets/supermarkets, hospitals/clinics/health centers, public offices, elderly care service centers, other care service centers and bus/underground stations. Social support: existence of close relatives, close friends/neighbors and visits from people other than cohabitants in the last month.</td>
</tr>
</tbody>
</table>

(Continued to the next page)
Table 2. Continued

<table>
<thead>
<tr>
<th>Study (yr)</th>
<th>Number of participants</th>
<th>Average age (y)</th>
<th>Sex</th>
<th>Sample source</th>
<th>Study type</th>
<th>Measurements conducted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee et al. (2020)</td>
<td>907</td>
<td>84.8</td>
<td>Female (78.2%) Male (21.8%)</td>
<td>Elderly people belonging to life centers in Houston, Chicago, and Seattle.</td>
<td>Cross-sectional</td>
<td>Outdoor environment of the place of residence (Living Centers): quality of the design of the outdoor areas or corridors, comfort in reaching the outdoor areas, physical comfort in the outdoor areas and satisfaction with the use of the outdoor areas.</td>
</tr>
<tr>
<td>Curl et al. (2020)</td>
<td>129</td>
<td>70</td>
<td>Female (81%) Male (19%)</td>
<td>Elderly members of community group networks in Greater Christchurch, New Zealand.</td>
<td>Cross-sectional</td>
<td>Outdoor activities assessed through 9 of the 16 items of the FES-I scale: going to the store; walking up or down stairs, walking in the neighborhood; walking on a slippery surface; walking in a crowded place, walking on an uneven surface; walking up or down a slope, using public transportation; crossing the street. Difficulties in walking in the neighborhood: presence/absence of footpaths, condition of footpaths, slope, width of footpath, obstacles on footpath, puddles or leaves, steps or stairs, busy roads, crosswalk facilities, street lighting, traffic speed and crime. Self-report of perceived accessibility based on the Lättman et al.’s scale (Accessibility of the Built Environment for the Satisfaction of Needs).</td>
</tr>
<tr>
<td>Romli et al. (2021)</td>
<td>1,489</td>
<td>68.5</td>
<td>Female (56.3%) Male (43.7%)</td>
<td>Elders included in the first wave of the Malaysian Elders Longitudinal Research (MELoR) project. Representatives of three cultural ethnicities: Malay, Chinese, and Indian.</td>
<td>Cross-sectional</td>
<td>Hazards in the home using the HOME FAST tool. It covers 7 key areas: flooring, furniture, lighting, bathroom, storage, stairs, and mobility.</td>
</tr>
<tr>
<td>Canever et al. (2021)</td>
<td>308</td>
<td>64.5</td>
<td>Female (57.8%) Male (42.2%)</td>
<td>Elderly community members registered in the three Basic Health Units of Balneário Arroio do Silva (Brazil).</td>
<td>Cross-sectional</td>
<td>Perception of the neighborhood-built environment assessed through the Neighborhood Environment Walkability Scale: infrastructure (presence of sidewalks, green and recreational areas, hills, trash and sewage); traffic in the neighborhood (safety and pollution); and general safety in the neighborhood (lighting and walking safety).</td>
</tr>
</tbody>
</table>

FES-I, Falls Efficacy Scale International; HOME FAST, Home Falls and Accidents Screening Tool.

also improved significantly, from 36.9 ± 12.9 at baseline to 31.5 ± 11.8 at the final evaluation (z = -2.69, p = 0.007). Likewise, 57% of the participants reported a subjective decrease in their fear of falling, with a high appreciation of the use of this innovative strategy (8.4 ± 0.8 on an appreciation scale of 0–10).

In contrast, three cross-sectional studies evaluated the relationship between the fear of falling and environmental hazards within a dwelling. First, they applied a home safety checklist and showed that the greatest fear of falling was associated with walking on a slippery surface, while the lowest fear was associated with getting dressed or undressed. Likewise, the use of inappropriate footwear, slipping on uneven surfaces, and reaching objects in high places showed the highest mean scores in people with a fear of falling. A significant relationship was observed between housing safety status, prevalence of falls, and fear of falling (p < 0.0001). A second study showed similar results regarding demanding physical activities reported by hypertensive older adults and the intensity of their fear of falling, including walking on slippery surfaces, walking on uneven surfaces, walking up or down a slope, climbing or descending stairs, reaching for an object or bending, and taking a bath or shower.

The fear of falling is also higher when hazards are present in the environment of older people; for instance, the fear of falling is significantly higher than that in individuals living in safer places (p = 0.001). The third study applied an instrument to identify hazards in housing, which showed a higher frequency (30%) in toilet and bathroom areas (no grab bar, no non-slip mat, distant toilet), slippery floors, housing without access to headlights, and
Factors associated with falls and fear of falling.

Fear of falling as a disturbance in everyday life.

Older adults with Parkinson disease

Participants

25 Females
12 Older adults

Older adults and their caregivers at a compassionate community elders

Sample source

Autonomy with personal care.

The environment.

9 Older adults
4 Caregivers

13 Older adults
3 Caregivers

Factors associated with a fear of falling; one study reported a greater effect of inadequate footwear. Binary logistic regression analysis of the total score of the instrument showed no significant association with fear of falling (Exp(β) = 1.010, p = 0.694); however, further analysis of the instrument subscales showed a lower probability of association between a high fear of falling and housing hazards (p = 0.023) and higher with functional problems (p < 0.001). Neither domain (environmental hazards and functional problems) was associated with activity restriction due to a fear of falling. 34

Concerning the barriers around the home and their relationship to the fear of falling, one study evaluated the perceived level of outdoor qualities in older adults who were classified as frequent and infrequent users of hallways and outdoor living areas. The researchers asked the participants about the design quality, physical comfort, and their perceived satisfaction with such areas. The results showed a greater fear of falling among individuals who were not frequently outdoors (odds ratio [OR] = 0.597, p = 0.023 for infrequent outdoor use and OR = 0.418, p = 0.003 for frequent outdoor use), as well as a low perceived level of the general design qualities of the outdoor areas and comfort when using these areas (OR = 0.522, p = 0.004 for infrequent users and OR = 0.414, p = 0.002 for frequent users). Additionally, adequate corridor design (OR = 0.614; 95% confidence interval [CI], 0.405–0.931), comfort levels in the use of outdoor areas (OR = 0.657; 95% CI, 0.437–0.989), and frequency of use of outdoor areas (OR = 0.538; 95% CI, 0.368–0.787) were associated with a decreased fear of falling outdoors after adjusting for individual factors (age, sex, health status, history of falls, vision impairment, and mobility aids). 35

Finally, two qualitative studies described the environmental factors associated with a fear of falling; one study reported a greater fear of falling among older adults in assisted living facilities reported with poor nighttime lighting and poor ambulatory surfaces in their housing. 36 A second qualitative follow-up study evaluating the results of adaptations made to older adults’ bathrooms showed that, at 23 months, older adults reported that they continued to use their walk-in shower without any difficulty; they noted that this adaptation had reduced the hazard and led to a larger and safer space with less fear of falling or injury. Similarly, the new bathroom reduced the physical burden on caregivers to assist with bathing, which led to better self-care and autonomy. 37

Fear of Falling and Factors Related to Neighborhood Built Environment

Among the factors related to neighborhood environment, a randomized CT assessed the effects of an intervention based on white noise therapy and walking on walking time, anxiety, and fear of falling in older adult patients with mild dementia. The intervention aimed to block external sounds to reduce the detection of ambient noise and disperse other noises in an irregular and open space, allowing individuals to focus on and detect specific sounds. The results showed a decrease in the fear of falling in both groups (experimental group, walking plus white noise; control group, walking only), with a significant difference in the experimental group with a confidence level of 99% (p < 0.01) and an 11.5-point decrease compared to the control group. 38

In contrast, a longitudinal study evaluating outdoor mobility trajectories in vulnerable older adults showed four latent trajectories: those with low mobility frequency, high mobility, decreasing mobility over time, and those who did not go outdoors regularly.
prevent their living spaces from shrinking with age. Additionally, required high functional reserves to overcome these barriers and mental barriers were more common, and older adults in these sites were more likely to be housebound compared to older adults who went out more frequently (OR = 3.55; 95% CI, 1.91–6.59) and also showed a higher probability of older age (OR = 1.92; 95% CI, 1.25–2.97). Similarly, approximately 14% of respondents lived in a block with mixed land use, 24% had barriers at their home entrance, and the mean sidewalk accessibility score was 3.5 ± 1 on a scale of 0–6.

Five cross-sectional studies reported an association of fear of falling with neighborhood aspects such as living in a neighborhood with many broken sidewalks, drainage ditches, presence of strangers, worse perceived accessibility and neighborhood conditions, living near places with garbage accumulation and/or places with open sewers, living in places with high crime rates, and low social support. In contrast, Lee et al. reported a lower likelihood of fear of falling in older adults who perceived that their neighborhoods had well-lit streets, well-maintained streets, and low traffic speed (OR = 0.324; 95% CI, 0.162–0.646). Likewise, Lee et al. described a lower fear of falling in adults living near supermarkets, stores or free markets, commercial businesses, bus stops, parks, plazas, walking tracks, bike lanes and/or sports courts, and outdoor gyms, as well as those living in places with sidewalks on most streets, with level streets, and those considered safe for walking during the day and at night; as well as those residing near a bus stop, and having an outdoor gym and safe places to walk.

**Fear of Falling and Factors Related to the City Built Environment**

Only one study addressed this category. This study assessed fear of falling and mobility in the living spaces of five cities with significantly different socioeconomic and cultural characteristics in middle- and high-income countries. The results demonstrated that fear of falling was related to mobility in living spaces and that the strength of the association differed between cities. Before adjusting for confounders, the relationship between the fear of falling and living space was significant for the overall sample of the five cities. After adjustment, the relationship remained significant for three of the five cities; in the other two sites, this association was weak and was explained mainly by functional and clinical factors. In these two cities, the scores were significantly worse, physical environmental barriers were more common, and older adults in these sites required high functional reserves to overcome these barriers and prevent their living spaces from shrinking with age. Additionally, the authors explained that these people lacked the financial means to compensate for the effect of environmental challenges on their living spaces; thus, they relied mainly on their functional reserves.

**Fear of Falling, People, and their Relationships**

Five studies evaluating aspects related to neighborhood social support and safety reported significant differences between the perception of high social support and reduced fear of falling (OR = 0.842; 95% CI, 0.772–0.919). These studies defined social support as the cumulative effects of the existence of close relatives, friends/neighbors, and visits received by people other than cohabitants in the last month. These characteristics were more significant in individuals with a history of falls. A second study reported that the likelihood of having a fear of falling outdoors was almost two times that of those who perceived that their neighborhood had many strangers (OR = 2.520; 95% CI, 1.238–5.129). In contrast, another study found that the perception of safety from crime influenced physical activity in frail older adults and that the fear of falling was a mediating factor in the relationship between safety from crime and physical activity. Likewise, a study reported that older adults living in places with high crime rates were more likely to report fear of falling (OR = 2.62; 95% CI, 1.50–4.56). Finally, qualitative studies indicated that a fear of falling involved difficulty spending time with friends and family due to constant worry about falling and an inability to engage in joint activities due to loss of self-confidence.

**Fear of Falling, Attitudes, and Values**

Four qualitative studies reported on attitudes regarding the fear of falling; these studies revealed behaviors or predispositions such as feeling ashamed of public stigmatization due to falling in front of an acquaintance. Fear of falling was seen as a dichotomous condition that protected against harm since it generated a greater awareness of the dangers of the environment and cautious behaviors; moreover, potential danger manifested in a feeling of discomfort owing to the lack of control of such dangers. Thus, slippery surfaces, snow, or rain were reported as the greatest risks for falls and generated greater concern and fear of consequences. In contrast, two studies reported that adults with a fear of falling felt vulnerable due to the feeling of aging, awareness of falls, and disability symptoms that led them to perceive danger in everyday environments. Another qualitative study reported an unwillingness to accept age-related changes in physical capacity, poor disposition towards walking aids, and misconceptions about falls and fear of falling as inevitable situations that cannot be controlled by the person himself/herself, but rather by spiritual forces. This study also identified...
caution and greater care to perform activities, as well as avoidance of activities when fear of falling is present.  

**DISCUSSION AND CONCLUSION**

When analyzing the results from the environmental factors contemplated in the healthy aging model, results were found for three of them. In the first instance, it can be said that most of the studies evaluated factors related to the built environment, specifically the home and neighborhood. A second aspect is that which shows the relationships of the older adult with his or her family and community; however, only some results are described from the perception of support and social security in the neighborhood. Third, we identified some results related to the attitudes of older adults about a fear of falling. We did not identify studies on the fear of falling and health policies, systems, or services provided.

As the built environment was the main component identified in this review, it is necessary to comment that its measurement is diverse depending on the interests of the authors. In this sense, four studies evaluated or performed intervention of aspects related to the housing environment through validated scales or checklists. On the other hand, six of these studies were dedicated to measuring or intervening aspects of the neighborhood environment through various instruments assessing perception in terms of discomfort, accessibility, or use of different neighborhood elements. Finally, three studies that assessed both aspects of the built environment (home and neighborhood) using different instruments were identified. This can be explained by the fact that the built environment has been addressed from environmental gerontology by different disciplines and theoretical perspectives through disability models, neighborhood models, land use, and person-environment adjustment, among others. However, most of the studies analyzed in this review did not specify the theoretical perspective underlying their work.

The main results of studies on the built environment showed that poor lighting, irregular or slippery floors, bathrooms and showers without grab bars, the presence of stairs, and objects in high places were the factors most related to the fear of falling. Likewise, home exterior design was of vital importance for older adults to decide to use it frequently. People with a fear of falling do not go out frequently in the house with exteriors that are considered unsafe or uncomfortable. This is an important aspect to consider, as adults with a fear of falling who do not go outdoors are four times more likely to be confined and have difficulty walking. Among the characteristics of the neighborhood environment, irregular sidewalks, poor street lighting, garbage, noise, and poor accessibility to places of commerce, are perceived as unsafe factors for mobility in adults with a fear of falling. As the built environment is a space that has been planned, shaped, and used to meet the needs of daily life, neighborhood characteristics can greatly affect the life and health of individuals, influencing their decisions, the risks to which they are exposed, and the resources they can access.

A higher frequency of fear of falling has been reported among older adults in neighborhood environments compared to home environments. Deshpande et al. attributed this difference to greater demands to control balance and maintain stability in the neighborhood environment so that the fear of falling in the neighborhood environment may precede that in the home environment. Likewise, people who express fear of falling inside the home, in general, have a lower functional capacity than those who experience a fear of falling only related to activities in the neighborhood.

Environmental gerontology has shown that built environments of the home and neighborhood are particularly important for the functional health and well-being of older adults; however, the specific predictors of the built environment that influence the onset or progression of the fear of falling have not been identified. Therefore, it is important to continue investigating this subject, as the WHO has proposed strategies to achieve age-friendly environments through compliance with a set of basic indicators that include the physical and social environment. Among these indicators is the accessible physical environment, assessed through quality of life in the neighborhood, ease of walking, accessibility of public spaces and buildings, accessibility of public transport vehicles, accessibility of public transport stops, and accessibility of housing.

In contrast, studies have reported a negative correlation between the perception of social support and fear of falling, while the perception of an unsafe neighborhood or one with many strangers increases the probability of fear of falling in older adults. Thus, fear of falling acts as both an outcome variable derived from poor safety and a mediating factor between the presence of delinquency and the performance of physical activity. The World Report on Aging and Health described the importance of older adults being able to create and maintain relationships as a fundamental aspect of the environment in which they live. The relationships they establish with children, partners, family, friends, neighbors, colleagues, acquaintances, and the community, in general, generate feelings of trust and belonging to certain groups that can provide support and contribute to well-being. Based on this concept, the results of the present review only show some existing relationships between older persons and their community environment; therefore, this knowledge also warrants attention from empirical evidence.
Regarding the attitudes of older adults, the qualitative results of this review illustrated some ways by which older adults react to a fear of falling and identified signs of embarrassment, vulnerability, dual sensations of danger/protection, poor disposition to walking aids, and erroneous thoughts about possible ways of addressing concerns about falling. These aspects are important to consider when developing interventions to avoid or reduce the fear of falling. Likewise, these attitudes must be investigated and validated from a quantitative perspective to provide generalizable results that contribute to the profile that characterizes a person with a fear of falling.

Finally, all the included studies evaluated individual covariates (age, sex, comorbidities, hospitalizations, presence of falls, physical capacity, visual acuity, polypharmacy, perception of health status, etc.) as mediating aspects between the presence of a fear of falling and the environment. Kakhki et al. reported that people with functional problems had a higher probability of presenting a high degree of fear of falling within the dwelling. Likewise, Lee et al. showed that comfort levels in outdoor living areas and their frequency of use were associated with a decreased fear of falling after adjusting for individual factors such as age, sex, health status, history of falls, vision problems, and use of mobility aids. These findings demonstrated the importance of considering individual variables when evaluating the relationship between the fear of falling and the environment as conditions that cannot be seen in isolation, given the variability in the aging process. Thus, the same environment can have different effects on individuals.

In conclusion, our results confirmed that the relationships between the fear of falling and environmental factors are mainly evidenced in the aspects of the built environment. The evidence supporting these relationships was derived from cross-sectional studies that have mostly performed multivariate analyses, taking into account mediating covariates related to intrinsic capacity (especially physical and functional aspects). Older adults with a fear of falling are characterized by perceptions that the built environments are dangerous when they do not meet the requirements of safety, accessibility, and comfort, as well as the importance of living in communities where crime levels are controlled and where social support is provided to older adults to improve their insecurity and feelings of vulnerability.

The limitations of this review include the lack of generalizability of the results regarding the relationships between the fear of falling and the environment owing to the level of evidence. Likewise, it is difficult to make conclusion regarding environmental factors because different studies have approached this concept from different theoretical perspectives and paradigms.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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None.

AUTHOR CONTRIBUTIONS

Conceptualization: CLVR; Data curation: CLVR, CLC; Investigation: CLVR; Methodology: CLVR; Supervision: CLC; Writing-original draft: CLVR; Writing-review & editing: CLC.

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Best Practice Recommendations for Geriatric Dysphagia Management with 5 Ws and 1H

Ebru Umay¹, Sibel Eyigor², Gulistan Bahat³, Meltem Halili⁴, Esra Giray⁵, Pelin Unsal⁶, Zeliha Unlu⁷, Canan Tikiz⁸, Meltem Vural⁹, Asli Tufan Cincin⁶, Serkan Bengisu⁸, Eda Gurcay¹⁰, Kemal Keseroglu¹¹, Banu Aydeniz¹², Elif Celik Karaca¹², Burak Karaca¹³, Ahmet Yalcin¹⁴, Cemile Oezsurekci¹⁵, Dilek Seyidoglu¹⁶, Ozlem Yilmaz¹⁶, Sibel Alicura¹¹, Serhat Tokgoz¹⁷, Barin Selcuk¹⁸, Ekin Ilke Sen¹⁹, Ali Yavuz Karahan¹⁹, Ayse Yaliman¹⁹, Serdar Ozkok¹, Birkan Ilhan¹¹, Merve Guner Oytun⁰, Zeynel Abidin Ozturk²², Sibel Akin¹³, Betul Yavuz¹³, Mazlum Serdah Akaltun²⁵, Aylin Sari²⁶, Murat Inanir²⁷, Meral Bilgilişoy²⁸, Zuhal Çalışkan²⁹, Guleser Saylan¹¹, Tuğçe Ozer¹¹, Yasemin Eren³⁰, Derya Hopanci Bicakli¹⁶, Dilek Keskin³¹, Zekeriya Ulger³², Aylin Demirhan³³, Yalkin Calik³⁴, Bulent Saka³, Zeynep Aykin Yigman³⁵, Erhan Arif Ozturk¹

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INTRODUCTION

In our aging world, human life expectancy is increasing with advances in medicine and improvements in living conditions. Consequently, the size of the older population is increasing worldwide. This increase brings with it many new terms, situations, and challenges. With aging, progressive physical impairments and functional disabilities occur as a part of the natural process.

As with all organ systems and tissues of the body, changes in swallowing occur with aging. Aging is an independent risk factor for dysphagia. Dysphagia symptoms occur in approximately 1/3 of healthy older adults and 2/3 of hospitalized older people. Presbyphagia is a condition characterized by structural and functional changes in the swallowing mechanism in healthy older individuals along with the normal aging process. All stages of swallowing are affected. The changes observed in presbyphagia include reduced bolus control, preparation, and transport; delayed swallow triggering and initiation; delayed opening of the upper and lower esophageal sphincters (UOS and LOS, respectively); and decreased esophageal peristalsis and dysfunction.

Considering etiologic causes besides presbyphagia, the most common cause of dysphagia in older adults is secondary dysphagia due to neurogenic causes such as stroke. The number of causes of secondary dysphagia increases with age. This further complicates swallowing function in older adults. Therefore, knowing, recognizing, and managing presbyphagia is important.

In recent years, research on dysphagia in older adults has increased. However, recommendations for geriatric dysphagia management in the literature have generally comprised chapters in the management guidelines of secondary causes such as stroke for a single limited part of dysphagia such as diagnosis, for treatment from the point of view of a single discipline, or for a single stage of swallowing such as oropharyngeal dysphagia (OPD). Dysphagia is now defined as a geriatric syndrome, and physician/health care professionals caring for older patients require comprehensive and clinical practice recommendations for dysphagia diagnosis, treatment, and follow-up. Moreover, dysphagia does not consist only of OPD because esophageal dysphagia (ED) also occurs not uncommonly in older adults; however, no guidelines yet exist for the management of ED in the geriatric population.

To address this gap, both in our country and worldwide, this study aimed to provide recommendations for clinical practice from the perspective of experienced multidisciplinary specialists, based on the questions “who, why, where, when, what, and how.”

METHODS

This study was performed between February and May 2021 via e-mail using the three-round modified Delphi survey method.

Aim, Definitions, and Focus of the Recommendations

This study defined dysphagia as any disorder in the transfer of oral food to the stomach. Thus, the term included both OPD and ED. The recommendations are intended for all individuals 65 years of age and older, regardless of the presence of any specific disease. We developed recommendations for older adults, from diagnosis to...
treatment and follow-up, under the headings of the 5Ws (who, why, what, where, and when) and 1H (how) question method. These recommendations are not specific to any disease and should not be applied to individuals under 65 years of age.

Methodology for Generating the Recommendations

A multidisciplinary expert group created the recommendations. We initially formed an expert task force comprising a geriatrician, a gastroenterologist, and two physiatrists, who then selected consultant experts. The selection criteria for the consultant experts included at least 5 years of experience in the care of geriatric patients or patients with dysphagia and active treatment or follow-up of these patients. In addition, we required that the consultants have knowledge regarding the diagnosis and treatment of dysphagia from experts in fields not specifically focused on dysphagia. Moreover, experts from all regions of the country (north, south, east, and west) were recruited to avoid a single-region view. Thus, we invited 20 physiatrists, 20 geriatricians, 10 gastroenterologists, five neurologists, five otolaryngologists, five speech-language pathologists (SLPs), five dietitians, two dentists, two general surgeons, and two social workers to participate via e-mail.

We then formed a consultant expert group comprising the 48 invited experts (18 physiatrists, 14 geriatricians, five otolaryngologists, two gastroenterologists, two neurologists, two dietitians, two dentists, one SLP, one general surgeon, and one social worker) who agreed to answer each questionnaire from their perspectives as experienced professionals in geriatrics and/or dysphagia in 38 different centers in 14 cities. Although the study started with 48 professionals, different numbers participated in each Delphi round, from 48 experts in the first round to 42 and 39 experts (29 centers and 14 cities) in rounds two and three, respectively.

We created consensus recommendations through a seven-step process. In the first step, the task force searched the main bibliographic databases (PubMed, EMBASE, and Cochrane Library) using the keywords "older," "older adult," and "dysphagia."

Guidelines, meta-analyses, systematic reviews, and randomized and nonrandomized comparative studies were first evaluated to establish appropriate question patterns. The abstracts of the identified literature were read, and the entire article was screened when necessary. The literature search included the last decade up to January 2021. Later, the task force team created six open-ended and unlimited commentary questions, suitable for the following 5Ws and 1H question patterns: "Who, why, where, when, with what, and how should dysphagia be evaluated and treated?" These six-question words, also known as journalistic questions, allowed us to examine all aspects of the subject. This question model, which is also a creative thinking technique, was used to describe the problem.29,30

In the second step, the six-question survey created by the task force was sent via e-mail to the consultant expert group members who agreed to participate in the study. The purpose of this (first) Delphi round was to identify the management, diagnosis, rehabilitation, and follow-up of dysphagia in older adults to understand potential problems and make recommendations. For this reason, the experts were asked to submit their detailed and unlimited opinions and suggestions within 1 week.

In the third step, the suggestions and comments of the 48 consultant experts invited by the task force were collected and 429 items were created (who-why 120 items, when 20 items, with what 82 items, and how 200 items).

In the fourth step (second Delphi round), a draft of the survey containing the majority opinions was sent back to the consultant group by task force and the feedback of their opinions was expected within 4 weeks.

In the fifth step, the task force revised the survey according to the responses from the consulting experts. During the revision, we removed items defined as overall divergence (OD) and, when available, added suggested explanations to the items. In addition, the task force listed items in the risk factor/symptom-sign showing an overall consensus (OC) for both dysphagia and aspiration under the “who-why” heading. Finally, 328 items were created (who-why 115 items, when 7 items, where 5 items, with what 52 items, and how 149 items).

In the sixth step, the final version of the survey was shared with the consulting expert group (third Delphi round), with a 4-week period to respond. The experts were asked to reconsider questions that were particularly close to consensus.

In the seventh step, the task force created the final version of 216 items (who-why 7 items, when 7 items, where 5 items, with what 51 items, and how 146 items), based on the responses received from the consultant experts (Figs. 1, 2).

Strength and Classification of Recommendations

The consultant experts rated all recommendations on a 10-point scale (from 0 point “I totally disagree” to 10 point “I totally agree”). This 10-point scale was divided into three terms that indicated the strength of agreement in response to each statement. While many methods have been applied in the literature to evaluate the strength of recommendations, three measures—percentage (%), median value, and interquartile range [IQR]—were used to increase the strength of the recommendations according to each item.31-33 The strengths of the recommendations were classified as OC (agreement rate between 8 and 10 points ≥ 80%, median value 9–10, and IQR ≤ 2); approaching consensus (AC), which indicated no
**Summary of the recommendations**

### When

- **Screening time for dysphagia in the elderly should be determined individually**
  - All seniors aged ≥80 years should be screened at least once a year (screening test)
  - Elderly aged ≥65 years with any dysphagia related-risk factor OR -related symptom/sign should be screened at least once a year (screening test)
  - Elderly aged ≥65 years with any dysphagia related-severe risk factor OR aspiration related-symptom/sign should be screened at least once a year (screening test + clinical evaluation)
  - Elderly aged ≥65 years and hospitalized for any reason, should be questioned in terms of dysphagia during each visit.

### Where

- **Screening**: primary health care centers/telehealth and telemedicine
- **Clinical and instrumental evaluation**: secondary and/or tertiary health center
- **Education**

### Who-Why

- **All seniors aged ≥80 years**
- **Elderly people aged ≥65 years with any dysphagia related-risk factor AND/OR -related symptom/sign**

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**Fig. 1.** Summary of the recommendation I. Recommendations for older adults, from diagnosis to treatment and follow-up, under the headings of the 5Ws (who, why, what, where, and when) and 1H (how) question method.
Summary of the recommendations—II

<table>
<thead>
<tr>
<th>With what</th>
<th>How</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Basic screening test</strong></td>
<td><strong>Oropharyngeal Dysphagia</strong></td>
</tr>
<tr>
<td>1. Risk factor+symptom/sign list</td>
<td>First-line rehabilitation modalities</td>
</tr>
<tr>
<td>2. Simple screening test questions:</td>
<td>Education and information</td>
</tr>
<tr>
<td>&quot;Do you have difficulty swallowing in solid foods/liquids?&quot;</td>
<td>Oral hygiene—oral care</td>
</tr>
<tr>
<td>&quot;Do you experience coughing, choking or obstruction during/after feeding in solid food/liquid?&quot;</td>
<td>Positioning and posture modification</td>
</tr>
<tr>
<td>&quot;Do you think there is any difference or change in feeding in solid food/liquid compared to your younger self?&quot;</td>
<td>Diet (Bolus volume, texture) modification</td>
</tr>
<tr>
<td>3. Eating assessment tool (EAT-10)</td>
<td>Feeding route modification (Artificial nutrition)</td>
</tr>
<tr>
<td>4. Swallowing disturbances questionnaire (SDQ)</td>
<td>Dental care and prostodontic rehabilitation</td>
</tr>
<tr>
<td>5. Observation of a meal (pandemic)</td>
<td>Nutritional rehabilitation</td>
</tr>
<tr>
<td><strong>Clinical evaluation</strong></td>
<td>Second-line rehabilitation modalities</td>
</tr>
<tr>
<td>1. Clinical evaluation of dysphagia should include detailed medical history (anamnesis) including questioning of risk factors and symptoms, general systemic examination, evaluation of dysphagia signs, and bedside swallowing test (BST).</td>
<td>Head and neck exercises (ROM and Strengthening)</td>
</tr>
<tr>
<td>2. The systemic examination should include examination of the neurological, cardiopulmonary, gastrointestinal, dental and musculoskeletal systems that may be associated with dysphagia.</td>
<td>Breathing exercises (inspiratory and EMST)</td>
</tr>
<tr>
<td>3. The BST should be chosen individually and pathology-specific.</td>
<td>Psychological support (patient/caregiver)</td>
</tr>
<tr>
<td>4. Suggested bedside swallowing test</td>
<td>Home program</td>
</tr>
<tr>
<td>- Volume-viscosity swallowing test</td>
<td></td>
</tr>
<tr>
<td>- Water swallow test with pulse oximetry</td>
<td></td>
</tr>
<tr>
<td>- Gugging Swallowing Screen test</td>
<td></td>
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<tr>
<td>- Observation of a meal (pandemic)</td>
<td></td>
</tr>
<tr>
<td><strong>Instrumental evaluation</strong></td>
<td></td>
</tr>
<tr>
<td>1. Multidisciplinary team</td>
<td></td>
</tr>
<tr>
<td>2. After suspicious clinical evaluation</td>
<td></td>
</tr>
<tr>
<td>3. For treatment selection and follow-up</td>
<td></td>
</tr>
<tr>
<td><strong>Suggested Methods</strong></td>
<td></td>
</tr>
<tr>
<td>Oropharyngeal Dysphagia</td>
<td></td>
</tr>
<tr>
<td>A. Flexible fiberoptic nasoendoscopy</td>
<td></td>
</tr>
<tr>
<td>B. Videofluoroscopy</td>
<td></td>
</tr>
<tr>
<td>C. Magnetic resonance, tomography, siltigraphy*</td>
<td></td>
</tr>
<tr>
<td>Esophageal Dysphagia</td>
<td></td>
</tr>
<tr>
<td>A. Videofluoroscopy</td>
<td></td>
</tr>
<tr>
<td>B. Pharyngoesophagography / esophagography</td>
<td></td>
</tr>
<tr>
<td>C. Upper gastrointestinal endoscopy</td>
<td></td>
</tr>
<tr>
<td>D. Manometry</td>
<td></td>
</tr>
<tr>
<td>E. Magnetic resonance, tomography, siltigraphy*</td>
<td></td>
</tr>
<tr>
<td>Sarcopenic Dysphagia</td>
<td></td>
</tr>
<tr>
<td>A. Magnetic resonance imaging</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Oropharyngeal Dysphagia</th>
<th>Esophageal Dysphagia</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-line rehabilitation modalities</td>
<td>First-line rehabilitation modalities</td>
</tr>
<tr>
<td>Environmental modification</td>
<td>Education and information</td>
</tr>
<tr>
<td>Oral sensorial stimulation (Thermal, touch and pressure)</td>
<td>Oral hygiene—oral care</td>
</tr>
<tr>
<td>Second-line rehabilitation modalities</td>
<td>Positioning and posture modification</td>
</tr>
<tr>
<td>Swallowing maneuvers</td>
<td>Diet (Bolus volume, texture) modification</td>
</tr>
<tr>
<td>Oropharyngeal exercises (ROM, Strengthening and CTAR)</td>
<td>Feeding route modification (Artificial nutrition)</td>
</tr>
<tr>
<td>Electrical stimulation (Oropharyngeal motor level)</td>
<td>Dental care and prostodontic rehabilitation</td>
</tr>
<tr>
<td>Third-line rehabilitation modalities</td>
<td>Nutritional rehabilitation</td>
</tr>
<tr>
<td>Transcranial electrical stimulation</td>
<td>Second-line rehabilitation modalities</td>
</tr>
<tr>
<td>Transcranial magnetic stimulation</td>
<td>Head and neck exercises (ROM and Strengthening)</td>
</tr>
<tr>
<td>Electrical stimulation (Oropharyngeal sensorial level)</td>
<td>Breathing exercises (inspiratory and EMST)</td>
</tr>
<tr>
<td>Biofeedback</td>
<td>Psychological support (patient/caregiver)</td>
</tr>
</tbody>
</table>

Follow-up

The follow-up time may vary depending on the patient’s personal characteristics, type and etiology of dysphagia.

Nutritional assessment and evaluation of rehabilitation modalities given

<table>
<thead>
<tr>
<th>Pneumonia history</th>
<th>Pneumonia finding</th>
<th>Hospitalization history</th>
<th>Aspiration findings/symptoms</th>
<th>Alarm symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mainnutrition</td>
<td>Dehydration</td>
<td>Weight loss</td>
<td>Cognitive dysfunction, delirium</td>
<td>Oral hygiene</td>
</tr>
<tr>
<td>Dental care</td>
<td>Sarcopenia</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*: it is for selected cases, it is not first option;
SLP, speech language pathologist; ROM, range of movement; CTAR, Chin Tuck Against Resistance; EMST, expiratory muscle strength training.

Fig. 2. Summary of the recommendation II. Recommendations for older adults, from diagnosis to treatment and follow-up, under the headings of the 5Ws (who, why, what, where, and when) and 1H (how) question method.
OC but substantial support (agreement rate between 8 and 10 points of 65%–79%, median value 8–10, and IQR ≤ 3); and OD, which indicated significantly different opinions within the group (agreement rate between 8 and 10 points of < 65%, median value < 8, or IQR > 3). The recommendations in this paper were “recommended and should be” for OC (strong recommendation), “considered and may be” for AC (weak recommendation), and “not recommended and should not be used” for OD.

**Statistical Analysis**

IBM SPSS Statistics for Windows (version 25.0; IBM Corp., Armonk, NY, USA) was used to perform the statistical analysis. The strength of agreement was calculated for each item according to proportions (8%–10% response), median values, and IQR using the Kappa method.\(^{34,35}\)

**Ethical Approval**

All procedures performed in studies involving human participants were in accordance with the ethical standards of the University of Health Sciences Turkey, Ankara Diskapi Training and Research Hospital (IRC No. 2021/103-02) and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. This study complied the ethical guidelines for authorship and publishing in the Annals of Geriatric Medicine and Research.\(^ {36}\) In addition, signed informed consent was obtained from each participant before study.

**RESULTS**

In the first Delphi round, a 429-item survey was prepared in line with the recommendations of the consultant expert group and answers to the six open-ended questions created by the task force. In the second Delphi round, 76.5% of these items were accepted as OC and AC and 101 items were removed. In the third Delphi round, 65.9% of these items were accepted as OC and AC, 112 items were removed, and 216 items were finalized. Tables 1–4 show the distributions of the strengths of the recommendations from the third Delphi round.

Of the recommendations in six sections, 144 were strong and 52 were weak, and 20 were not recommended: who-why section (7 strong recommendations), when section (5 strong and 2 weak recommendations), where section (5 strong recommendations), what section (37 strong recommendations, 5 weak recommendations, and 9 do not recommend), how section (90 strong recommendations, 45 weak recommendations, and 11 do not recommend).

**Who-Why Sections**

The three strong recommendations in the Who section included “dysphagia should be considered in older adults aged ≥ 80 years (regardless of symptoms/signs and risk factors), and aged ≥ 65 years with any risk factor for dysphagia AND/OR with any symptoms/signs associated with dysphagia.” In the Why section, we created four lists for the dysphagia and aspiration-related risk factors and symptoms/signs specified in the Who section.

**When Section**

The five strong recommendations in this section were “Older people identified in the Who section should be screened at least once a year” and “For the diagnosis of dysphagia, screening tests and clinical evaluations should be performed at least once yearly in all older people aged ≥ 65 years with any severe risk factor AND/OR with any symptoms/signs associated with dysphagia.”

**Where Section**

The five strong recommendations in this section were “While the dysphagia screening test can be performed in older adults at primary healthcare centers, clinical evaluation should be performed at secondary and tertiary health centers in older patients with dysphagia as a result of screening” and “To screened older adults for dysphagia starting from primary care, education on this subject should be included in the curriculum in medical faculties and all health-related faculties (such as emergency medical technician training and nursing)” as well as “The telehealth/telemedicine system can also be used to perform screening tests for dysphagia.”

**What Section**

The 37 strong recommendations included diagnosis management, the definition of multidisciplinary teams, formal and non-formal screening tests that can be applied, the definition of clinical evaluation, swallowing tests that can be applied, and instrumental evaluation methods.

**How Section**

The 90 strong recommendations included rehabilitation management, the general characteristic of dysphagia rehabilitation, modalities (education and information, dietary modification, artificial route modification, and nutritional rehabilitation as first-line modalities for both OPD and ED and positioning, postural modifications, oral hygiene, oral/dental care, swallowing maneuvers and sensory stimulation as first-line modalities for OPD), follow-up management (team, methods, and follow-up lists) as well as sarcopenic dysphagia (SD) and frailty-related dysphagia (FRD) man-
Table 1. Distributions of the strength of the recommendations for the 3th Delphi Round-1

<table>
<thead>
<tr>
<th>WHO-WHY</th>
<th>8%-10%</th>
<th>IQR</th>
<th>Median</th>
<th>SOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. WHO-WHY</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A1. All individuals ≥ 80 years old</td>
<td>89.2</td>
<td>2.0</td>
<td>10.0</td>
<td>OC</td>
</tr>
<tr>
<td>A2. Elderly people aged ≥ 65 years with any dysphagia related-risk factor</td>
<td>97.3</td>
<td>0.0</td>
<td>10.0</td>
<td>OC</td>
</tr>
<tr>
<td>A3. Elderly people aged ≥ 65 years with any dysphagia related-symptom/sign</td>
<td>91.9</td>
<td>1.0</td>
<td>10.0</td>
<td>OC</td>
</tr>
<tr>
<td>Dysphagia-related risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progressive/non-progressive central neurological diseases</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Connective tissue disease</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Radiotherapy and surgery history of head, neck, anterior mediastinum and gastrointestinal tract</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conditions that cause cognitive dysfunction,</td>
<td>100</td>
<td>0.0</td>
<td>10.0</td>
<td>OC</td>
</tr>
<tr>
<td>Recent history of tracheostomy, intubation and mechanical ventilation,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of sarcopenia and frailty,</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Drug use that may affect swallowing</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Other risk factors assessed in Delphi Round-3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer history of head, neck, anterior mediastinum and gastrointestinal tract</td>
<td>83.8</td>
<td>2.0</td>
<td>9.0</td>
<td>OC</td>
</tr>
<tr>
<td>Lack of teeth that can affect chewing function</td>
<td>67.8</td>
<td>3.0</td>
<td>9.0</td>
<td>AC</td>
</tr>
<tr>
<td>Presence of respiratory system disease (such as COPD, pulmonary fibrosis and asthma)</td>
<td>83.0</td>
<td>2.0</td>
<td>9.0</td>
<td>OC</td>
</tr>
<tr>
<td>Temporomandibular joint problems, oral structural deformity and malocclusion</td>
<td>66.5</td>
<td>3.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>Presence of gastrointestinal tract diseases such as gastroesophageal reflux, peptic ulcer, achalasia</td>
<td>81.9</td>
<td>2.0</td>
<td>9.0</td>
<td>OC</td>
</tr>
<tr>
<td>Multiple drug use (polypharmacy)</td>
<td>88.4</td>
<td>2.0</td>
<td>9.0</td>
<td>OC</td>
</tr>
<tr>
<td>Recent long-term use of nasogastric tube</td>
<td>89.2</td>
<td>2.0</td>
<td>9.0</td>
<td>OC</td>
</tr>
<tr>
<td>Hospitalization due to acute attacks of comorbidities</td>
<td>75.7</td>
<td>2.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>Prolonged hospital stay</td>
<td>83.8</td>
<td>2.0</td>
<td>9.0</td>
<td>OC</td>
</tr>
<tr>
<td>Decreased hand grip-and general muscle-strength, difficulty getting out of bed and chair</td>
<td>78.4</td>
<td>2.0</td>
<td>9.0</td>
<td>AC</td>
</tr>
<tr>
<td>Slow walking speed, difficulty climbing stairs</td>
<td>70.3</td>
<td>3.0</td>
<td>9.0</td>
<td>AC</td>
</tr>
<tr>
<td>Decreased overall muscle mass and muscle wasting</td>
<td>79</td>
<td>2.0</td>
<td>9.0</td>
<td>AC</td>
</tr>
<tr>
<td>Functional dependence, limitation in activities of daily living and immobilization</td>
<td>66.1</td>
<td>3.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>Tiredness and weakness in the last few months</td>
<td>65.4</td>
<td>2.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>Any reason to develop delirium</td>
<td>78.3</td>
<td>2.0</td>
<td>9.0</td>
<td>AC</td>
</tr>
<tr>
<td>Aspiration-related (severe) risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progressive/non-progressive central neurological diseases</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer, radiotherapy and surgery history of head, neck, anterior mediastinum and gastrointestinal tract</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conditions that cause cognitive dysfunction,</td>
<td>97.3</td>
<td>1.0</td>
<td>10.0</td>
<td>OC</td>
</tr>
<tr>
<td>Recent history of tracheostomy, intubation and mechanical ventilation,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recent long-term use of nasogastric tube,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of sarcopenia and frailty</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other severe risk factors assessed in Delphi Round-3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple comorbidities</td>
<td>78.8</td>
<td>2.0</td>
<td>9.0</td>
<td>AC</td>
</tr>
<tr>
<td>Presence of respiratory system disease</td>
<td>78.4</td>
<td>3.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>Any reason to develop delirium</td>
<td>73.0</td>
<td>2.0</td>
<td>9.0</td>
<td>AC</td>
</tr>
<tr>
<td>Presence of gastrointestinal tract diseases such as gastroesophageal reflux, peptic ulcer, achalasia</td>
<td>68.5</td>
<td>3.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>Dysphagia-related symptoms/signs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in eating habits,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difficulty in chewing,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spillage of food from the mouth during feeding,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residual food in the mouth,</td>
<td>97.3</td>
<td>1.0</td>
<td>10.3</td>
<td>OC</td>
</tr>
<tr>
<td>Drooling,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coughing, choking and voice change during/after swallowing,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased need for throat clearing,</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Continued to the next page)
Table 1. Continued

<table>
<thead>
<tr>
<th>Symptom Description</th>
<th>8%-10%</th>
<th>IQR</th>
<th>Median</th>
<th>SOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sticky feeling the throat during/after swallowing</td>
<td>94.6</td>
<td>1.0</td>
<td>10.0</td>
<td>OC</td>
</tr>
<tr>
<td>Retrosternal obstruction/stuck/sticky feeling during/after feeding</td>
<td>69.4</td>
<td>3.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>Painful swallowing</td>
<td>86.7</td>
<td>2.0</td>
<td>8.0</td>
<td>OC</td>
</tr>
<tr>
<td>Repeated swallowing and need for multiple swallowing</td>
<td>66.7</td>
<td>3.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>Progressive swallowing difficulty</td>
<td>65.4</td>
<td>2.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>Delayed pharyngeal phase</td>
<td>94.6</td>
<td>1.0</td>
<td>10.0</td>
<td>OC</td>
</tr>
<tr>
<td>Head and posture change during feeding</td>
<td>70.3</td>
<td>3.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>Presence of signs of lower respiratory tract infection</td>
<td>83.8</td>
<td>2.0</td>
<td>9.0</td>
<td>OC</td>
</tr>
<tr>
<td>History of pneumonia more than 3 times a year</td>
<td>65.3</td>
<td>3.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>Presence of tachypnea</td>
<td>71.9</td>
<td>3.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>Involuntary weight loss</td>
<td>67.6</td>
<td>3.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>Movement disorder and weakness in the tongue and lip muscles</td>
<td>72.9</td>
<td>3.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>Low tongue pressure</td>
<td>75.7</td>
<td>3.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>Decreased oral sensation</td>
<td>79.2</td>
<td>2.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>General malaise/fatigue, decreased muscle strength</td>
<td>79.2</td>
<td>2.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>Low body mass index, cachexia</td>
<td>79.2</td>
<td>2.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
</tbody>
</table>

**Aspiration-related symptoms/signs**

I. Weakened or absent voluntary cough reflex,
II. Coughing/choking and voice change during/after swallowing,
III. Shortness of breath/bruising,
IV. Drooling,
V. Increased need for throat clearing,
VI. Repetitive and multiple swallowing,
VII. Feeling of having something stuck in the throat while swallowing,
VIII. Decrease in laryngeal elevation,
IX. Presence of signs of lower respiratory tract infection
X. Decrease in oxygen saturation with pulse oximetry during/after feeding

**Other aspiration-related symptoms/signs assessed in Delphi Round-3**

<table>
<thead>
<tr>
<th>Symptom Description</th>
<th>8%-10%</th>
<th>IQR</th>
<th>Median</th>
<th>SOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrosternal obstruction/stuck/sticky feeling during/after feeding</td>
<td>69.4</td>
<td>3.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>History of pneumonia more than 3 times a year</td>
<td>86.7</td>
<td>2.0</td>
<td>8.0</td>
<td>OC</td>
</tr>
<tr>
<td>Weakness in chewing muscles</td>
<td>66.7</td>
<td>3.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>Decreased bite force, low bite pressure</td>
<td>65.4</td>
<td>2.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
</tbody>
</table>

**B. WHEN**

B1. All elderly people aged ≥ 80 years should be screened for dysphagia at least once a year with a simple screening test (regardless of symptoms and risk factors.
B2. Screening time for dysphagia in the elderly should be determined individually.
B3. All elderly people aged ≥ 65 years, with any risk factor should be screened with a simple screening test for dysphagia at least once a year.
B4. All elderly people aged ≥ 65 years, with any dysphagia symptoms/signs should be screened for dysphagia at least once a year with a simple screening test.
B5. For the diagnosis of dysphagia, screening test and clinical evaluation should be performed at least once a year in all elderly people aged ≥ 65 years and with any severe risk factor.
B6. For the diagnosis of dysphagia, screening test and clinical evaluation should be performed at least once a year for all elderly people aged ≥ 65 years with any aspiration-related dysphagia symptoms and signs.
B7. All elderly people aged ≥ 65 years, hospitalized for any reason, should be questioned in terms of dysphagia during each visit.

(Continued to the next page)
Table 1. Continued

| WHERE | C1. All elderly people aged ≥ 65 years can be screened for dysphagia with a simple screening test in primary health care centers. | 91.9 | 1.0 | 10.0 | OC |
| C2. Elderly people who are thought to have dysphagia as a result of screening in primary care should only be evaluated in a secondary and/or tertiary health center. | 83.8 | 2.0 | 9.0 | OC |
| C3. In order for the elderly to be screened for dysphagia starting from primary care, education on this subject should be included in the curriculum in medical faculties. | 89.2 | 2.0 | 10.0 | OC |
| C4. In order for the dysphagia screening test to be performed in the elderly starting from primary care, education on this subject should be included in the curriculum in all health-related faculties (such as emergency medical technician, nursing). | 89.2 | 2.0 | 9.0 | OC |
| C5. The telehealth/telemedicine system can also be used in the screening test for dysphagia (this method should be used in special cases such as pandemics). | 91.9 | 2.0 | 10.0 | OC |

IQR, interquartile range; SOA, strength of agreement; AC, approaching consensus; OC, overall consensus; OD, overall divergence.

Table 2. Distributions of the strength of the recommendations for the 3th Delphi Round-2

<table>
<thead>
<tr>
<th>WHAT</th>
<th>Diagnosis management</th>
<th>8%-10%</th>
<th>IQR</th>
<th>Median</th>
<th>SOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1. The screening test for dysphagia can be administered by a trained health care professional (for example, a trained rehabilitation nurse).</td>
<td>86.5</td>
<td>1.75</td>
<td>10.0</td>
<td>OC</td>
<td></td>
</tr>
<tr>
<td>D2. Clinical evaluation for the diagnosis of dysphagia should be performed by a SLP, if possible, or if not available, by physicians and/or a trained nurse.</td>
<td>89.2</td>
<td>2.0</td>
<td>9.25</td>
<td>OC</td>
<td></td>
</tr>
<tr>
<td>D3. If possible, screening for dysphagia by a trained team member assigned in a multidisciplinary team may facilitate diagnosis, treatment and follow-up.</td>
<td>83.9</td>
<td>2.0</td>
<td>9.0</td>
<td>OC</td>
<td></td>
</tr>
<tr>
<td>D4. Although clinical and further evaluation for the diagnosis of dysphagia varies according to the conditions and possibilities of each center, it should be done in a multidisciplinary team.</td>
<td>91.9</td>
<td>1.0</td>
<td>10.0</td>
<td>OC</td>
<td></td>
</tr>
<tr>
<td>D5. In the broadest form among the multidisciplinary team, primary care physician, home care services and health personnel in the elderly care center in primary care; neurologist, physiatrist, geriatrician, otorharyngologist, gastroenterologist, internal medicine, general surgery, radiology and psychiatry specialists in the secondary and tertiary care, dental physician, SLP, nurse, dietitian, psychologist, physiotherapist and social worker should be included. Family and caregivers should also be included in this team.</td>
<td>94.4</td>
<td>0.75</td>
<td>10.0</td>
<td>OC</td>
<td></td>
</tr>
<tr>
<td>D6. If there is not a SLP in the multidisciplinary team, one of the branches of geriatrics, physical medicine and rehabilitation, neurology, otorharyngology and gastroenterology should take primary responsibility for the coordination and organization of the team, depending on the type of dysphagia (oral, pharyngeal, esophageal).</td>
<td>86.5</td>
<td>1.0</td>
<td>10.0</td>
<td>OC</td>
<td></td>
</tr>
</tbody>
</table>

Screening tests

D1. Risk factor + symptom/sign lists can be used as a screening test for dysphagia.
D2. The following 3 questions can be used as a dysphagia screening test in the elderly: "Do you have difficulty swallowing in solid foods/liquids?"
"Do you experience coughing, choking or obstruction during/after feeding in solid food/liquid?"
"Do you think there is any difference or change in feeding in solid food/liquid compared to your younger self?"
D3. Eating assessment tool (EAT-10) can be used as a dysphagia screening tool.
D4. Swallowing disturbances questionnaire (SDQ) can be used as a dysphagia screening tool.
D5. Observation of mealtime can be used as a screening tool for dysphagia.

Clinical evaluation

D1. Clinical evaluation of dysphagia should include detailed medical history (anamnesis) including questioning of risk factors and symptoms, general systemic examination, evaluation of dysphagia findings, and bedside swallow test.
D2. General systemic examination should include examination of the neurological, cardiopulmonary, gastrointestinal, dental, and musculoskeletal systems that may be associated with dysphagia.
D3. Neurological examination should include consciousness and cranial nerve reflexes associated with swallowing, speech, voice, coordination, involuntary movement and motor planning.

(Continued to the next page)
Table 2. Continued

<table>
<thead>
<tr>
<th>Item</th>
<th>8%-10%</th>
<th>IQR</th>
<th>Median</th>
<th>SOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>D4. Cardiopulmonary examination should include auscultation, pulse and respiratory rate, and cough reflex.</td>
<td>94.4</td>
<td>1.0</td>
<td>10.0</td>
<td>OC</td>
</tr>
<tr>
<td>D5. Gastrointestinal examination should include inspection, bowel auscultation, palpation assessment for localized tenderness, palpable mass and lymphadenopathy.</td>
<td>91.9</td>
<td>1.0</td>
<td>10.0</td>
<td>OC</td>
</tr>
<tr>
<td>D6. Dental examination should include evaluation of oral hygiene, teeth, denture fit, malocclusion, tone and sensation of muscles and soft tissues in the oral cavity.</td>
<td>94.6</td>
<td>1.0</td>
<td>10.0</td>
<td>OC</td>
</tr>
<tr>
<td>D7. Musculoskeletal examination should include assessment of posture, mobility, oropharyngeal and postural structures, range of motion, muscle strength and tone of the temporomandibular joint and extremities.</td>
<td>94.6</td>
<td>1.0</td>
<td>10.0</td>
<td>OC</td>
</tr>
<tr>
<td>D8. Bedside swallow test should be chosen individually and according to the pathology, based on the suspected OPD or ED with the screening test.</td>
<td>97.3</td>
<td>0.75</td>
<td>10.0</td>
<td>OC</td>
</tr>
<tr>
<td>D9. Volume-Viscosity Swallowing Test (VVST) can be used as a bedside screening test after the examination.</td>
<td>94.6</td>
<td>1.88</td>
<td>10.0</td>
<td>OC</td>
</tr>
<tr>
<td>D10. The Sydney Swallow Questionnaire (SSQ) can be used as a bedside screening test after the examination.</td>
<td>69.4</td>
<td>2.38</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>D11. The Yale Swallowing Protocol can be used as a bedside screening test after the examination.</td>
<td>69.4</td>
<td>2.88</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>D12. The 3 oz water swallow test can be used as a bedside screening test after the examination.</td>
<td>77.8</td>
<td>2.0</td>
<td>9.0</td>
<td>AC</td>
</tr>
<tr>
<td>D13. Water swallow test with pulse oximetry can be used as bedside screening test after examination.</td>
<td>81.1</td>
<td>1.75</td>
<td>10.0</td>
<td>OC</td>
</tr>
<tr>
<td>D14. The Gugging Swallowing Screen test (GUSS) can be used as a bedside screening test after the examination.</td>
<td>81.1</td>
<td>2.0</td>
<td>9.5</td>
<td>OC</td>
</tr>
<tr>
<td>D15. Observation of mealtime can be used as a clinical assessment (for the Pandemic process).</td>
<td>81.8</td>
<td>2.0</td>
<td>9.0</td>
<td>OC</td>
</tr>
</tbody>
</table>

**Instrumental evaluation**

D1. Instrumental evaluation should be made after clinical evaluations. | 97.3 | 0.0 | 10.0 | OC |
D2. Instrumental evaluation is not required for all patients. It should be done if there is any doubtful clinical evaluation. | 94.6 | 1.0 | 10.0 | OC |
D3. If the patient has a serious risk factor and/or symptom-sign for dysphagia, further evaluation should be performed after clinical evaluation. | 97.3 | 0.0 | 10.0 | OC |
D4. The choice of advanced evaluation method should be decided by a multidisciplinary team. | 97.3 | 0.0 | 10.0 | OC |
D5. The choice of advanced evaluation method should be decided according to the underlying pathology, dysphagia, and the patient's current characteristics. | 94.6 | 0.75 | 10.0 | OC |
D6. The choice of the advanced evaluation method should be decided according to the facilities and conditions of the center performing the evaluation. | 94.4 | 0.75 | 10.0 | OC |
D7. FEES is an effective method for OPD. | 94.4 | 0.75 | 10.0 | OC |
D8. Evaluation of VF swallowing is an effective method for OPD. | 89.2 | 0.75 | 10.0 | OC |
D9. Evaluation of electrophysiological dysphagia limit is an effective method for OPD. | 47.6 | 3.75 | 7.75 | OD |
D10. Ultrasonographic evaluation of oropharyngeal structures is an effective method for OPD. | 37.1 | 4.25 | 7.0 | OD |
D11. Accelerometric evaluation is an effective method for OPD. | 22.9 | 2.75 | 6.0 | OD |
D12. Tongue pressure measurement is an effective method for the diagnosis of OPD. | 38.9 | 3.75 | 7.0 | OD |
D13. Magnetic resonance imaging, computed tomography and scintigraphy may be effective methods in the diagnosis of OPD; they may not be suitable for every patient and are not the first-line methods. | 88.9 | 1.75 | 10.0 | OC |
D14. VF evaluation is an effective method for ED. | 83.8 | 1.75 | 10.0 | OC |
D15. Barium swallow pharyngoesophagography/esophagography is an effective method for ED. | 86.5 | 1.38 | 10.0 | OC |
D16. Upper gastrointestinal endoscopy is an effective method for ED. | 83.8 | 1.0 | 10.0 | OC |
D17. Manometry is an effective method for ED. If possible, high-resolution manometry should be used. | 81.1 | 1.0 | 10.0 | OC |
D18. Muscle ultrasonography is an effective method for ED. | 13.9 | 3.0 | 5.25 | OD |
D19. Endoscopic ultrasonography and ultrasound elastography are effective methods for ED. | 44.4 | 3.0 | 8.0 | OD |
D20. Magnetic resonance imaging, computed tomography and scintigraphy may be effective methods in the diagnosis of ED; they may not be suitable for every patient, and they are not the methods of choice in the first-line. | 86.5 | 1.88 | 10.0 | OC |
Table 2. Continued

<table>
<thead>
<tr>
<th></th>
<th>8%-10%</th>
<th>IQR</th>
<th>Median</th>
<th>SOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>D21.</td>
<td>For SD, imaging of muscle wasting with magnetic resonance imaging is an effective method for diagnosis.</td>
<td>69.4</td>
<td>3.0</td>
<td>9.25</td>
</tr>
<tr>
<td>D22.</td>
<td>For SD, imaging of muscle wasting with computed tomography is an effective method for diagnosis.</td>
<td>51.4</td>
<td>5.0</td>
<td>7.25</td>
</tr>
<tr>
<td>D23.</td>
<td>For SD, imaging of muscle wasting with ultrasonography is an effective method for diagnosis.</td>
<td>55.6</td>
<td>4.63</td>
<td>8.0</td>
</tr>
<tr>
<td>D24.</td>
<td>Advanced assessment methods can also be used for treatment selection and follow-up.</td>
<td>97.2</td>
<td>1.0</td>
<td>10.0</td>
</tr>
</tbody>
</table>

IQR, interquartile range; SOA, strength of agreement; AC, approaching consensus; OC, overall consensus; OD, overall divergence; ENMG, electroneuromyography; VF, videofluoroscopy; FEES, fiberoptic endoscopic evaluation of swallowing; OPD, oropharyngeal dysphagia; ED, esophageal dysphagia; SD, sarcopenic; SLP, speech language pathologist.

Table 3. Distributions of the strength of the recommendations for the 3th Delphi Round-3

<table>
<thead>
<tr>
<th></th>
<th>8%-10%</th>
<th>IQR</th>
<th>Median</th>
<th>SOA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>E. HOW</strong></td>
<td><strong>Rehabilitation management</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E1.</td>
<td>A management algorithm (in terms of diagnosis and treatment) created by a multidisciplinary team should be used in the management of both OPD and ED in the elderly.</td>
<td>97.2</td>
<td>0</td>
<td>10.0</td>
</tr>
<tr>
<td>E2.</td>
<td>The tools/methods used in this algorithm may change in accordance with the current facilities and possibilities of each center in terms of personnel and equipment.</td>
<td>88.9</td>
<td>0</td>
<td>10.0</td>
</tr>
<tr>
<td>E3.</td>
<td>Patients who do not have dysphagia but have more than one serious risk factor should also be included in a rehabilitation program that includes oral hygiene, compensatory methods such as modifications and a follow-up program.</td>
<td>86.1</td>
<td>1.0</td>
<td>10.0</td>
</tr>
<tr>
<td>E4.</td>
<td>Both OPD and ED rehabilitation should be personalized.</td>
<td>97.2</td>
<td>0</td>
<td>10.0</td>
</tr>
<tr>
<td>E5.</td>
<td>Both OPD and ED rehabilitation should be pathology specific. Dysphagia characteristics should be well defined before rehabilitation.</td>
<td>94.4</td>
<td>0</td>
<td>10.0</td>
</tr>
<tr>
<td>E6.</td>
<td>Rehabilitation of both OPD and ED should be specific to the etiology.</td>
<td>80.6</td>
<td>2.0</td>
<td>10.0</td>
</tr>
<tr>
<td>E7.</td>
<td>Determination and treatment of the underlying cause is the first-line method in the rehabilitation of both OPD and ED.</td>
<td>97.2</td>
<td>0</td>
<td>10.0</td>
</tr>
<tr>
<td>E8.</td>
<td>Treatment of the underlying cause should include elimination of correctable risk factors for dysphagia.</td>
<td>100</td>
<td>0</td>
<td>10.0</td>
</tr>
<tr>
<td>E9.</td>
<td>Treatment of the underlying cause of ED may be drugs and may be the first-line method.</td>
<td>100</td>
<td>1.0</td>
<td>10.0</td>
</tr>
<tr>
<td>E10.</td>
<td>Treatment of the underlying cause of ED may be a surgical method and may be the first-line method.</td>
<td>94.4</td>
<td>1.0</td>
<td>10.0</td>
</tr>
<tr>
<td>E11.</td>
<td>Treatment of the underlying cause of ED may be botulinum injection and may be the first-line method.</td>
<td>94.4</td>
<td>1.0</td>
<td>10.0</td>
</tr>
<tr>
<td>E12.</td>
<td>Treatment of the underlying cause of OPD may be a surgical method and may be the first-line method.</td>
<td>94.4</td>
<td>1.0</td>
<td>10.0</td>
</tr>
<tr>
<td>E13.</td>
<td>Treatment of the underlying cause of OPD may be a medical drug and may be the first-line method.</td>
<td>94.4</td>
<td>1.0</td>
<td>10.0</td>
</tr>
<tr>
<td>E14.</td>
<td>Treatment of the underlying cause of OPD may be botulinum injection.</td>
<td>88.9</td>
<td>1.88</td>
<td>10.0</td>
</tr>
</tbody>
</table>

**Rehabilitation-compensatuar methods**

<table>
<thead>
<tr>
<th></th>
<th>8%-10%</th>
<th>IQR</th>
<th>Median</th>
<th>SOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>EA1.</td>
<td>EDUCATION AND INFORMATION is an effective treatment method in the rehabilitation of OPD.</td>
<td>100.0</td>
<td>0</td>
<td>10.0</td>
</tr>
<tr>
<td>EA2.</td>
<td>Education and information is the first-line treatment method for OPD.</td>
<td>100.0</td>
<td>0.75</td>
<td>10.0</td>
</tr>
<tr>
<td>EA3.</td>
<td>Education and information is an effective treatment method for ED.</td>
<td>100.0</td>
<td>1.0</td>
<td>10.0</td>
</tr>
<tr>
<td>EA4.</td>
<td>Education and information is the first line treatment method for ED.</td>
<td>100.0</td>
<td>1.38</td>
<td>10.0</td>
</tr>
<tr>
<td>EA5.</td>
<td>In the rehabilitation of dysphagia in the elderly, education and information should include the patient, patient relatives and caregivers.</td>
<td>100.0</td>
<td>0</td>
<td>10.0</td>
</tr>
<tr>
<td>EA6.</td>
<td>Active participation of the patient, their relatives and caregivers should be ensured in the rehabilitation of dysphagia in the elderly.</td>
<td>100.0</td>
<td>1.0</td>
<td>10.0</td>
</tr>
<tr>
<td>EA7.</td>
<td>POSITIONING AND POSTURAL MODIFICATIONS are effective methods in the rehabilitation of OPD.</td>
<td>100.0</td>
<td>0.75</td>
<td>10.0</td>
</tr>
<tr>
<td>EA8.</td>
<td>Positioning and postural modifications are the first-line treatment method for OPD.</td>
<td>89.5</td>
<td>2.0</td>
<td>10.0</td>
</tr>
</tbody>
</table>

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(Continued to the next page)
Table 3. Continued

| EA | Positioning and postural modifications are effective methods in the rehabilitation of ED in the elderly. | 73.7 | 2.75 | 8.5 | AC |
| EA10. | Positioning and postural modifications are the first-line treatment method for ED. | 73.5 | 2.75 | 8.0 | AC |
| EA11. | ENVIRONMENTAL MODIFICATION is an effective method in the rehabilitation of OPD. | 65.4 | 3.0 | 8.0 | AC |
| EA12. | Environmental modification is the first-line treatment method for OPD. | 65.2 | 3.0 | 8.0 | AC |
| EA13. | Environmental modification is an effective method in the rehabilitation of ED in the elderly. | 52.6 | 3.75 | 6.0 | OD |
| EA14. | DIETARY MODIFICATION is an effective method in the rehabilitation of OPD. | 100.0 | 0.75 | 10.0 | OC |
| EA15. | Dietary modification is the first-line treatment for OPD. | 91.2 | 1.0 | 10.0 | OC |
| EA16. | Dietary modification is an effective method in the rehabilitation of ED. | 81.5 | 2.0 | 9.0 | OC |
| EA17. | Dietary modification is the first-line treatment for ED. | 80.6 | 2.0 | 9.0 | OC |
| EA18. | SWALLOWING MANEUVERS are effective methods in the rehabilitation of OPD. | 94.1 | 2.0 | 10.0 | OC |
| EA19. | Swallowing maneuvers are the second line treatment method for OPD. | 76.4 | 2.0 | 9.0 | OC |
| EA20. | Swallowing maneuvers are effective methods in the rehabilitation of ED. | 61.1 | 3.0 | 8.0 | OC |
| EA21. | ARTIFICIAL ROUTE MODIFICATIONS are effective methods in the rehabilitation of OPD. | 100.0 | 1.0 | 10.0 | OC |
| EA22. | Alternative feeding route modification is the first line treatment method for OPD. | 94.4 | 1.0 | 10.0 | OC |
| EA23. | Alternative feeding route modification is an effective method in the rehabilitation of ED. | 88.9 | 1.0 | 10.0 | OC |
| EA24. | Alternative feeding route modification is the first-line treatment method for ED. | 85.3 | 2.0 | 9.5 | OC |
| EA25. | ORAL HYGIENE AND ORAL CARE are effective methods in the rehabilitation of OPD. | 85.3 | 2.0 | 9.0 | OC |
| EA26. | Oral hygiene and oral care is the first line treatment method for OPD. | 94.3 | 1.0 | 10.0 | OC |
| EA27. | Oral hygiene and oral care are effective methods in the rehabilitation of ED. | 66.1 | 2.0 | 10.0 | OC |
| EA28. | Oral hygiene and oral care is the first line treatment method for ED. | 77.8 | 2.75 | 9.0 | OC |

**Rehabilitation-therapeutic methods**

| EB1. | DENTAL CARE AND PROSTHODONTIC REHABILITATION are effective methods in the rehabilitation of OPD. | 100.0 | 1.0 | 10.0 | OC |
| EB2. | Dental care and prosthodontic rehabilitation are the first line treatment method for OPD. | 88.9 | 1.75 | 8.0 | OC |
| EB3. | Dental care and prosthodontic rehabilitation are effective in rehabilitation of ED. | 66.7 | 2.75 | 8.0 | AC |
| EB4. | Dental care and prosthodontic rehabilitation are the first line treatment method for ED. | 66.1 | 3.0 | 8.0 | AC |
| EB5. | SENSORY STIMULATIONS INCLUDING THERMAL, TACTILE AND PRESSURE are effective methods in the rehabilitation of OPD. | 100.0 | 1.0 | 10.0 | OC |
| EB6. | Sensory stimulation is the first line treatment method for OPD. | 88.9 | 1.75 | 8.0 | OC |
| EB7. | JOINT RANGE OF MOVEMENT (OROPHARYNGEAL) EXERCISES are effective methods in the rehabilitation of OPD. | 90.9 | 2.0 | 9.5 | OC |
| EB8. | Joint range of movement exercises are the second line treatment method for OPD. | 77.8 | 3.0 | 8.0 | AC |
| EB9. | OROPHARYNGEAL MUSCLE STRENGTHENING and RESISTANT EXERCISES (INCLUDING CTAR) are effective modalities in rehabilitation of OPD. | 100.0 | 1.75 | 10.0 | OC |
| EB10. | Oropharyngeal muscle strengthening and resistance exercises are the second line treatment methods for OPD. | 75.8 | 3.0 | 8.0 | AC |
| EB11. | HEAD AND NECK (CERVICAL SPINE) JOINT RANGE OF MOVEMENT EXERCISES are effective methods in the rehabilitation of OPD. | 69.3 | 3.0 | 8.0 | AC |
| EB12. | Head and neck range of motion exercises are the second line treatment method for OPD. | 67.6 | 3.0 | 8.0 | AC |
| EB13. | Head and neck range of motion exercises are an effective method in the rehabilitation of ED. | 67.0 | 3.0 | 8.0 | AC |
| EB14. | Head and neck range of motion exercises are the second line treatment method for ED. | 65.1 | 3.0 | 8.0 | AC |
| EB15. | HEAD AND NECK (CERVICAL SPINE) STRENGTHENING EXERCISES are effective methods in the rehabilitation of OPD. | 65.6 | 3.0 | 8.0 | AC |
| EB16. | Head and neck strengthening exercises are the second line treatment method for OPD. | 68.1 | 3.0 | 8.0 | AC |
| EB17. | Head and neck strengthening exercises are effective methods in the rehabilitation of ED. | 65.6 | 2.75 | 8.0 | AC |
| EB18. | Head and neck strengthening exercises are the second line treatment method for ED. | 68.1 | 3.0 | 8.0 | AC |
| EB19. | EXPIRATORY MUSCLE STRENGTHENING EXERCISES are effective methods in the rehabilitation of OPD. | 88.9 | 1.0 | 10.0 | OC |

(Continued to the next page)
| EB20. | Expiratory muscle strengthening exercises are the second line treatment method for OPD. | 85.3 | 2.75 | 9.5 | AC |
| EB21. | Expiratory muscle strengthening exercises are effective methods in the rehabilitation of ED. | 87.1 | 2.0 | 9.0 | AC |
| EB22. | Expiratory muscle strengthening exercises are the second line treatment method for ED. | 65.6 | 3.0 | 8.0 | AC |
| EB23. | INSPIRATORY RESPIRATORY MUSCLE STRENGTHENING EXERCISES are effective methods in the rehabilitation of OPD. | 89.1 | 2.0 | 10.0 | OC |
| EB24. | Inspiratory respiratory muscle strengthening exercises are the second line treatment method for OPD. | 67.8 | 3.0 | 8.0 | AC |
| EB25. | Inspiratory respiratory muscle strengthening exercises are effective methods in the rehabilitation of ED. | 65.3 | 3.0 | 8.5 | AC |
| EB26. | Inspiratory respiratory muscle strengthening exercises are the second line treatment method for ED. | 68.9 | 2.75 | 8.0 | AC |
| EB27. | OROPHARYNGEAL MOTOR NEUROMUSCULAR ELECTRIC STIMULATION is an effective method in rehabilitation of OPD. | 88.9 | 1.25 | 10.0 | OC |
| EB28. | Oropharyngeal motor neuromuscular electrical stimulation is the second line treatment method for OPD. | 77.8 | 2.25 | 9.5 | AC |
| EB29. | TRANSCRANIAL ELECTRIC STIMULATION is an effective method in the rehabilitation of OPD. | 69.6 | 3.0 | 9.0 | AC |
| EB30. | Transcranial electrical stimulation is the third line treatment method for OPD. | 66.7 | 2.75 | 9.0 | AC |
| EB31. | Transcranial electrical stimulation is an effective method in the rehabilitation of ED. | 52.6 | 4.0 | 6.0 | OD |
| EB32. | SENSORY NEUROMUSCULAR ELECTRIC STIMULATION is an effective method in the rehabilitation of OPD. | 72.2 | 3.0 | 10.0 | AC |
| EB33. | Oropharyngeal sensory neuromuscular electrical stimulation is the third line treatment for OPD. | 83.3 | 2.0 | 9.0 | AC |
| EB34. | TRANSCRANIAL MAGNETIC STIMULATION is an effective method in the rehabilitation of OPD. | 66.7 | 3.0 | 8.0 | AC |
| EB35. | Transcranial magnetic stimulation is the third line treatment method for OPD. | 72.2 | 3.0 | 8.0 | AC |
| EB36. | Transcranial magnetic stimulation is an effective method in the rehabilitation of ED. | 47.8 | 3.75 | 5.0 | OD |
| EB37. | BIOFEEDBACK is an effective method in the rehabilitation of OPD. | 66.7 | 3.0 | 8.0 | AC |
| EB38. | Biofeedback is the third line treatment method for OPD. | 72.2 | 2.75 | 9.0 | AC |
| EB39. | Biofeedback is an effective method in the rehabilitation of ED. | 48.1 | 4.5 | 5.0 | OD |
| EB40. | ACUPUNCTURES are effective methods in the rehabilitation of OPD. | 57.8 | 5.0 | 5.5 | OD |
| EB41. | Acupuncture is an effective method in the rehabilitation of ED. | 46.5 | 6.0 | 5.5 | OD |
| EB42. | KINESIO TAPING is an effective method in the rehabilitation of ED. | 44.7 | 5.5 | 5.0 | OD |
| EB43. | DRUG THERAPY is an effective method in the treatment of OPD and ED. | 45.5 | 4.5 | 5.0 | OD |
| EB44. | Nutritional rehabilitation is an effective method in the treatment of OPD. | 94.1 | 1.0 | 10.0 | OC |
| EB45. | Nutritional rehabilitation is the first line treatment for OPD. | 88.2 | 1.0 | 10.0 | OC |
| EB46. | Nutritional rehabilitation is an effective method in the treatment of ED. | 89.1 | 1.5 | 10.0 | OC |
| EB47. | Nutritional rehabilitation is the first line treatment for ED. | 88.3 | 0.5 | 10.0 | OC |
| EB48. | All elderly people with suspected both OPD and ED should be nutritionally evaluated. | 97.1 | 1.0 | 10.0 | OC |
| EB49. | Every elderly person diagnosed with both OPD and ED should be evaluated nutritionally. | 94.3 | 0.5 | 10.0 | OC |
| EB50. | Nutritional evaluation can be done by a diettitian, if possible, or by physicians and other trained health personnel; if possible, within the multidisciplinary team that programs dysphagia management. | 94.2 | 1.0 | 10.0 | OC |
| EB51. | A formal test should be used for nutritional assessment. | 97.1 | 1.0 | 10.0 | OC |
| EB52. | In the rehabilitation of OPD, compensatory and therapeutic methods should be used together as a combination therapy. | 98.2 | 0 | 10.0 | OC |
| EB53. | In the rehabilitation of ED, compensatory and therapeutic methods should be used together as a combination therapy. | 94.3 | 0.5 | 10.0 | OC |
| EB54. | PSYCHOLOGICAL SUPPORT-REHABILITATION for the patient is an effective method in the treatment of OPD. | 77.8 | 2.5 | 10.0 | AC |
| EB55. | Psychological support-rehabilitation for the patient is the second line method for OPD. | 68.5 | 3.0 | 8.0 | AC |
Table 3. Continued

<table>
<thead>
<tr>
<th>EB56. Psychological support-rehabilitation for the patient is an effective method in the treatment of ED.</th>
<th>8%-10%</th>
<th>IQR</th>
<th>Median</th>
<th>SOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>EB57. Psychological support-rehabilitation for the patient is the second line method for ED.</td>
<td>66.7</td>
<td>3.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>EB58. PSYCHOLOGICAL SUPPORT-REHABILITATION for the caregiver is an effective method in the treatment of OPD.</td>
<td>78.2</td>
<td>2.0</td>
<td>9.5</td>
<td>AC</td>
</tr>
<tr>
<td>EB59. Psychological support-rehabilitation for the caregiver is the second line method in treatment for OPD.</td>
<td>68.8</td>
<td>2.75</td>
<td>9.0</td>
<td>AC</td>
</tr>
<tr>
<td>EB60. Psychological support and rehabilitation for the caregiver is an effective method in the treatment of ED.</td>
<td>69.4</td>
<td>3.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
<tr>
<td>EB61. Psychological support-rehabilitation for the caregiver is the second line method in treatment for ED.</td>
<td>66.3</td>
<td>3.0</td>
<td>8.5</td>
<td>AC</td>
</tr>
<tr>
<td>EB62. Rehabilitation applications in the form of a home program are an effective method in the treatment of OPD.</td>
<td>78.0</td>
<td>2.75</td>
<td>9.0</td>
<td>AC</td>
</tr>
<tr>
<td>EB63. Rehabilitation applications in the form of a home program are an effective method in the treatment of ED.</td>
<td>67.6</td>
<td>3.0</td>
<td>8.0</td>
<td>AC</td>
</tr>
</tbody>
</table>

**Follow-up**

| EA1. In general, the follow-up time in elderly patients with dysphagia should be arranged according to the patient's personal characteristics, type and etiology of dysphagia, so the follow-up period may vary from person to person. | 100.0 | 0 | 10.0 | OC |
| EA2. The follow-up time and follow-up method in elderly patients with dysphagia should be decided by a multidisciplinary team. | 94.1 | 0 | 10.0 | OC |
| EA3. In the follow-up of elderly patients with dysphagia, tests applied for screening can be used. | 85.0 | 2.0 | 10.0 | OC |
| EA4. Clinical evaluation methods can be used in the follow-up of elderly patients with dysphagia. | 81.3 | 0.25 | 10.0 | OC |
| EA5. Bedside swallow tests can be used for follow-up in elderly patients with dysphagia. | 90.2 | 1.25 | 10.0 | OC |
| EA6. FEES as the instrumental methods, can be used for follow-up. | 86.7 | 0.25 | 10.0 | OC |
| EA7. Videofluoroscopy, as the instrumental methods, can be used for follow-up. | 44.1 | 3.25 | 8.0 | OD |
| EA8. Ultrasononography, one of the advanced evaluation methods, can be used for follow-up. | 42.9 | 3.75 | 8.0 | OD |
| EA9. If the elderly patient with dysphagia, who is taken to rehabilitation program with therapeutic methods, is hospitalized, swallowing difficulty should be questioned at each visit, weekly clinical evaluation, and instrumental evaluation method at admission and discharge. | 95.2 | 0.25 | 10.0 | OC |
| EA10. If the elderly patient with dysphagia, who is admitted to the rehabilitation program with therapeutic methods, is an outpatient, the swallowing difficulty should be questioned before each treatment, a weekly clinical evaluation, and an instrumental evaluation method at the beginning and end of the treatment should be followed up. | 100.0 | 0 | 10.0 | OC |
| EA11. Patients who were included in the rehabilitation program with compensatory methods, are evaluated according to the patient’s compliance with the treatment, stabilization of dysphagia, risk of developing complications, frequency of complications and level of control; first once a week, then every 15 days, then monthly or at 2 months, then at 3-6 monthly intervals. It can be followed up with clinical evaluation in the short-term follow-up period and instrumental evaluation methods in the long-term follow-up periods. | 95.6 | 0.25 | 10.0 | OC |
| EA12. In elderly patients with dysphagia treated with surgical methods (in- and out-patient), follow-up intervals should be decided according to the surgical method applied and personal characteristics. | 95.2 | 0 | 10.0 | OC |
| EA13. In elderly patients with dysphagia treated with chemodenervation method, follow-up intervals should be decided according to the patient's condition. | 95.0 | 0.25 | 10.0 | OC |
| EA14. In elderly patients with dysphagia treated with drug therapy, follow-up intervals should be decided according to the patient's condition. | 100.0 | 0.25 | 10.0 | OC |
| EA15. In all elderly patients included in the rehabilitation program, the follow-up of dysphagia and the follow-up of nutritional status should be combined. | 100.0 | 0 | 10.0 | OC |
| EA16. A formal test can be used to monitor nutritional status. | 90.5 | 0 | 10.0 | OC |
| EA17. Eating-nutritional characteristics such as appetite status, 3-day food consumption record, number of meals, and hydration status can be questioned to monitor nutritional status. | 81 | 0.5 | 10.0 | OC |
| EA18. Follow-up should include reassessment of the continuation and modification of compensatory modalities such as diet, posture modification, maneuvers, and alternative feeding. | 95.2 | 0.25 | 10.0 | OC |

(Continued to the next page)
Table 3. Continued

<table>
<thead>
<tr>
<th>8%-10%</th>
<th>IQR</th>
<th>Median</th>
<th>SOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>100.0</td>
<td>0</td>
<td>10.0</td>
<td>OC</td>
</tr>
<tr>
<td>97.3</td>
<td>0</td>
<td>10.0</td>
<td>OC</td>
</tr>
</tbody>
</table>

Follow-up list

- History of pneumonia
- Pneumonia symptoms/signs
- Hospitalization history
- Aspiration symptoms/signs
- Alarm symptoms
- Malnutrition
- Dehydration
- Weight loss
- Cognitive dysfunction, delirium
- Oral hygiene
- Dental care
- Sarcopenia

Other items evaluated in Delphi Round-3

- Muscle weakness
- Functional independence, state of mobilization

Table 4. Distributions of the strength of the recommendations for the 3rd Delphi Round-4

<table>
<thead>
<tr>
<th>8%-10%</th>
<th>IQR</th>
<th>Median</th>
<th>SOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>100.0</td>
<td>0</td>
<td>10.0</td>
<td>OC</td>
</tr>
</tbody>
</table>

Sarcopenia related dysphagia

S1. Definition: SD is the presence of dysphagia in the presence of generalized sarcopenia (imaging confirming the loss of swallowing muscles, exclusion of other causes other than sarcopenia as the cause of dysphagia, and specifying sarcopenia as the main cause of dysphagia even if other causes accompany). Define, probable and/or possible sarcopenia dysphagia should be rehabilitated.

S2. Since isolated dysphagia rehabilitation will not be sufficient in SD rehabilitation, additional rehabilitation applications are required.

S2a. Rehabilitation components of SD should consist of patient education, increasing physical activity, muscle strengthening exercises and nutritional support.

S2b. Muscle strengthening should include oropharyngeal and generalized muscle strengthening exercises.

S2c. Measures such as ensuring oral hygiene to increase oropharyngeal muscle strength, treatment of periodontal diseases and use of appropriate prostheses should be added to the rehabilitation program.

S2d. Neuromuscular electrical stimulation method can be added to the treatment when the exercise program for muscle strengthening is insufficient.

S3. Nutritional support should include providing adequate calorie and protein intake, vitamin D supplementation, and the use of nutritional supplements that are likely to increase protein synthesis in suitable patients.

Frailty-related dysphagia

K1. Since frailty includes the effects on physical, psychological, cognitive and social functions, cognitive dysfunction, psychological dysfunction such as depressive mood, dependence in daily living activities and social isolation may predispose to the development of dysphagia.

K1a. In the presence of frailty (feeling of fatigue/burnout, low muscle strength, involuntary weight loss, slowing of walking speed, decrease in physical activity), oral phase dysphagia which includes dysfunction in chewing functions, may be observed. This potentiates each other with presbyphagia.

K1b. Frailty can be due to many reasons such as cognitive, psychological, multiple diseases, polypharmacy. Frailty screening tests should be performed, followed by a comprehensive geriatric evaluation.

IQR, interquartile range; SOA, strength of agreement; AC, approaching consensus; OC, overall consensus; OD, overall divergence; OPD, oropharyngeal dysphagia; ED, esophageal; FEES, Fiberoptic endoscopic evaluation of swallowing
This study presents the opinions and recommendations regarding “geriatric and dysphagia” from experienced multidisciplinary experts from many regions of Turkey. We collected and analyzed expert opinions according to the three-round Delphi method to determine the extent of consensus on the content and effectiveness of management methods in older adults with both OPD and ED. We divided this study into sections and subsections based on the 5Ws and 1H question pattern, including detailed diagnosis, treatment, and follow-up. Moreover, the 216-item recommendations were designed to be as detailed as possible and shed light on almost all potential questions and problems in clinical practice.

### DISCUSSION

**Who**

In the “who” section, we sought to answer the question “who should be considered for dysphagia?” Accordingly, we created three strong recommendations: “dysphagia should be considered in all older adults aged ≥ 80 years (regardless of symptoms/signs and risk factors), and in those ≥ 65 years of age with any risk factor for dysphagia AND/OR with any symptoms/signs associated with dysphagia.” We added an explanation to avoid the use of unnecessary, excessive and/or wrong methods: “These recommendations primarily suggest a simple screening test. However, this does not mean that clinical evaluation and further evaluation are unnecessary.”

Depending on the decrease in reserves with aging, anatomical, physiological, and functional changes in swallowing functions and in the systems of the whole body are defined as “presbyphagia.” These changes in swallowing function begin at 65 years of age. Although the rate of presbyphagia varies according to the diagnosis method, dysphagia occurs in 15%–70% of adults aged > 65 years, with the highest rate in adults aged ≥ 80 years. Therefore, we recommended a simple screening test for all older people aged ≥ 80 years with a high risk of dysphagia.

### Risk factors associated with dysphagia and aspiration

Presbyphagia, which is age-related, is a natural physiological condition. The secondary causes of dysphagia complicate this situation. The most feared complication of dysphagia is aspiration, pneumonia, and the associated 30%–50% increase in mortality.
ty.\textsuperscript{14,41,42} Therefore, it is important to be aware of the dysphagia-related risk factors that may complicate presbyphagia. Among the causes of dysphagia, the most common causes of OPD are neurological diseases, particularly stroke.\textsuperscript{3,4,6,17,20,43,44} Disorders causing cognitive dysfunction, the presence of malignancy, history of radiotherapy/surgery, respiratory diseases such as chronic obstructive pulmonary disease (COPD), and medical factors such as the use of tracheostomy and mechanical ventilation have a high sensitivity in predicting aspiration pneumonia (AP).\textsuperscript{3,12,19}

ED occurs 16% less often than OPD and its incidence increases with age. In some cases, such as esophageal cancer, this rate rises to 70%.\textsuperscript{15,45} Although it can vary regionally, the most common cause of ED is gastroesophageal reflux (GER).\textsuperscript{4,6} In addition, structural and inflammatory problems of the gastrointestinal tract (GIT), such as stricture, web, ring, malignancy, esophagitis, and/or motility disorders, can cause ED in older people.\textsuperscript{23,47}

In addition, conditions such as Parkinson disease, myotonic dystrophy, and myasthenia gravis; infectious conditions such as candida; some connective tissue diseases; multiple comorbidities; multiple drug therapy (polypharmacy); and the use of swallowing-related drugs can cause both OPD and ED.\textsuperscript{30,49}

The present study defined the following as dysphagia-related risk factors by OC: progressive/non-progressive central neurological diseases (stroke, dementia, Parkinson disease, myasthenia gravis, multiple sclerosis, motor neuron disease, and neuromuscular diseases); connective tissue diseases (scleroderma, systemic lupus erythematosus, polymyositis, dermatomyositis, Sjogren's syndrome); respiratory system diseases (COPD, lung fibrosis, and asthma); history of head, neck, anterior or mediastinum, and GIT cancer and radiotherapy and surgery to these regions; high comorbidity burden; multiple comorbidities; polypharmacy; drug use that may affect swallowing; recent history of tracheostomy, intubation, and mechanical ventilation; recent long-term use of nasogastric tube; conditions that cause cognitive dysfunction; the presence of sarcopenia and frailty; GIT diseases such as GER, peptic ulcer, and achalasia; and prolonged hospitalization.

The same risk factors were also assessed for their relationships with aspiration. Progressive/non-progressive central neurological diseases; history of head, neck, anterior mediastinum, and GIT cancer and radiotherapy and surgery to these regions; recent history of tracheostomy, intubation, and mechanical ventilation; recent long-term use of a nasogastric tube; conditions that cause cognitive dysfunction; and presence of sarcopenia and frailty were accepted as OC as aspiration-related risk factors. These factors are also reported in the literature as predictors of aspiration.\textsuperscript{3,50}

SD and FRD, which are among the risk factors for both dysphagia and aspiration, are discussed in detail in the “How” section.

**Symptoms/signs associated with dysphagia and aspiration**

The strongly recommended (OC) symptoms/signs suggestive of dysphagia were: change in eating habits (volume and consistency modification); difficulty in chewing; spillage of food from the mouth during feeding; food residue in the mouth; drooling, coughing, choking, and change of voice during/after feeding; increased need for throat clearing; choking while swallowing; sticky feeling; retrosternal obstruction/stuck/sticky feeling after swallowing; painful swallowing; repeated swallowing; need for multiple swallowing; progressive swallowing difficulty; prolonged swallowing time; delayed pharyngeal phase; head and posture changes during feeding; the presence of signs of lower respiratory tract infection; and a history of > 3 cases of pneumonia per year.

Among these symptoms/signs, retrosternal obstruction/stuck/sticky feeling, painful swallowing, and progressive swallowing difficulty especially after swallowing were characteristic of ED. Recommendation studies stated that painful swallowing should be considered an important symptom of ED.\textsuperscript{23,43}

We also compiled the following strongly recommended list of symptoms/signs that may be associated with aspiration: weakened or absent voluntary cough reflex, coughing/choking during/after feeding, change of voice (wet and hoarse voice) during/after feeding, shortness of breath/bruising, drooling, increased need for throat clearing, repetitive and multiple swallowing, feeling that something is stuck in the throat during swallowing, decrease in laryngeal elevation, presence of signs of lower respiratory tract infection (fever, cough, increased spumum, tachypnea), decreased oxygen saturation by pulse oximetry during/after feeding, and a history of pneumonia > 3 times a year.

**When-Where**

In these sections, we sought answers to the question “when and where should dysphagia be screened/evaluated in older people?” We made seven and five recommendations in response to “when” and “where,” respectively. Among these recommendations, 10 were strong and 2 were weak. Consistent with the answer to the “who” question, “all older people aged ≥ 80 years regardless of the presence of symptoms and/or risk factors, and those aged ≥ 65 years with risk factors and/or dysphagia symptom-signs should be screened once a year with a simple screening test for dysphagia” was accepted as a strong recommendation. In addition, we also recommended that “screening test and clinical evaluation should be performed at least once a year in people aged ≥ 65 years with severe aspiration-related risk factors and/or symptoms/signs.”

In recent years, annual wellness visits have been recommended for people aged ≥ 65 years, especially as a cancer screening and prevention strategy\textsuperscript{51} to potentially reduce mortality and morbidity. Considering the impact of dysphagia on morbidity and mortality, screening should be performed at least once a year when adding
screening for dysphagia to these annual well-being visits.

In this paper, we rejected the recommendation for screening two and four times a year due to the potential increase in workload. Instead, we added a weak recommendation that the screening time could be individually adjusted.

However, a screening test alone is not sufficient in patients with aspiration-related risk factors/symptom-signs; thus, clinical evaluation should be added to examinations in these patients. Screening tests are considered the first-line method for diagnosis in the literature. However, in recent years, these tests have been recommended to be completed with a comprehensive clinical examination for both OPD and ED. Since the present paper is intended for application in clinical practice, we recommended clinical evaluations in addition to screening tests only in cases accompanied by aspiration-related parameters.

In addition, we strongly recommended screening tests in primary health care centers, while clinical and instrumental evaluations should be performed in secondary and tertiary care centers.

Many medical branches such as general practitioners, dentists, social workers and geriatrics, gastroenterology, neurology, otorhinolaryngology, physical medicine and rehabilitation, and surgery may encounter older patients, from general practices, which are primary health centers, to tertiary hospitals. Therefore, screening is the first-line recommendation to both detect vulnerable patients and prevent unnecessary/excessive referrals to secondary and tertiary centers.

An important point here is to reveal the need for dysphagia education in all health professionals caring for geriatric patients. The experts in the present study expressed hesitations about where and by whom the evaluations would be done. In the literature, the need for education on the diagnosis, treatment, and possible complications of dysphagia is a general problem; moreover, all experts strongly accepted the recommendation for more education on this issue.

What
This section sought to answer the question “what should be evaluated in older adults with dysphagia?” to create recommendations for methods for diagnosing dysphagia. Accordingly, the diagnosis of dysphagia was evaluated under four subsections: management principles, screening tests, and clinical and instrumental evaluations.

Management principles
Since aging is a natural process of life, it is practically impossible to carry out a detailed evaluation in all older people to identify presbyphagia and dysphagia. Therefore, the proposed diagnosis algorithm in the present study was first-line screening tests, second-line clinical evaluation, and third-line instrumental evaluation.

Because swallowing is a sensorimotor complex behavior that involves many systems, starting from the central nervous system to the stomach, and is shaped by the sequential coordinated movement of these systems, many medical branches and healthcare professionals in clinical practice may encounter older people with dysphagia. Guidelines on dysphagia management, as well as meta-analyses and reviews, suggest the need for multidisciplinary team efforts. In the present study, although the team members in each center could change according to circumstances and capabilities, we suggested the establishment of a multidisciplinary team and formulated six strong recommendations. However, since multidisciplinary teams are not universal in clinical practice for the first-line simple screening for dysphagia, we created a recommendation that “if possible, performing the dysphagia screening test by a trained team member assigned in a multidisciplinary team may provide convenience in terms of diagnosis, treatment, and follow-up.” In addition, since dysphagia is not only a condition involving the patient but also a social health problem involving caregivers, we strongly recommended including patients and their relatives in the management team.

In addition, SLPs specialized in dysphagia are primarily responsible for dysphagia management worldwide. However, other health specialists play a more active role due to their low number in some places such as our country. For this reason, we recommended that other medical specialists may play an active role in the absence of SLPs both in terms of clinical evaluation and primary responsibility.

Screening tests
Among 25 initial items for simple screening tests, based on the recommendations of the consultant experts, five of the items were accepted at the end of the third Delphi round (four strong and one weak). Thus, we recommended three informal/subjective screening tests and two formal/objective tests:

1. Lists of risk factors + symptoms/signs that can be used as a screening test for dysphagia.
2. Three questions that can be used as a screening test for dysphagia:
   - “Do you have difficulty in swallowing solid foods/liquids?”
   - “Do you experience coughing, choking, or obstruction during/after feeding with solid food/liquid?”
   - “Do you think there is any difference or change in feeding with solid food/liquid compared to your younger self?”
Almost all studies in older adults have reported changes in eating habits (reduced volume, changed consistency, and increased meal times) with increasing age.\(^{6,38,48,52}\) Bolus formation and chewing ability especially decrease owing to age-related changes in swallowing function, in addition to changes in the choice of food consistency.\(^{13}\) Therefore, we accepted that the symptom of changes in eating habits and difficulty with solid foods/liquids, especially in older adults, may be appropriate screening questions for the diagnosis of geriatric dysphagia. In addition, changes in eating habits are an important symptom of OPD and presbyphagia and are an alarm symptom in severe esophageal pathologies such as peptic stricture and esophageal cancer in ED. Thus, we included this symptom in our three-question survey. This survey can be used when assessing the signs/symptoms of dysphagia in older people. In addition, we also added a key finding suggesting bolus aspiration, “coughing, choking and feeling of obstruction during/after feeding,” a question sentence. This question is also important because studies in older adults reported coughing and choking during feeding as the most common symptoms of aspiration.\(^{11,38,52}\) We also strongly recommended “observation of a patient’s mealtime in their natural home environment can be used as a screening test” in special conditions such as pandemic conditions, in which patients cannot come to centers or in which distancing is required. Observation of mealtime, foods that he/she can eat or avoid, food selection, and whether there are signs of aspiration during feeding can suggest the presence of dysphagia.

Among the evaluated objective screening tests, the Eating Assessment Tool-10 (EAT-10) was strongly recommended.\(^{13,57}\) The EAT-10 is a self-administered, questionnaire-based test that evaluates dysphagia symptoms and severity without any food intake. This test is commonly applied as a screening test in older adults; besides evaluating the symptoms of OD, it also includes questions related to painful swallowing, the feeling that something is stuck in the throat, and difficulty in swallowing solid food, which are among the symptoms of ED. Therefore, the tool is also valid for ED.\(^{9,65}\) Since the present study aimed to evaluate both OPD and ED, we considered the EAT-10 to be suitable for screening.

**Clinical evaluation**

In this subsection, the experts voted on 24 recommendations in the first Delphi round. Among the 15 recommendations created in the third Delphi round, 12 were strong and three were weak.

According to the World Health Organization (WHO); clinical evaluation involves the organized and targeted assessments of all components that comprise a function such as swallowing, as well as their relationships with each other.\(^{50}\) Thus, the goal of the clinical evaluation of swallowing functions is to understand the nature of swallowing functions. Therefore, we strongly recommended that “the clinical evaluation of dysphagia should include a detailed medical history (anamnesis) with questions about risk factors and symptoms, general systemic examination, evaluation of dysphagia signs, and a bedside swallowing test (BST)” and “the general systemic examination should include an examination of the neurological, cardiopulmonary, gastrointestinal, dental and musculoskeletal systems that may be associated with dysphagia.” We also detailed the symptoms/signs to be evaluated in systems related to swallowing to facilitate use in practice.

Seven of the 15 recommendations in this subsection are related to BSTs. BSTs are often used for the diagnosis of OPD. Researchers have frequently used various questionnaire screening tests including aspiration symptoms/findings and the water-swallow test (WST) in dysphagia studies among healthy older people.\(^{40,59,60}\) In this paper, we strongly recommended the volume viscosity swallowing test (VVST), Gugging Swallowing Screen test (GUSS), and WST with pulse oximetry. The VVST is performed with three different volumes (5, 10, and 20 mL) and three different viscosities (liquid, mildly thick, and extremely spoon-thick), while the GUSS test applies different food consistencies (solid, semisolid, and liquid) and amounts of food/liquid.\(^{13,61,62}\) These two tests are among the best BSTs as they resemble real swallowing functions with foods consumed in daily life (solid, semisolid, and liquid) and minimize the risk of aspiration during the evaluation.\(^ {43}\) The VVST can be used in patients with potential difficulty in swallowing liquids of different viscosities, while the GUSS can be used in patients with potential difficulty in swallowing liquids and solid foods. Although the guidelines for patients with stroke recommend the GUSS, some reviews on OD in older adults have recommended the VVST.\(^ {5,64}\) The WST with pulse oximetry has been recommended as a test of choice in patients with aspiration symptoms with liquid.\(^ {63}\) Although the WST is relatively easy to perform compared to other tests and is often used in the literature, other tests are recommended owing to the lower specificity and sensitivity of the WST and risk of aspiration compared to other tests.\(^ {60}\)

In addition, we strongly recommended that “the BST should be chosen individually and pathology-specifically, according to the suspected OPD or ED with the screening test.” As mentioned above, any of these three tests can be selected based on the symptoms/signs reported in the patient’s history and the examination features. We did not describe a specific BST for ED. This is because in OPD, symptoms occur during or immediately after swallowing, whereas in ED, symptoms such as delayed passage into the esophagus and a sensation of obstruction in the throat, chest, and/or epigastrum/retrosternal occur after the bolus is swallowed. Studies have rec-
ommended ruling out OPD primarily in patients with dysphagia symptoms/signs.23 For these reasons, we recommended the GUSS, which also includes evaluation with solid food, as a swallow test in patients with suspected ED.

Instrumental evaluation
The third Delphi resulted in 24 recommendations (15 strong, one weak, and eight non-recommendations). As a general recommendation, instrumental evaluation for dysphagia was recommended in suspected cases after clinical evaluation (such as the presence of severe risk factors and/or aspiration-related symptoms/signs). We strongly recommended that “the choice of instrumental method should be determined within a multidisciplinary team based on the characteristics of the underlying pathology, the type of dysphagia, the patient, and the center performing the evaluation” and that “these instrumental methods would be useful in treatment selection and follow-up.” This subsection also discussed instrumental methods in detail.

Videofluoroscopy (VF) and flexible fiberoptic endoscopic evaluation of swallowing (FEES) are the most widely studied and recommended gold standard methods in the diagnosis of OPD.24,40,48 The choice of method depends on the advantages and disadvantages.43 We recommended both FEES and VF as first-line methods for OPD diagnosis.

In contrast, the recommended methods of assessment in ED include barium swallow pharyngoesophagography/esophagography, upper gastrointestinal system endoscopy, and manometry (high-resolution manometry if possible).24,43 Guidelines and meta-analyses recommend barium radiography first to rule out structural and inflammatory causes, followed by manometry to assess motility disorders. Endoscopy has been proposed as a first-line modality in instrumental evaluation, especially in patients with symptoms of persistent dysphagia.24,25,43,58 In the present study, we added the VF as this method allows evaluation of the mouth to the LES, including the observation of UES patency and bolus transport. In addition, the American College of Radiology recommends the VF for dysphagia.67

As in other guidelines, we recommended magnetic resonance imaging (MRI), computed tomography (CT), and scintigraphy as non-first-line methods in difficult cases for both dysphagia types.23

How
This section sought answers to the question “how should dysphagia be treated and followed up?” Dysphagia treatment was categorized as management/general principles and rehabilitation modalities.

Management/general principles
This subsection included 14 strong recommendations.

The primary goal in the management of dysphagia is to prevent the development of dysphagia. Thus, the first-line treatment is the elimination of factors that can cause dysphagia before using rehabilitation modalities.23,43 In OPD, first-line modalities include surgery (in the presence of tumors and cervical osteophytes), medical treatment (in cases such as myasthenia gravis and oral candidiasis), and botulinum injection (in the presence of saliorrhea and dystonia).23,43 Similarly, the use of antiviral, antifungal, and antibiotic drugs in infectious esophagitis causing ED and medical treatment of GER and gastroparesis are first-line treatment modalities.23,43 The use of proton pump inhibitors for 4 weeks, especially in GER, reduces the incidence of GER worldwide and the incidence of ED as a result of this decrease.23 Similarly, the first-line treatment modalities include surgical treatment (cricopharyngeal myotomy and dilatation in stenosis, obstruction and neural relaxation disorder of UES, and resection of diverticulum and tumors) and botulinum toxin injection (application into the cricopharyngeal muscle to reduce UES pressure and facilitate bolus passage).23,43 In this study, we accepted as a strong recommendation that “determination of the underlying cause and its treatment should be the first-line treatment modality in the rehabilitation of both OPD and ED, and the treatment of the underlying cause should include the elimination of correctable risk factors for dysphagia.”

Another special point of this study was that we separately evaluated rehabilitation modalities that can be applied for both OPD and ED in detail. OPD management has been evaluated in detail due to aspiration complications and recommendations have been made for OPD. The aim of the rehabilitation modalities used in these guidelines is to improve the speed, strength, and range of movement (ROM) of the swallowing muscles (therapeutic methods) and to modify swallowing mechanics to improve bolus transfer and prevent or minimize aspiration (compensatory methods).11,68 Combination therapy has been recommended in both older people and patients with OPD.23,11,12,25,68 For example, in patients who cannot be fed orally, nutritional support may be provided using alternative feeding methods; however, oral stimulation and salivary swallowing exercises may also be combined with this therapy to stimulate swallowing function. Moreover, in patients who can be partially orally fed, a combination of compensatory methods such as diet and postural modification may be used, while both compensatory and therapeutic methods may form the treatment components in patients who can be fully orally fed. The treatment of dysphagia may vary individually and may change according to structural, functional, and/or anatomic dysfunction.63 For these reasons, “the selection of rehabilitation modalities ‘using
a management algorithm created by a multidisciplinary team may vary based on the existing facilities and facilities at each center in terms of personnel and equipment; considering the person’s general physical condition, cognitive and respiratory functions, and motivation as well as specific factors related to the person, pathology, and etiology, and dysphagia characteristics (such as affected areas, severity and prognosis) should be well defined” were accepted as strong recommendations. Moreover, we also recommended that “older people without dysphagia but with more than one severe risk factor should be included in a rehabilitation program that includes compensatory methods such as oral hygiene and some modifications, and a follow-up program.” Studies on neurologic dysphagia have reported greater effects of multidisciplinary and early treatment compared to mid- and late-term treatment, as well as significantly reduced AP. \(^{12,43}\) Given the presence of presbyphagia in older adults, early treatment becomes even more important.

**Rehabilitation modalities**

In this subsection, we generated 91 recommendations (35 strong, 45 weak, and 11 non-recommendations) for both OPD and ED. We then evaluated these modalities separately and defined each as first-, second-, and third-line methods to create a treatment algorithm.

While most of the recommended modalities for OPD were strong recommendations, most of the recommendations for ED were weak. The reason for this may be that rehabilitation modalities for ED are not widely used and that in our country and worldwide, recommendations for rehabilitation modalities for this situation are lacking.

(1) First-line treatment modalities

- **Education and information (OPD-ED):** Most older people lack information about their nutritional status and proper diet. \(^{40}\) Reviews and studies have reported that patient perception, motivation, willingness to change, technical knowledge, and health literacy affect treatment compliance in patients with dysphagia. \(^{11,12,14}\) Thus education is important in the rehabilitation of dysphagia. Therefore, we strongly recommended that: “education and information involving patients and their relatives are effective rehabilitation modalities for older adults with both OPD and ED and are recommended as a first-line treatment method.”

- **Oral hygiene-oral care and dental care-prosthodontic rehabilitation (OPD-ED):** “Oral hygiene, dental care, and prosthodontic rehabilitation are effective rehabilitation modalities and are recommended as a first-line treatment methods for older adults with both OPD and ED” (strong recommendation strength for OPD, weak recommendation for ED) (OPD: oral hygiene is a strong recommendation, dental care is a weak recommendation; ED: both weak recommendations).

Regular oral hygiene and dental care reduce the colonization of virulent bacteria and the incidence of AP, increase sensory sensitization, and improve the sensitivity of the cough reflex. \(^{45,71}\) Studies on oral hygiene are often based on OPD. However, GER, the most common cause of ED, also affects the oral region. \(^{71}\) The major oral symptom of GER is dental erosion. In addition, it can also cause tonsillitis, oral mucosa atrophy, glossitis, xerostomia, and dysgeusa. Moreover, in the presence of GER, microaspiration of bacteria into the oral flora along with saliva contents may occur due to esophageal dysmotility, damaged swallowing coordination, and decreased sensitivity of pharyngeal and laryngeal protective reflexes. Therefore, regardless of the pathology of dysphagia, we recommended oral hygiene and oral/dental care.

- **Positioning and posture modification (OPD-ED):** “Positioning and postural modifications are effective rehabilitation modalities and are recommended as first-line treatment methods for older adults with both OPD and ED” (strong recommendation for OPD, weak recommendation for ED).

A supine position of at least 60°, and ideally 90°, can prevent residual, penetration, and aspiration by altering swallowing structures to protect the respiratory tract and also affects the esophageal phase with gravity. \(^{12,22,26,43,44,52}\) However, no study has provided strong evidence for positioning. Therefore, our recommendations are important to the literature.

Our consultant experts recommended positioning patients with OPD in a sitting position as much as possible and using head and posture modifications for OPD. The most common postural modification considered to be effective is the chin-tuck position (98%), which prepares the airway for swallowing by reducing the rate of bolus passage, especially in patients with preterm escape. \(^{44}\) In contrast, our experts recommended the use of trunk modification for ED, most commonly an upright sitting position (91%). Lifting the head while lying down and remaining in a sitting position for at least 30 minutes after meals were among the recommendations for postural modification in patients with GER.

- **Dietary (bolus volume, texture, consistency) modification (OPD-ED):** “Dietary modifications are effective modalities for older adults with both OPD and ED and are recommended as a first-line treatment method” (strong recommendation).

Dietary modifications are the most recommended compensatory methods for treating dysphagia. Modifications such as volume, viscosity, bolus, and texture changes are common methods, especially for OPD. \(^{3,13,14,26,48,52,69}\) In older adults with chronic dysphagia, texture modification such as pureeing and mincing, and thickened fluids such as nectar, honey, and pudding consistencies are moder-
ately recommended. Studies in patients with neurogenic dysphagia and liquid aspiration have shown that viscosity changes reduce the risk of AB.

Dietary modification is 96% effective in patients with ED, depending on the etiology. Modifications such as reduced portions and increased meal numbers, providing bite-sized food, removing problematic food (such as hard solids) from the meal, eating slowly, and drinking liquid with each bite can also be implemented in these patients.

However, these modifications may negatively affect quality of life, especially in older patients. In fact, dietary modification is an unconscious compensatory method used by older adults against changes observed in presbyphagia. Studies have shown that older adults have difficulty swallowing, especially solid food, and that patients unconsciously eliminate solid food from their diets and modify it by prolonging the meal time or consuming less. We believe that if this is done under the supervision of a health professional, the effects reported as negative will disappear. In support of this, nutritional management guidelines also strongly recommend the use of dietary modifications to ensure adequate and balanced nutrition in older patients.

Feeding route modification (artificial feeding) (OPD-ED):

“Feeding route modification is effective and is recommended as a first-line treatment method for older adults with both OPD and ED” (strong recommendation).

The main task of the swallowing function is the intake of necessary and sufficient macro- and micro-nutrients, energy, and calories for the body. Although the oral route is the priority, the natural oral route may not always be able to meet the body’s needs or the use of this route may involve a risk of aspiration. Nasogastric (NG), percutaneous endoscopic gastrostomy, or jejunostomy (PEG/PEJ) tubes can be used as life-extending procedures. Guidelines and reviews have reported that their use in patients with OPD greatly reduces the incidence of AP and ensures adequate and balanced nutrition. NG should be chosen in patients who require short-term tube feeding (2–4 weeks), while PEG/PEJ should be used in patients who require or are expected to require enteral feeding long-term (> 28 days). This study recommended the use of enteral feeding tubes for both types of dysphagia, as needed. However, to avoid overuse/unnecessary use, this method has been conditioned to be useful for “patients with severe dysphagia and/or high dysphagia risk and/or malnutrition/malnutrition risk and/or patients with > 25% residue and/or > 10% aspiration in all volumes and liquids/nutrients.”

Nutritional rehabilitation (OPD-ED):

“Nutritional rehabilitation is an effective modality and is recommended as a first-line treatment method for older adults with both OPD and ED” (strong recommendation).

Malnutrition and dehydration are major complications of dysphagia that are associated with morbidity and mortality. Although protein and energy requirements decrease with age, they may increase with disease, inflammation, fever, and physical activity and cause increased morbidity and mortality. This situation should not be seen only as a nutritional deficiency; thus, the experts strongly recommended that “nutrition should be evaluated and treated in a multidisciplinary team, with a dietician if possible; if there is no dietician, this should be done by physicians or trained health personnel.”

Malnutrition is defined as unintentional weight loss > 10% in 6 months or markedly reduced BMI (< 20 kg/m²). Therefore, malnutrition can be evaluated with measurements such as weight and BMI. However, guidelines recommend the use of a formally validated test for nutritional assessment; among these tests, the most commonly used and recommended is the Mini Nutritional Assessment-Short Form (MNA-SF). This study recommended the use of the MNA-SF at a rate of 95.3%. The Nutrition Risk Score-2002 (NRS-2002) and Global Leadership Initiative on Malnutrition (GLIM) tests were also recommended at rates of 92%, while the Malnutrition Universal Screening Tool was recommended at a rate of 87%. The GLIM is a combination of at least one phenotype criterion (i.e., involuntary weight loss, low BMI, or decreased muscle mass) and one etiology criterion (i.e., reduced food intake/malabsorption or severe inflammatory disease). Recent guidelines recommend the GLIM criteria.

Although there is no definitive evidence regarding the effect of oral nutritional supplements (ONS), ONS added to the hospital diet affects functional recovery in older adults and patients with stroke, malnutrition, and cancer. In addition, recent guidelines published in recent years report that ONS can be used to increase nutritional intake and achieve nutritional goals in older people with malnutrition or at risk of malnutrition. We recommended ONS to improve the nutritional status of older adults with dysphagia and to supplement deficiencies in appropriate patients in a team setting.

Oral sensory stimulation (thermal, touch, and pressure) (OPD)

“Oral sensory stimulation is an effective modality and is recommended as a first-line treatment method for older adults with OPD” (strong recommendation).

A loss of sense of taste, decreased numbers of sensory receptors, and changes in salivary rheology occur with aging regardless of OPD. The goal of oral sensory stimulation is to increase the sensitivity of these receptors and to initiate and accelerate the oropharyngeal swallowing response. Cold and tactile stimulation can improve the transition from the oral to the pharyngeal phase by in-
creasing oral awareness. 79) Almost all experts in this study (97.5%) recommended cold stimulation. Considering that there may be changes related to age, we strongly recommend the application of oral sensory stimulation in older adults with dysphagia/dysphagia risk.

(2) Second-line treatment modalities

- **Head and neck exercises (ROM and Strengthening) (OPD-ED)**

  “Head and neck exercises (ROM and strengthening) can be effective modalities for older adults with both OPD and ED and can be tried as a second-line treatment method” (weak recommendation).

  Exercises are inherently more active and effective methods than compensatory mechanisms. Head and neck ROM and strengthening exercises can be effective in creating the correct feeding posture for both OPD and ED.6,12,13,23,43,44 Among these, cervical flexion strengthening exercises (Shaker exercise) improve hyoid and laryngeal elevation, increase UES opening, reduce pharyngeal residuals, and improve dysphagia symptoms, especially in patients with neurogenic OPD.6,69 Moreover, lingual weakness is associated with muscle weakness in the head and neck muscles.69 The experts in the present study weakly recommended exercises as second-line treatment methods because older people with cognitive problems could find exercising difficult. For this reason, our experts requested that all exercise recommendations include the statement “appplicable to patients with adequate awareness and cognitive function.” Another important point here is that physical fitness should also be considered, as extreme exercise can cause trauma and fatigue in elderly patients.

- **Breathing exercises (inspiratory and expiratory muscle strengthening exercises (EMST)) (OPD-ED)**

  “Breathing exercises (inspiratory and EMST) are effective modalities for older adults with both OPD and ED (strong recommendation for OPD, weak recommendation for ED) and can be tried as a second-line treatment method” (weak recommendation).

  Swallowing and breathing are closely related because they share the same anatomical pathways. Swallowing often (75-95%) begins during the expiratory phase of respiration, inspiration is suppressed during bolus transport and continues with expiration after swallowing. This is a natural aspiration inhibitor. The cough reflex is another pillar of the anti-aspiration mechanism.80 Both of these aspiration protective mechanisms deteriorate with age, the cough reflex weakens, and inspiration instead of expiration following swallowing is observed three times more often compared to young people.80 In addition, lung elasticity and both inspiratory and expiratory muscle strength decrease, and compliance increases with age. Therefore, both inspiratory and expiratory muscles should be strengthened not only in patients with dysphagia but in all older people. Recent studies have assessed EMST applications, especially in patients with OPD. EMST increases the physiological load and strengthens the expiratory and suprahyoid muscles.81 While EMST may be effective compared to conventional treatments in improving the pharyngeal phase in patients with OPD, strong evidence is lacking.5,12,13 The present study recommended adding breathing exercises to dysphagia rehabilitation in all geriatric dysphagia patients, as permitted by cognitive functions, to maintain healthy oxygenation throughout the body.

- **Swallowing maneuvers (OPD)**

  “Swallowing maneuvers are an effective modality for older adults with OPD (strong recommendation) and can be tried as a second-line treatment method” (weak recommendation). “It is not an effective modality and is not recommended for older adults with ED.”

  Swallowing maneuvers are behavioral interventions used to establish safe and effective swallowing.62 Although evidence for their effectiveness is insufficient, these interventions are recommended in combination therapy for dysphagia.3 Implementation and adaptation difficulties negatively affect the implementation of maneuvers.83 In the present study, we asked our experts about the maneuvers they found most effective; 82% of them stated that the Mendelsohn maneuver can be effective in older patients, similar to the literature.84 This maneuver involves the voluntary holding of hyolaryngeal elevation during the peak phase of swallowing. However, it can cause muscle fatigue in older adults. The present study recommended the Mendelsohn maneuver in cognitively and physically fit patients.

- **Oropharyngeal exercises (ROM, strengthening, and chin tuck against [CTAR]) (OPD)**

  “Oropharyngeal exercises (ROM, strengthening, and CTAR) are modalities that can be used in older adults with OPD (strong recommendation) and can be tried as a second-line treatment method” (weak recommendation).

  Exercises have long been used for treating dysphagia. ROM exercises are recommended, especially for patients with head and neck cancer, to prevent impairments secondary to surgery and radiotherapy.85 These exercises may be effective in older adults with OPD due to the loss of elasticity in the tissues with aging. Recent studies have evaluated the effectiveness of tongue muscle strengthening exercises as tongue propulsion strength and squeezing pressure against the palate are closely related to swallowing disorders. Tongue strengthening exercises improve swallowing phase intervals and food intake in older patients.19,46 In addition, strengthening exercises of the swallowing muscles in the oropharyngeal areas provide formation and control of the bolus and re-
produce the risk of aspiration. Additionally, CTAR exercises to strengthen the suprahyoid muscles have been applied in recent years for treating dysphagia. This type of exercise is performed to strengthen the suprahyoid muscles. However, there is not yet strong evidence regarding its effectiveness. As with all exercises, the present study recommended that these exercises should be added to treatment in suitable older adults.

- **Electrical stimulation (oropharyngeal motor level)** (OPD)

  “Neuromuscular electrical stimulation (NMES) (motor level) is a modality that can be applied in older adults with OPD (strong recommendation) and can be tried as a second-line treatment method” (weak recommendation).

  NMES is increasingly used for treating dysphagia in recent years. It is also often used for treating neurologic OPD and is considered to increase muscle strength and achieve muscle contraction by stimulating motor nerves. Although studies and guidelines have reported its positive effect on the oropharyngeal phase, the efficacy findings have been inconsistent because of the lack of standardization in practice. While suprahyoid and infrahyoid region applications are reportedly effective in the oral phase, the effect on the pharyngeal phase alone is not sufficient. Besides these transcutaneous applications, the effectiveness of stimulations applied directly to the pharyngeal region has not been demonstrated. While there is a decrease in type II muscle fibers with aging, type I fibers are not much affected by age. This decrease in muscle fiber size causes progressive skeletal muscle loss, atrophy, weakness, and functional disability. NMES targets these type 2 fibers. Thus, transcutaneous NMES at the motor level has been accepted as a method that can be applied in older patients with OPD.

(3) Third-line treatment modalities

Third-line treatment modalities have been described only for older adults with OPD.

- **Electrical stimulation (Oropharyngeal sensory level)** (OPD)

  “Neuromuscular electrical stimulation (NMES) (sensory level) is a modality that can be tried in older adults with OPD and can be tried as a third-line treatment method” (weak recommendation).

  Sensory nerve fiber stimulation affects swallowing function through stimulation of the afferent sensory nerves and has an indirect effect on the swallowing muscles. This stimulation has been frequently studied in stroke patients and is reportedly more effective than motor-level applications. In addition, there remains no standardized application method such as motor-level applications. However, we recommended that this stimulation can be tried in patients who cannot tolerate NMES at the motor level.

- **Transcranial electrical stimulation and repetitive transcranial magnetic stimulation (rTMS)** (OPD)

  “Transcranial electrical stimulation and rTMS are modalities that can be tried as a third-line treatment method in older adults with OPD” (weak recommendation).

  Transcranial applications for treating dysphagia focus on adaptation, compensation, repair, and reorganization in the brain. Although it is reportedly a safe treatment method in patients with neurological dysphagia, results regarding its effectiveness are conflicting. Another method based on the same mechanism, rTMS, has shown increased popularity in recent years. Unlike other electrical stimulation applications, rTMS is reportedly particularly effective in the pharyngeal phase. However, as it requires special and costly equipment, this method was recommended to be tried in patients with OPD after other methods.

- **Biofeedback (OPD)**

  “Biofeedback is a modality that can be tried as a third-line treatment method in older adults with OPD” (weak recommendation). “It is thought to be ineffective in patients with ED and is not recommended.”

  Biofeedback is the training of the ability to provide coordination and timing of swallowing with visual, auditory, or sensory signals during swallowing muscle activity. It is effective in combination treatments in patients with OPD. In addition, a recent study in patients with amyotrophic lateral sclerosis and ED showed that biofeedback is a promising method. However, our experts made a weak recommendation in the presence of OPD because of the requirement for special training and equipment and serious patient cognitive skills. Among other modalities, it can be used in the presence of suitable conditions and patients.

**Home program (OPD-ED)**

This study weakly recommended that “home programs can be applied in older adults with OPD and ED.”

Home programs are widely used methods in clinical practice to maximize the benefits of rehabilitation. These programs apply personalized compensatory and therapeutic methods based on patient needs and are reportedly effective in adults. However, in geriatric patients, the effectiveness may vary depending on the patient’s cognitive and physical dysfunction, treatment compliance, and the presence of social support. Therefore, albeit with a weak recommendation, we believed that personalized home programs for older people will increase the continuum of treatment. Because changes in aging are progressive conditions, albeit slow, long-term rehabilitation will not occur with only expert-provided therapies.

**Follow-up**

While there were 45 recommendations in the first Delphi round, 21 items were accepted as strong recommendations at the end of the third Delphi round. The follow-up subsection was detailed as
much as possible to facilitate clinical practice. Nearly all management guidelines suggest follow-up time and methods specifically for individual patients. The present study recommended that the follow-up time and methods may vary according to individual patient characteristics, dysphagia pathology, and etiology and that decisions should be made according to these situations.

We recommended the use of screening tests, clinical evaluation methods, bedside swallow tests, and FEES from instrumental methods for follow-up. VF was not recommended to avoid radiation exposure in patients with repeated applications.

Decision-making requires a multidisciplinary team based on treatments such as surgery, chemodenervation, or medical treatment. Moreover, the follow-up intervals should be decided based on these varying circumstances. We recommend that patients receiving rehabilitation should be first evaluated together with nutritional rehabilitation and formal testing or evaluation of feeding-nutrition characteristics such as appetite status, food consumption record for 3 days, number of meals, and hydration status.

In addition, we detailed follow-up recommendations for rehabilitation modalities. Patients undergoing rehabilitation with compensatory methods should be followed up based on patient compliance, dysphagia progression, risk of developing complications, and severity of existing complications. Clinical and instrumental evaluations should be performed for short and long terms, respectively: initially once weekly, then every 15 days, then every 2 months, and finally at 3–6-month intervals. Furthermore, we recommended follow-up of inpatients who underwent rehabilitation programs with therapeutic methods by asking about swallowing difficulties at each visit, weekly clinical evaluations, and instrumental evaluation methods at admission and discharge. In contrast, we recommended follow-up of outpatients who underwent rehabilitation with therapeutic methods by asking about their symptoms/signs of swallowing difficulties before each treatment session as well as weekly clinical evaluations and instrumental evaluations at the beginning and end of the treatment. The recommended follow-up intervals varied for almost any application, especially the application of rehabilitative modalities, as compensatory methods are not curative modalities for dysphagia, and they still carry the risk of dysphagia, whereas therapeutic methods are likely to lead to changes in the nature of dysphagia for better or worse.

Apart from these principal recommendations, this study also included some symptoms/signs/risk factors that should be on a follow-up list. We recommended that the complications of dysphagia, especially the risk of silent aspiration, should be questioned and evaluated in terms of treatment continuity and modification. In addition, all members strongly recommended the inclusion of aspiration signs/symptoms, pneumonia history and/or signs, cognitive dysfunction, delirium, recent hospitalization history, alarm symptoms, malnutrition, dehydration, weight loss, oral hygiene, dental care, and sarcopenia as parameters on a follow-up list.

**How-special**

“Sarcopenia” and “frailty” are terms that have been introduced in recent years with respect to geriatric syndrome and have shown increasing importance for older people. Therefore, the need arose in our study to create a special section for SD and FRD. Twenty strong recommendations were made, including seven for SD and 13 for FRD.

Sarcopenia is characterized by a progressive and generalized loss of skeletal muscle mass in the whole body accompanied by a loss of either muscle strength or physical performance or both. The loss of muscle mass and strength in sarcopenia results in physical impairment, functional dependence, and maladaptation to stress and diseases. Sarcopenia affects up to 50% of older people. In addition to this increased sensitivity to stress and maladaptation, when many systems become deficient due to the effect of aging, a different multidimensional geriatric clinical syndrome called “frailty” develops.

Recent publications have highlighted the association between sarcopenia and frailty and dysphagia. The impairments and deficiencies in all systems that occur in sarcopenia and frailty naturally affect swallowing functions and cause dysphagia. Dysphagia itself can also cause these two conditions. Malnutrition and dehydration, the main complications of dysphagia, cause sarcopenia, immune system dysfunction, increased functional disability, and frailty. That is, just as sarcopenia and frailty are risk factors for dysphagia, dysphagia is also a risk factor for sarcopenia and frailty. The present study defined the presence of sarcopenia and frailty as both dysphagia- and aspiration-related risk factors.

SD is the presence of dysphagia (with imaging confirmation of the loss of swallowing muscles, exclusion of causes other than sarcopenia that may cause dysphagia, and specification of sarcopenia as the main cause of dysphagia, even with other accompanying causes) in the presence of generalized sarcopenia. Similar to our article, the literature for the diagnosis of SD recommends a screening test (EAT-10) within the recommended steps for generalized dysphagia, followed by a detailed clinical examination and a BST such as the WST with pulse oximetry, GUSS, or VVST. In the evaluation of swallowing muscles, the EWS-GOP stated that dual-energy X-ray absorptiometry (DEXA), bioelectrical impedance analysis (BIA), MRI, CT, and ultrasound can be used. The present study did not recommend the evaluation of the swallowing muscles with CT and ultrasound due to lack of
standardization, and weakly recommended the use of MRI, which is sensitive to the evaluation of soft tissues. DEXA and BIA were dropped after the first Delphi round because they are not universally available in clinical practice and require specialized equipment and personnel.

Based on the presence/absence of the parameters in the definition of SD, we created descriptions including definite-, probable- and/or possible-SD. Sarcopenia itself is associated with physical disability, poor quality of life, and even death. If dysphagia is added to this, it can be predicted that the complications of dysphagia will compound the complications of sarcopenia, resulting in increased morbidity and mortality. Therefore, the experts accepted the recommendation that “everyone should be rehabilitated, regardless of probable-, possible- or definite-SD.” However, since SD is a systemic condition, treatment applications are needed for both sarcopenia and dysphagia, just as treatment is applied for both dysphagia rehabilitation and loss of motor function in the extremities in patients with stroke. Our experts recommended that “the rehabilitation program should include patient education, increase in physical activity, muscle strengthening (exercises and oral-dental care), and nutritional support.” The muscle strengthening methods include strengthening exercises for both oropharyngeal (head-neck, tongue, and chewing muscles) and general muscles (the lower extremities, anti-gravity, postural muscles, and respiratory muscles). Increasing oropharyngeal muscle strength requires precautions such as ensuring oral hygiene, treating periodontal diseases, and using appropriate prostheses. When the exercise program for muscle strengthening is insufficient, the rehabilitation program was further elaborated with the NMES method. In addition, treatments should also include nutritional rehabilitation, including adequate calorie and protein intake (1.2–1.5 kg/day), the use of dietary supplements that are likely to increase protein synthesis, and vitamin D support when needed. Although aging is most commonly reported in the etiology of sarcopenia (primary sarcopenia), it can also develop as a result of conditions such as physical inactivity; malnutrition; organ failure; and malignant, endocrine, and metabolic diseases (secondary sarcopenia). Aging also paves the way for the development of secondary sarcopenia by increasing the risk of serious diseases such as cancer and causing both inactivity and malnutrition with presbyphagia in older patients with or without sarcopenia. Since the changes that occur with age are a natural consequence of life, it is important to treat the causes of secondary sarcopenia that can be corrected. Exercise plays a role in both the prevention and treatment of physical inactivity by increasing muscle strength throughout the body. In addition, malnutrition has a serious negative effect on type 2 muscle fibers, which provide rapid contraction in the swelling muscles. Therefore, nutritional support is recommended in SD. Recent geriatric studies have reported that the dietary supplementation of protein and amino acids is effective in improving muscle mass. Additionally, vitamin D plays a key role in muscle function and strength. Therefore, we recommend its use to increase muscle mass for treating SD in patients with vitamin D deficiency.

FRD is the presence of dysphagia in patients with frailty. In particular, in the presence of physical frailty syndrome (feeling of exhaustion/fatigue, low muscle strength, involuntary weight loss, reduced walking speed, and decreased physical activity), oral phase dysfunction, including chewing dysfunction (oral frailty) may occur. This condition mutually reinforces presbyphagia and may result in oropharyngeal residue, laryngeal penetration, and aspiration. As frailty affects physical, psychological, cognitive, and social functions, cognitive and psychological dysfunction such as depressive mood, social isolation, and dependence in activities of daily living also pave the way for the development of OPD. Morbidity and mortality rates increase by approximately 3–4-fold in the presence of FRD, regardless of physical frailty status. Therefore, the recognition and treatment of frailty is important. Studies recommend screening tests as a first-line method for the detection of frailty, consistent with our general recommendations, and comprehensive geriatric evaluations as a second-line method.

As with SD, additional rehabilitation is required in the presence of FRD. Because frailty is a biological syndrome with a complex and multifactorial etiology, occurring due to the decline of physiological reserves as a result of disease, malnutrition, and changes that occur with aging. Therefore, in addition to treating the cognitive, psychological, and social effects that constitute frailty, treatment of the correctable causes in the etiology such as obesity, polypharmacy, and multiple comorbidities should be included as a first-line method in rehabilitation programs. Because sarcopenia plays a key role in frailty, we also recommended adopting the recommendations for SD in these patients, including increased physical activity, muscle strengthening exercises, oral and dental care, and nutritional rehabilitation.

Limitations
We did not follow a systematic review approach. As systematic reviews should have specified inclusion and exclusion criteria and should include a detailed analysis and interpretation of the literature, this method is the subject of an article in itself. We could not follow the systematic review method in this study due to the desire to provide detailed recommendations formed as a common opinion of experts with clinical practice experience.
Conclusion
Despite the many recommendations and reviews worldwide on the management of dysphagia in geriatric patients, no study has evaluated all aspects of dysphagia in detail. This study applied a multidisciplinary approach to attempt to answer all potential questions and problems encountered in clinical practice regarding geriatric dysphagia. We discussed oropharyngoesophageal dysphagia in detail, from diagnosis to treatment, and created a 216-item recommendation list for the management of geriatric dysphagia, SD, and FRD.

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CONFLICT OF INTEREST
The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTIONS
Conceptualization: EU; Data curation: EU, SE, GB; Investigation: EU, SE, GB, MH; Methodology: EU, SE, GB, MH; Project administration: EU, SE; Supervision: EU; Writing-original draft: EU; Writing-review & editing: EU, SE, GB, MH, EG, PU, ZU, CT, MV, ATC, SB, EG, KK, BA, ECK, BK, AY, CO, DS, OY, SA, ST, BS, EIS, AYK, AY, SO, BI, MGO, ZAO, Sak, BY, MSA, AS, MI, MB, ZÇ, GS, TO, YE, DHB, DK, ZU, AD, YÇ, BS, ZAY, EAO.

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Validation of a Multi-Sensor-Based Kiosk in the Use of the Short Physical Performance Battery in Older Adults Attending a Fall and Balance Clinic

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Background: The Short Physical Performance Battery (SPPB) is a well-established functional assessment tool used for the screening and assessment of frailty and sarcopenia. However, the SPPB requires trained staff experienced in conducting the standardized protocol, which may limit its widespread use in clinical settings. The automated SPPB (eSPPB) was developed to address this potential barrier; however, its validity among frail older adults remains to be established. Therefore, this exploratory study compared the eSPPB and manual SPPB in patients attending a tertiary fall clinic in relation to their construct validity, discriminatory ability, and reliability.

Methods: We studied 37 community-dwelling older adults (mean age, 78.5 ± 6.8 years; mean FRAIL score, 1.2 ± 1.0; 65% pre-frail) attending a tertiary falls clinic. The participants used the mSPPB and eSPPB simultaneously. We evaluated the convergent validity, discriminatory ability, reliability, and agreement using partial correlation adjusted for age and sex, an SPPB cutoff of ≤8 to denote sarcopenia, intraclass correlation coefficients (ICC), and Bland-Altman plots, respectively.

Results: The eSPPB showed strong correlations with the mSPPB (r=0.933, p<0.01) and Berg Balance Scale (r=0.869, p<0.01), good discriminatory ability for frailty and balance, and good to excellent reliability (ICC=0.94; 95% confidence interval, 0.88–0.97). The Bland-Altman plots indicated good agreement with the mSPPB (mean difference, -0.2; 95% confidence interval, -3.2–2.9) without evidence of systematic or proportional biases.

Conclusion: The results of our exploratory study corroborated the construct validity, reliability, and agreement of the eSPPB with the manual SPPB in a small sample of predominantly pre-frail older adults with increased fall risk. Future studies should examine the scalability and feasibility of the widespread use of the eSPPB for frailty and sarcopenia assessment.

Key Words: Physical performance, Frailty, Sarcopenia
This study was conducted in community-dwelling older adults recruited from the Falls and Balance Clinic at Tan Tock Seng Hospital, a tertiary hospital in Singapore. We recruited participants from July 2020 to July 2021. The inclusion criteria included patients aged ≥ 65 years attending the Falls and Balance Clinic who were able to walk ≥ 100 m independently (with or without aid); those who scored ≥ 4 on the Abbreviated Mental Test (AMT), which corresponded to the cutoff for mild-moderate dementia in a local validation study; and those who could understand instructions and adhere to the study protocol. The exclusion criteria were (1) chair or bed-bound status, (2) AMT ≤ 3, and (3) inability to understand simple commands or provide consent. Informed written consent was obtained from the participants or their legally appointed representative, where appropriate, in the presence of a trained research assistant. Ethical approval was obtained from the Institutional Review Board of the National Healthcare Group (No. 2020/00038).

Manually Measured SPPB (mSPPB)
A trained physiotherapist conducted the mSPPB. In the balance test, the participants were asked to maintain three positions (side-by-side, semi-tandem, and tandem stances) for 10 seconds. To measure gait speed, the participants were timed with a stopwatch (Casio Model HS-3, with a measurement accuracy of up to 1/100-seconds) as they walked 4 m from a standing start. For the chair-stand test, the participants were timed for five consecutive sit-to-stand repetitions with their arms folded across their chest and ending with a fifth sit. We employed a sitting stop, as this was the prevalent practice for the timing of the chair stand test. This also allowed for comparability with the chair sensor of the eSPPB kiosk.

The eSPPB Kiosk
The eSPPB kiosk prototype was developed by Dyphi (Daejeon, Korea). We used the eSPPB setup described in the original validation study. In brief, the three SPPB components can be semi-automatically estimated. Balance was measured with a load cell array that could detect the location of the participant’s foot and measure the force applied to it. Gait speed was measured with a one-dimensional light detection and ranging (LiDAR) sensor that could measure the distance between the sensor and the participant. The chair stand test was performed five times using a combination of two sensors: a load cell-embedded chair to measure the weight of the participants and a LiDAR sensor to measure the distance between the participant and the chair. The three components were input directly into a program that allowed the conduction of SPPB in a standardized manner with graphic and voice instructions. The
eSPPB kiosk algorithm was used to calculate the score for each component based on previously published cutoff points.

Data Collection

Protocol for mSPPB and eSPPB
The participants performed the mSPPB and eSPPB simultaneously to optimize the reliability evaluation and avoid the need for repeated assessments. While the physical therapist instructed the participants and manually recorded timings for individual test sections of the mSPPB, the research assistant recorded their performance using the eSPPB. The research assistant aided with the setup of the eSPPB components and operated the eSPPB software during the assessment.

Other variables
We collected data on demographics, height, weight, and body mass index. The functional ability, basic activities of daily living (ADL), and physical activity were evaluated using the modified Barthel Index (MBI), Lawton and Brody’s instrumental ADL (iADL), and Frenchay Activities Index (FAI), respectively. Frailty status was measured using the FRAIL (fatigue, resistance, ambulation, illness, loss of weight) scale, a self-reported five-item scale that assesses the domains of fatigue, resistance, ambulation, illnesses, and loss of weight. Individuals who scored 1–2 were considered as pre-frail, whereas those who scored 3–5 were classified as frail. Fall efficacy and balance performance were measured using the Falls Efficacy Scale International (FES-I) and Berg Balance Scale (BBS), respectively.

Statistical Analysis
The sample size was calculated based on the evaluation of the intraclass correlation coefficient (ICC) between the mSPPB and eSPPB. Using an a priori postulated ICC of 0.80, a study power (1−β) of 0.80, and a half-width 95% confidence interval (CI) of ICC < 0.15, we required 35 participants for the study. Based on an anticipated dropout rate of 10%, we recruited 39 participants.

Descriptive and inferential statistics were analyzed using IBM SPSS Statistics for Windows (version 27.0; IBM, Armonk, NY, USA) and MedCalc for Windows (version 20.013; MedCalc Software, Ostend, Belgium). Two-sided p < 0.05 was considered statistically significant.

First, we performed descriptive statistics to assess the demographic and clinical characteristics of the study participants. Next, we examined the construct validity of the mSPPB and the eSPPB in two ways. First, for convergent validity, we evaluated the correlations with common geriatric parameters using a partial correlation coefficient adjusted for age and sex. Second, using a cutoff of ≤ 8 to denote sarcopenia, we performed independent samples t-tests to ascertain the ability to discriminate physical function, physical activity, frailty, balance performance, fear of falling, and physical performance between the ≤ 8 and > 8 subgroups. We then assessed the reliability of the mSPPB and eSPPB based on the ICCs of the total and component-specific scores. ICC values were indicated as: poor reliability (< 0.5), moderate reliability (0.5–0.75), good reliability (0.75–0.9), and excellent reliability (> 0.9). We also performed paired t-tests to compare the mean differences between the readings. Lastly, we constructed Bland-Altman plots to determine the agreements between the total and component-specific scores. Systematic bias was calculated as the mean difference between readings, and 95% limits of agreement were calculated as the bias ± 2 standard deviation for the differences between readings. Proportional bias was ascertained by inspecting the regression line and Pearson correlation to quantify the degree of bias.

RESULTS

Recruitment Flowchart
Of the 88 eligible participants, 35 (39.8%) declined further participation due to fear of technology, lack of time, or the coronavirus disease 2019 (COVID-19) situation. Of the 53 recruited participants, 16 were excluded from the study as they had incomplete data owing to technical issues that resulted in their data not being properly captured by the computer or them not being recognized by the sensors. Thus, the final sample comprised 37 participants who underwent both mSPPB and eSPPB assessments. Age, anthropometry, physical function, activity, and frailty status did not differ significantly between the included (n = 37) and excluded (n = 16) participants (Fig. 1).

Baseline Characteristics
The participants were predominantly female (62%) with a mean age of 78.5 ± 6.8 years. The AMT scores ranged from 6 to 10; while one participant had mild cognitive impairment, none had dementia. The mean FRAIL score was 1.2 ± 1.0; thus, most of the participants were pre-frail (65%). The mean mSPPB score was 6.6 ± 3.3, which is lower than the cutoff of ≤ 8 used to denote sarcopenia. The female participants were lighter, shorter, and had lower MBI and BBS scores. Our participants from the Falls and Balance Clinic were slightly older and appeared to be frailer than those of original validation study derived from a rehabilitation clinic. This is evidenced by the lower BBS, mSPPB, and eSPPB and higher FRAIL
scores obtained in our study (Table 1).

**Convergent Validity**

Not surprisingly, we observed a strong correlation between the mSPPB and eSPPB total scores ($r = 0.933$, $p < 0.01$). Both mSPPB and eSPPB total scores showed strong correlations with the BBS ($r = 0.900$ and $r = 0.869$, respectively, $p < 0.01$), moderate correlation with the MBI ($r = 0.507$ and $r = 0.508$, $p < 0.01$) and iADL ($r = 0.465$ and $r = 0.530$, $p < 0.05$), and weak to moderate correlations with the FRAIL scale ($r = -0.441$ and $r = -0.383$, $p < 0.05$). Neither mSPPB nor eSPPB was correlated with the FAI or FES-I.

**Discriminatory Ability for Outcomes**

Using a cutoff of ≤ 8 to denote sarcopenia, both mSPPB and eSPPB were associated with significantly higher FRAIL scores (mSPPB: $1.5 \pm 1.0$ vs. $0.4 \pm 0.5$, $p = 0.013$; eSPPB: $1.5 \pm 1.0$ vs. $0.6 \pm 0.6$, $p = 0.010$), lower BBS scores (mSPPB: $38.2 \pm 10.0$ vs. $50.8 \pm 2.9$, $p = 0.008$; eSPPB: $36.6 \pm 9.8$ vs. $50.2 \pm 2.8$, $p = 0.005$), and lower SPPB total scores (mSPPB: $5.0 \pm 2.4$ vs. $10.5 \pm 1.0$, $p = 0.003$; eSPPB: $4.4 \pm 2.2$ vs. $10.1 \pm 1.3$, $p = 0.001$). The domain-specific scores for balance, gait speed, and chair stand were also significantly lower in the ≤ 8 subgroups for both the mSPPB and eSPPB (Table 2).

**Total/Domain Scores and ICCs**

We observed no significant differences in the mean mSPPB and eSPPB total and domain scores. Relative to the mSPPB, the eSPPB showed excellent reliability for the total score (ICC = 0.94; 95% confidence interval).

The subdomains of the mSPPB and eSPPB showed similar results as the total scores, with a moderate to strong correlation with the BBS (lowest $r = 0.460$ for eSPPB gait speed, and highest $r = 0.831$ for eSPPB balance), moderate correlations with the MBI and iADL, and weak to moderate correlations with the FRAIL scale. The FAI was only moderately correlated with eSPPB gait speed but was not correlated with the rest of eSPPB subdomains or with mSPPB. None of the subdomains in either the mSPPB or eSPPB were correlated with the FES (Table 2).

### Table 1. Baseline characteristics of the current and original validation studies

<table>
<thead>
<tr>
<th></th>
<th>Current study</th>
<th>Original study (Jung et al.16)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male (n = 14)</td>
<td>Female (n = 23)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>76.9 ± 6.4</td>
<td>79.5 ± 7.0</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>70.1 ± 14.1</td>
<td>53.2 ± 11.6</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.6 ± 0.08</td>
<td>1.5 ± 0.1</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.0 ± 5.0</td>
<td>25.0 ± 6.0</td>
</tr>
<tr>
<td>MBI Total (0–100)</td>
<td>98.0 ± 2.5</td>
<td>93.7 ± 7.1</td>
</tr>
<tr>
<td>iADL (0–32)</td>
<td>19.7 ± 3.2</td>
<td>17.6 ± 4.6</td>
</tr>
<tr>
<td>FRAIL total (0–5)</td>
<td>0.8 ± 0.8</td>
<td>1.4 ± 1.1</td>
</tr>
<tr>
<td>Robust</td>
<td>6 (43)</td>
<td>4 (17)</td>
</tr>
<tr>
<td>Pre-frail</td>
<td>8 (57)</td>
<td>16 (70)</td>
</tr>
<tr>
<td>Frail</td>
<td>0 (0)</td>
<td>3 (13)</td>
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<tr>
<td>FAI total (0–45)</td>
<td>26.4 ± 9.5</td>
<td>26.6 ± 11.8</td>
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<tr>
<td>BBS total (0–56)</td>
<td>47.2 ± 3.2</td>
<td>39.2 ± 11.8</td>
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<tr>
<td>FES-I total (16–64)</td>
<td>28.8 ± 11.1</td>
<td>29.6 ± 10.2</td>
</tr>
<tr>
<td>mSPPB (0–12)</td>
<td>7.6 ± 2.8</td>
<td>6.0 ± 2.5</td>
</tr>
<tr>
<td>eSPPB (0–12)</td>
<td>8.1 ± 3.2</td>
<td>5.7 ± 3.2</td>
</tr>
</tbody>
</table>

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

BMI, body mass index; MBI, modified Barthel Index; iADL, instrumental activities of daily living; FRAIL, fatigue, resistance, ambulation, illness, loss of weight; FAI, Frenchay Activities Index; BBS, Berg Balance Scale; FES-I, Falls Efficacy Scale International; mSPPB, manual Short Physical Performance Battery; eSPPB, automated Short Physical Performance Battery.

*p<0.01, **p<0.05.
Table 2. Convergent validity of mSPPB versus eSPPB and their subdomains

<table>
<thead>
<tr>
<th></th>
<th>MBI</th>
<th>iADL</th>
<th>FES</th>
<th>FRAIL</th>
<th>FAI</th>
<th>BBS</th>
</tr>
</thead>
<tbody>
<tr>
<td>mSPPB total</td>
<td>0.507*</td>
<td>0.465**</td>
<td>0.077</td>
<td>-0.441**</td>
<td>0.305</td>
<td>0.900*</td>
</tr>
<tr>
<td>Balance</td>
<td>0.494*</td>
<td>0.413**</td>
<td>-0.082</td>
<td>-0.292</td>
<td>0.253</td>
<td>0.789*</td>
</tr>
<tr>
<td>Gait speed</td>
<td>0.282</td>
<td>0.470**</td>
<td>0.150</td>
<td>-0.505*</td>
<td>0.299</td>
<td>0.662*</td>
</tr>
<tr>
<td>Chair stand</td>
<td>0.430**</td>
<td>0.269</td>
<td>0.121</td>
<td>-0.297</td>
<td>0.201</td>
<td>0.718*</td>
</tr>
<tr>
<td>eSPPB total</td>
<td>0.508*</td>
<td>0.530*</td>
<td>0.138</td>
<td>-0.383**</td>
<td>0.362</td>
<td>0.869*</td>
</tr>
<tr>
<td>Balance</td>
<td>0.569*</td>
<td>0.499*</td>
<td>0.100</td>
<td>-0.239</td>
<td>0.380</td>
<td>0.831*</td>
</tr>
<tr>
<td>Gait speed</td>
<td>0.163</td>
<td>0.411**</td>
<td>0.286</td>
<td>-0.430**</td>
<td>0.409**</td>
<td>0.460**</td>
</tr>
<tr>
<td>Chair stand</td>
<td>0.309</td>
<td>0.287</td>
<td>0.068</td>
<td>-0.233</td>
<td>0.132</td>
<td>0.555*</td>
</tr>
</tbody>
</table>

Partial correlation adjusted for age and gender.

mSPPB, manual Short Physical Performance Battery; eSPPB, automated Short Physical Performance Battery; MBI, modified Barthel Index; iADL, instrumental activities of daily living; FES, Falls Efficacy Scale; FRAIL, fatigue, resistance, ambulation, illness, loss of weight; FAI, Frenchay Activities Index; BBS, Berg Balance Scale.
*p<0.01, **p<0.05.

Table 3. Characteristics and comparisons of the means of SPPB scores of ≤8 and >8

<table>
<thead>
<tr>
<th></th>
<th>mSPPB ≤ 8 (n = 26)</th>
<th>mSPPB &gt; 8 (n = 11)</th>
<th>p-value</th>
<th>eSPPB ≤ 8 (n = 23)</th>
<th>eSPPB &gt; 8 (n = 14)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBI total</td>
<td>93.9 ± 6.8</td>
<td>98.6 ± 1.8</td>
<td>0.091</td>
<td>93.3 ± 7.0</td>
<td>98.2 ± 2.1</td>
<td>0.033**</td>
</tr>
<tr>
<td>iADL</td>
<td>17.2 ± 4.4</td>
<td>21.1 ± 1.8</td>
<td>0.13</td>
<td>17.2 ± 4.4</td>
<td>20.1 ± 3.2</td>
<td>0.115</td>
</tr>
<tr>
<td>FRAIL total</td>
<td>1.5 ± 1.0</td>
<td>0.4 ± 0.5</td>
<td>0.013**</td>
<td>1.5 ± 1.0</td>
<td>0.6 ± 0.6</td>
<td>0.010**</td>
</tr>
<tr>
<td>FAI total</td>
<td>24.5 ± 10.8</td>
<td>31.2 ± 9.6</td>
<td>0.756</td>
<td>24.6 ± 11.3</td>
<td>27.5 ± 9.1</td>
<td>0.972</td>
</tr>
<tr>
<td>BBS total</td>
<td>38.2 ± 10.0</td>
<td>50.8 ± 2.9</td>
<td>0.008*</td>
<td>36.6 ± 9.8</td>
<td>50.2 ± 2.8</td>
<td>0.005*</td>
</tr>
<tr>
<td>FES-I total</td>
<td>27.3 ± 9.4</td>
<td>34.6 ± 11.6</td>
<td>0.343</td>
<td>27.4 ± 9.5</td>
<td>30.3 ± 9.7</td>
<td>0.919</td>
</tr>
<tr>
<td>SPPB total (0–12)</td>
<td>5.0 ± 2.4</td>
<td>10.5 ± 1.0</td>
<td>0.003*</td>
<td>4.4 ± 2.2</td>
<td>10.1 ± 1.3</td>
<td>0.001*</td>
</tr>
<tr>
<td>Balance (0–4)</td>
<td>1.7 ± 1.1</td>
<td>3.2 ± 1.0</td>
<td>0.003*</td>
<td>1.5 ± 1.1</td>
<td>3.4 ± 0.8</td>
<td>0.001*</td>
</tr>
<tr>
<td>Gait speed (0–4)</td>
<td>1.8 ± 0.9</td>
<td>3.6 ± 0.7</td>
<td>0.007*</td>
<td>1.6 ± 0.8</td>
<td>3.4 ± 0.8</td>
<td>0.002*</td>
</tr>
<tr>
<td>Chair stand (0–4)</td>
<td>1.5 ± 1.5</td>
<td>3.6 ± 0.5</td>
<td>0.003*</td>
<td>1.3 ± 1.4</td>
<td>3.4 ± 1.1</td>
<td>0.003*</td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation.

mSPPB, manual Short Physical Performance Battery; eSPPB, automated Short Physical Performance Battery; MBI, modified Barthel Index; iADL, instrumental activities of daily living; FRAIL, fatigue, resistance, ambulation, illness, loss of weight; FAI, Frenchay Activities Index; BBS, Berg Balance Scale; FES-I, Falls Efficacy Scale International.
*p<0.01, **p<0.05.

CI, 0.88–0.97) and gait speed domain (ICC = 0.94; 95% CI, 0.89–0.97), and good reliability for the balance and chair stand domains (ICC 0.86–0.89). The confidence intervals were wider for the balance and chair stand domains (95% CI, 0.75–0.93 and 0.81–0.94, respectively) than those of the total score and gait speed domain. Our reliability results were similar to those of the original study, which also showed good to excellent reliability for total SPPB scores and its domains161 (Table 4).

Bland-Altman Plots

The Bland-Altman plot showed good agreement for the eSPPB and mSPPB total scores, with most values within the limits of agreement. We observed no evidence of systematic (mean difference = -0.2; 95% CI, -3.2–2.9) or proportional (r = 0.102, p = 0.546) biases. Similarly, the domain-specific scores showed good agreement for balance (mean difference = 0.1; 95% CI, -1.3–1.5; r = -0.225, p = 0.181), gait speed (mean difference = -0.2; 95% CI, -1.7–1.3; r = -0.100, p = 0.555), and chair stand (mean difference = -0.1; 95% CI, -1.6–1.3; r = 0.019, p = 0.912), with most values within the limits of agreement (91.9%, 97.3%, and 94.6%, respectively). We observed no evidence of systematic or proportional biases in the domain-specific scores (Fig. 2).

DISCUSSION

Since the original validation study of the automated multi-sensor-based kiosk for SPPB, emerging evidence from retrospective analyses of clinical populations supports the application of the eSPPB
in real-world clinical settings. To our knowledge, this exploratory study is the first to compare the validity, reliability, and agreement of the eSPPB with those of the mSPPB among predominantly pre-frail older adults attending a fall and balance clinic. Similar to the original validation study involving a less frail population, we observed no significant differences in the total and domain scores of the eSPPB and mSPPB. In addition, our study builds upon the body of evidence by corroborating the construct validity, good-to-excellent reliability, and good agreement without systematic or proportional biases between the eSPPB and mSPPB readings for total and domain scores.

As the criteria for referral to our Falls and Balance Clinic is recurrent falls and/or unsteady gait, it was unsurprising that the overall mean score for both the eSPPB and mSPPB was < 8, suggesting that a significant number of our participants were already in the sarcopenia category. This was consistent with the results of studies that reported an association between sarcopenia and an increased risk of falls. In contrast, the higher SPPB scores (mean, 9.9–10.2 for the mSPPB) in our study may reflect the less frail nature of our population compared to those with sarcopenia.

Table 4. Comparisons of total/domain SPPB scores and ICCs

<table>
<thead>
<tr>
<th></th>
<th>Current study</th>
<th>Original study (Jung et al.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mSPPB</td>
<td>eSPPB</td>
</tr>
<tr>
<td>Total score (0–12)</td>
<td>6.62 ± 3.26</td>
<td>6.57 ± 3.38</td>
</tr>
<tr>
<td>Balance (0–4)</td>
<td>2.14 ± 1.25</td>
<td>2.24 ± 1.40</td>
</tr>
<tr>
<td>Gait speed (0–4)</td>
<td>2.38 ± 1.16</td>
<td>2.32 ± 1.20</td>
</tr>
<tr>
<td>RCST (0–4)</td>
<td>2.11 ± 1.61</td>
<td>2.00 ± 1.60</td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation.
SPPB, Short Physical Performance Battery; ICC, intraclass correlation coefficient; eSPPB, automated Short Physical Performance Battery; mSPPB, manual Short Physical Performance Battery; RCST, repeated chair stand test; CI, confidence interval.

Fig. 2. Bland-Altman plots comparing the agreements between the mSPPB and eSPPB for total score (A) and domain scores for balance (B), gait speed (C), and repeated chair stand (D). eSPPB, automated Short Physical Performance Battery; mSPPB, manual Short Physical Performance Battery.
Our study results supported the construct validity of the eSPPB in at-risk older adults by demonstrating its convergent validity in terms of balance performance, physical function, and physical activity. Notably, the correlation coefficient with the BBS score was higher in our study than that in the original validation study. Although the exact reason remains to be elucidated, one possibility is the closer relationship between the balance sub-domain and BBS in frailer older adults at increased risk of falls, which further affirms the convergent validity of the eSPPB in this at-risk population. Our results also corroborated the discriminatory ability of frailty, balance performance, and SPPB scores using a cutoff of ≤ 8 to denote sarcopenia. In support of this, participants scoring ≤ 8 on both the eSPPB and mSPPB were also in the pre-frail range, based on the FRAIL scale. This was consistent with previous studies that showed that SPPB score of ≤ 8 was a useful measure for identifying sarcopenia and physical frailty phenotype in community-dwelling older adults.

Our study also demonstrated excellent reliability for total scores and good to excellent reliability for domain scores between the eSPPB and the mSPPB. In relation to the original validation study, it was reassuring that the ICC in our study was comparable to that of the total score and higher for the balance and gait speed domain scores, albeit lower for the chair stand despite the frailter population. However, caution is needed when interpreting ICCs, as the values can be affected by samples heterogeneity, which exemplifies the concept of signal-to-noise ratio, wherein the proportion of variance is due to differences between subjects instead of the assessments performed. Despite the good reliability, balance and chair stand showed the lowest ICC and widest confidence intervals among the domains, suggesting the need to address technical issues related to sensors in frailler older adult populations.

In addition, we observed good agreement between the SPPB total score, with almost all data points lying within the 95% limits of agreement. The absolute difference in mean scores of 0.2 for SPPB total score in our study was lower than the minimally significant change of 0.3–0.8 points reported in the LIFE-P study. We also observed no evidence of systematic or proportional biases. Examination of the domain scores showed the highest number of outliers in the balance and chair stand assessments, with 8.1% and 5.4% of data points, respectively, beyond the limits of agreement. These outliers could have resulted from technical challenges in the sensing of balance and chair pads.

Our study has several limitations. Due to the cross-sectional design, we were unable to assess the test-retest reliability of the eSPPB or evaluate its predictive validity via longitudinal outcomes. As an exploratory study, our sample size was small, precluding comparisons between sexes or other subgroups. In addition, our results pertain to a predominantly pre-frail at-risk patient group attending the Falls and Balance Clinic and may not be generalizable to a wider population of frail older persons. As our study sample included no individuals with dementia, our results cannot be extrapolated to patients with dementia. We employed the sitting stop for the chair-stand test to allow comparability with the chair sensor of the SPPB. A recent study indicated that the timings for standing versus sitting stop in the chair stand test may not be comparable; therefore, our results may not be generalizable to settings where a standing stop is the prevalent practice. We also did not collect data pertaining to the feasibility and user acceptability of the eSPPB from the participants’ perspective. Future studies in larger populations with greater proportions of frail older adults are needed to examine the feasibility and acceptability of the eSPPB for widespread use in clinical settings.

In summary, the results of our exploratory study corroborated the construct validity, reliability, and agreement of the eSPPB with the mSPPB in a small sample of predominantly pre-frail older adults with increased fall risk. In addition, the balance and chair stand domains were associated with potential technical issues that need to be addressed to improve the reliability and agreement of the readings. This study paves the way for future studies examining the scalability and feasibility of the widespread use of eSPPB for frailty and sarcopenia detection in the clinical setting.

ACKNOWLEDGMENTS

The authors thank Ms. Loo Yen Leng, Ms. Lee Jin Yih, Ms. Audrey Yeo Jing Ping, and Ms. Kalene Pek for their invaluable assistance with this study. We also express our gratitude to the study participants who graciously consented to participate in the study, as well as the doctors, nurses, and physiotherapists of the Falls and Balance Clinic at Tan Tock Seng Hospital who helped us to perform this study.

CONFLICT OF INTEREST

Dr. Hee-Won Jung cofounded Dyphi, Inc., a startup company for sensor technology. The authors declare no conflicts of interest.

FUNDING

None.

AUTHOR CONTRIBUTIONS

Conceptualization, OEH, LH, NHI, LWS; Data curation, HHCH, LWS; Investigation, CNT, FG; Methodology, OEH, LH, LWS;...
REFERENCES


INTRODUCTION

The proportion of the geriatric population in society is gradually increasing. According to a World Health Organization report, the number of people aged ≥ 60 years, which was one billion in 2020, is expected to increase at an unprecedented rate to 2.1 billion by 2050. National data reveal that the older population will double by 2060. With an increase in the geriatric population, geriatric syndromes are of increasing importance. Geriatric syndromes are common, complex, and costly health conditions in older individuals. Sarcopenia, which causes physical disability with a progressive and generalized decrease in skeletal muscle strength and mass, is also defined as geriatric syndrome.

In general, 5%–13% of people aged 60–70 years and 11%–50% of people aged ≥ 80 years have sarcopenia. A systematic study, reported sarcopenia in at least one of 20 members of the community, with the incidence increasing to up to one in three in frail older individuals. Sarcopenia is associated with many clinical consequences such as falls, fractures, physical disability, and increased mortality, causing high personal, social, and economic burdens. Sarcopenia is also associated with many chronic and endocrine comorbidities such as diabetes mellitus, depression, and cardiovascular diseases. However, the relationship of sarcopenia with cognitive function remains unclear. Sarcopenia and cognitive disorders share many co-occurrence mechanisms, which has prompted researchers to investigate the relationship between cognitive and...
In this context, the present study investigated the relationship between sarcopenia and cognitive function in older adults.

Materials and Methods

Study design and participants
This study included 201 participants aged > 65 years at Department of Family Medicine, the Health Sciences University Kartal Dr. Lutfi Kirdar City Hospital, Istanbul, Turkey, between July 1, 2020, and January 31, 2021. The Kartal Dr Lutfi Kirdar City Hospital Clinical Research Ethics Committee approved this study (No. 2020/514/180/33). Informed consent was obtained from all participants at the beginning of the study. This study complied with the ethical guidelines for authorship and publishing in the Annals of Geriatric Medicine and Research. We calculated the sample size for a known population with an unknown prevalence within the 95% confidence interval. We evaluated all participants and collected data on their anthropometric measurements. The same examiner performed all measurements. Body mass index (BMI) was calculated as body weight (kg)/height squared (m²). Body analyses of the patients were performed using an Omron Karada Scan device on an empty stomach, without metal, and with bare feet.

Sarcopenia assessment
Sarcopenia was diagnosed according to the European Working Group on Sarcopenia in Older People (EWGSOP2) criteria. We also screened all patients based on the SARC-F (strength, assistance with walking, rising from a chair, climbing stairs, and falls) questionnaire. We considered participants with a SARC-F total score ≥ 4 to be at risk for sarcopenia. The handgrip strength of patients with sarcopenia risk was evaluated using a Baseline Digital Smedley hand dynamometer. We asked the participants were asked to keep their elbows close to the body, flex the elbow to 90°, and grasp the dynamometer and squeeze as hard as possible. We used the highest value of three measurements for analysis. We defined probable sarcopenia as handgrip strength < 27 kg in male participants and < 16 kg in female participants.

We applied bioelectrical impedance analysis (BIA) to evaluate the skeletal muscle masses of participants with probable sarcopenia. Jannsen et al. defined skeletal muscle index (SMI) as the percentage of total body mass (skeletal mass/body weight × 100), and expressed SMI% in units. A low SMI was considered normal if it was greater than one standard deviation from the sex-specific mean for young adults (18–39 years) based on data from the Third National Health and Nutrition Examination Survey (NHANES III). Patients with values one standard deviation below the mean were defined as having sarcopenia. The present study used cutoff values of < 37% (for male) and < 27.6% (for female), with participants with values these cutoffs categorized as having sarcopenia.

We conducted a 4-m walking speed test to evaluate the physical performance of the participants, with times ≤ 0.8 m/s indicating severe sarcopenia.

Cognitive function
We used the Standardized Mini-Mental Test (SMMT) and Standardized Mini-Mental Test for the Untrained (SMMT-E) to evaluate the cognitive status of the participants. Participants who correctly completed all test areas received the maximum total score of 30. We defined normal cognitive function as scores of ≥ 24 points, mild dementia as scores of 18–24, and severe dementia as scores ≤ 18.

Statistical analysis
Study data were analyzed using IBM SPSS Statistics for Windows, version 21.0 (IBM, Armonk, NY, USA). Descriptive criteria (frequencies, percentages, means, medians, standard deviations, and minimum-maximum values) were reported. We applied Kolmogorov-Smirnov tests to assess normality. Pearson and Spearman correlation tests were used to evaluate the relationships between continuous variables. Chi-square test was used. Statistical significance was set at p < 0.05.

Results
This study included a total of 201 participants—44.3% (n = 89) male and 55.7% (n = 112) female. The mean age of the participants was 73.3 ± 6.0 years. Most the participants were married (69.2%; n = 139), high school graduates (29.4%; n = 59), and retired (61.7%; n = 124). The mean BMI was 27.9 ± 4.1 kg/m². According to BMI classification, approximately half of the participants (46.8%; n = 94) were overweight. The general characteristics of the participants are presented in Table 1.

In this study, 10.9% (n = 22) of the participants were at risk for sarcopenia. To confirm the diagnosis of sarcopenia, we evaluated the participants’ muscle mass and handgrip strength, which showed that 6.0% (n = 12) of the participants had definite sarcopenia. The results of walking tests to assess the sarcopenia severity revealed severe sarcopenia in 33.3% (n = 4) of the participants (Fig. 1).

Examination of the relationship between demographic data and sarcopenia status showed a significant difference between the presence of sarcopenia and age. In this study, 16.7% (n = 2) of participants with sarcopenia were aged ≥ 85 years compared to 3.2%...
Table 1. Demographic features of the study participants (n=201)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>73.3 ± 6.0</td>
</tr>
<tr>
<td>65–74</td>
<td>109 (54.2)</td>
</tr>
<tr>
<td>75–84</td>
<td>84 (41.8)</td>
</tr>
<tr>
<td>≥ 85</td>
<td>8 (4.0)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>89 (44.3)</td>
</tr>
<tr>
<td>Female</td>
<td>112 (55.7)</td>
</tr>
<tr>
<td>Education (y)</td>
<td></td>
</tr>
<tr>
<td>≤ 8</td>
<td>97 (48.3)</td>
</tr>
<tr>
<td>≥ 9</td>
<td>104 (51.7)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>139 (69.2)</td>
</tr>
<tr>
<td>Single</td>
<td>7 (3.5)</td>
</tr>
<tr>
<td>Widow/divorced</td>
<td>55 (27.4)</td>
</tr>
<tr>
<td>Working status</td>
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</tr>
<tr>
<td>Retired</td>
<td>124 (61.7)</td>
</tr>
<tr>
<td>Employed</td>
<td>11 (5.5)</td>
</tr>
<tr>
<td>Non-employed</td>
<td>66 (32.8)</td>
</tr>
<tr>
<td>Living condition</td>
<td></td>
</tr>
<tr>
<td>Alone</td>
<td>36 (17.9)</td>
</tr>
<tr>
<td>Wife/husband and children</td>
<td>158 (78.6)</td>
</tr>
<tr>
<td>Mother/father</td>
<td>6 (3.0)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Income (Turkish lira)</td>
<td></td>
</tr>
<tr>
<td>≤ 2,200</td>
<td>63 (31.3)</td>
</tr>
<tr>
<td>≥ 2,201</td>
<td>138 (68.7)</td>
</tr>
</tbody>
</table>

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

We observed no significant differences between other demographic characteristics and sarcopenia (Table 2).

Evaluation of the cognitive functions of the participants using SMMT showed a mean SMMT score of 26.2 ± 3.3. While 80.6% (n = 162) of the group had a normal cognitive function, 19.4% (n = 39) showed impairment. Our examination of the association between cognitive impairment and SARC-F revealed that 8.6% (n = 14) and 20.5% (n = 8) of participants with normal cognitive function and cognitive impairment, respectively, were at risk of sarcopenia (p = 0.045). We next assessed the relationship between cognitive function and sarcopenia status, finding that 3.7% (n = 6) of participants with normal cognitive function were sarcopenic, compared to 15.4% (n = 6) of participants with cognitive impairment (p = 0.006) (Table 3).

DISCUSSION

This study aimed to determine the prevalence of sarcopenia and investigate the relationship between sarcopenia and cognitive function in older individuals. It was found that 10.9% (n = 22) of participants was risky for sarcopenia and that 6.0% of the participants had definite sarcopenia. The rate of sarcopenia was significantly higher in older individuals with cognitive impairment compared to those without cognitive impairment (15.4% vs. 3.7%).

Epidemiological studies on the prevalence of sarcopenia have reported sarcopenia in 5%–13% of people aged 60–70 years and 11%–50% of people aged > 80 years. Differences in sarcopenia definitions, cutoff values, measurement methods, and formulations have led to different prevalence reports in the literature. BIA underestimates fat mass, overestimates muscle mass, and shows a small margin of error in estimating skeletal muscle mass. Kim et al. reported sarcopenia frequencies of 14.2% in female and 5.1% in male based on the SMI. The authors also reported different sarcopenia frequencies using different methods to assess muscle mass. In our study, the overall incidence of sarcopenia was 5.9%, while it was 8.0% in female and 3.3% in male. The frequency of sarcopenia was 25% in participants aged ≥ 85 years, with a significan-
sarcopenia. Given the progressive decrease in muscle mass with age, this result was expected. However, the frequency of sarcopenia in our study was relatively low, even in those aged > 85 years. We attribute this finding to the living conditions of the older individuals in this study. Physical inactivity and obesity are important risk factors for sarcopenia. As our study area was an island, the inhabitants have high physical activity levels.

We observed no significant difference in the presence of sarcopenia between sexes. In their meta-analysis including 58,404 patients, Shafiee et al. \(^{17}\) reported a similar prevalence of sarcopenia between sexes, consistent with our findings. The relationship between sex and sarcopenia has been inconsistent in the literature. Some studies reported a higher reduction in muscle mass in male than in female. \(^{18,19}\) Iannuzzi-Sucich et al. \(^{20}\) reported the highest prevalence of sarcopenia (52.9%) in male aged > 80 years compared to 31.0% among female of the same age. Various endogenous and exogenous factors determine the prevalence of sarcopenia in both sexes. Hormonal changes that play a role in decreasing muscle mass occur more slowly in male than in female. After the menopause transition, the concentrations of sex steroids containing both estrogen and androgen decrease significantly. The reduction in sex steroids in male is much slower than that in female. \(^{21}\)

In our study, the rate of sarcopenia was significantly higher in older individuals with cognitive impairments compared to those with normal cognitive functions. Ida et al. \(^{22}\) reported a significant

cant association between age and sarcopenia. Given the progressive decrease in muscle mass with age, this result was expected. However, the frequency of sarcopenia in our study was relatively low, even in those aged > 85 years. We attribute this finding to the living conditions of the older individuals in this study. Physical inactivity and obesity are important risk factors for sarcopenia. As our study area was an island, the inhabitants have high physical activity levels.

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In our study, the rate of sarcopenia was significantly higher in older individuals with cognitive impairments compared to those with normal cognitive functions. Ida et al. \(^{22}\) reported a significant
relationship between sarcopenia and mild cognitive impairment (MCI) using the Japanese version of the SARC-F in a study of Japanese participants with diabetes. Another study showed that physical performance but no other markers of sarcopenia were independently associated with cognitive impairment. Lee et al. reported that sarcopenia was associated with MCI in older Korean female. Moreover, a recent meta-analysis showed evidence regarding the relationship between sarcopenia and cognitive impairment.

This study is one of a few to assess sarcopenia and cognitive function in the Turkish population. However, our study had some limitations. First, because of the study area, the findings cannot be generalized. The study area was an island near a large metropolis (Istanbul) and the participants had higher socioeconomic status and average life expectancy than those of the general population. Moreover, as motor vehicles are not allowed on the island, the physical movement capacity of the participants was also higher than that of the general population. Additionally, the MMT is a screening tool that cannot diagnose dementia. Finally, the cross-sectional design does not show causality.

In conclusion, the results of our study revealed the frequency of cognitive impairment in older individuals at risk of sarcopenia and/or those diagnosed with sarcopenia. With the rapid increase in the geriatric population, neuropsychiatric diseases have become a critical public health problem worldwide and in our country. The correlation between SARC-F and SMMT findings suggests that patients at risk of sarcopenia can also be assessed for cognitive impairment.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST
The researchers claim no conflicts of interest.

FUNDING
None.

AUTHOR CONTRIBUTIONS
Conceptualization: BY, CO, HC, EES; Data curation: BY; Funding acquisition: BY, EES; Investigation: BY, CO; Methodology: CO, HC, EES; Project administration: BY; Supervision: CO, HC, EES; Writing-original draft: BY, CO, HC, EES; Writing-review & editing: BY, CO, HC, EES.

REFERENCES


Is Laparoscopic Common Bile Duct Exploration Safe for the Oldest Old Patients?

Hee Jin Yeon, Ju Ik Moon, Seung Jae Lee, In Seok Choi
Department of Surgery, Konyang University Hospital, Daejeon, Korea

Background: This study aimed to identify the risk factors for postoperative complications of laparoscopic common bile duct exploration (LCBDE) in the oldest old patients aged 80 years or older.

Methods: From March 2001 to October 2020, 363 patients underwent LCBDE with stone removal. Based on their ages, they were divided into two groups, those younger than 80 years (n=240) and those 80 years old or older (n=123). We compared patient demographics, disease characteristics, surgical outcomes, and postoperative complications based on these groups.

Results: The older group had a higher proportion of patients with a Charlson Comorbidity Index ≥5 (p<0.001) and the American Society of Anesthesiologist (ASA) physical status classification ≥3 (p<0.001). In addition, the older group had longer postoperative hospital stays than younger group (7.5 ± 6.1 days vs. 6.2 ± 3.9 days, p=0.013). However, there were no significant differences between groups according to the postoperative complications (13.8% vs. 20.3%, p=0.130). According to multivariate analysis, the risk factors for postoperative complications were Charlson Comorbidity Index ≥5 (odds ratio [OR]=2.307; 95% confidence interval [CI], 1.162–4.579; p=0.017) and operative time >2 hours (OR=3.204; 95% CI, 1.802–5.695; p<0.001).

Conclusion: In patients with Charlson Comorbidity Index <5 and operation time <2 hours, LCBDE with stone removal can be considered safe for the oldest old patients.

Key Words: Laparoscopy, Choledocholithiasis, Aged, Postoperative complications, Multivariate analysis

INTRODUCTION

Common bile duct (CBD) stones occur in 10%–15% of patients with gallstone disease. Up to approximately 4% of patients have symptoms related to CBD stones during the first year after cholecystectomy. The appropriate treatment for CBD stones remains controversial.

Endoscopic retrograde cholangiopancreatography (ERCP) with endoscopic sphincterotomy (EST) plus laparoscopic cholecystectomy (LC) as a two-stage treatment is reportedly a safer treatment method than one-stage treatment. Laparoscopic common bile duct exploration (LCBDE) with stone removal plus LC, a one-stage treatment, has been widely used in the treatment of bile duct stones since the 1980s with the development of laparoscopic surgery. With the recent development of surgical devices and technology, many centers and surgeons have tried to practice LCBDE, showing success in approximately 90% of patients. However, persistent and recurrent stones have been reported in 10% of patients. Previous studies reported no significant differences in the success and complication rates between one- and two-stage treatments. However, one-stage treatment allows shorter hospital stays, requires fewer procedures, and is cost-effective. Thus, the recent results of one-stage treatment are comparable or superior to those of two-stage treatment.

Life expectancy is gradually increasing with current trends in economic development and health promotion.
data from the National Statistical Office of South Korea, the population aged 65 years or older increased from 5.9% of the total population in 1995 to 15.7% of the total population in 2020. Life expectancy has also increased, reaching 82.3 years in 2016. As a result, the number of older patients undergoing surgical procedures is increasing. These patients often have chronic diseases such as high blood pressure, diabetes, heart disease, or cerebral infarction; therefore, we anticipate additional postoperative risks compared to those in younger patients. Recent studies on surgery in older patients showed that risk stratification with comorbidity better predicts postoperative outcomes than age. In contrast, Liu et al. reported that patients > 70 years of age had a higher preoperative risk for CBD stones, although the results were comparable between one- and two-stage treatments. However, no studies have compared the outcomes of LCBDE in patients aged ≥ 80 years.

Therefore, this retrospective single-center study investigated LCBDE outcomes in the oldest old patients to identify the factors associated with increased complications.

**MATERIALS AND METHODS**

**Patients**

Overall, 363 patients with CBD stones underwent LCBDE at a single center between January 2003 and October 2020. CBD stones were diagnosed using abdominal ultrasonography, abdominal computed tomography, magnetic resonance cholangiopancreatography (MRCP), and ERCP. We enrolled patients who underwent LCBDE plus LC without attempting ERCP, attempted preoperative ERCP but failed, and underwent only LCBDE because they had previously undergone LC. We also excluded patients who underwent LCBDE in combination with other surgeries. If LCBDE was repeated for stone recurrence after LCBDE, only the first surgery was included in the study. We retrospectively reviewed the medical records for the following data: (1) clinical characteristics such as age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, medical history including surgeries, Charlson Comorbidity Index, diameter of CBD, number of CBD stones, bilirubin level, preoperative intensive care unit (ICU) management history, and cause of ERCP failure, (2) surgical outcomes including clearance of CBD stones, CBD stone recurrence, operation time, estimated blood loss, open conversion, and postoperative hospital stays, and (3) postoperative complications graded according to the Clavien-Dindo classification. We retrospectively investigated the postoperative complications using patient medical records, including bile leakage, wound infection, pancreatitis, dysuria, pneumonia, and urinary tract infection (UTI), and Clavien-Dindo classifications of grade III or higher were classified as major complications. This study was approved by the Institutional Review Board of Konyang University Hospital (No. 2021-03-007). The informed consent was waived. This study complied with the ethical guidelines for authorship and publishing in the Annals of Geriatric Medicine and Research.

**LCBDE Technique**

Surgery was performed as previously described. The patients were placed in the supine position under general anesthesia. LCBDE was performed using a four-port method. A 12-mm port was used at the umbilicus for the camera, a 10-mm port was placed at the midclavicular line just above the nearest point from the CBD for the choledochoscope or fan retractor, and 5-mm ports were placed at the epigastric area and right anterior axillary line close to the right subcostal area. First, we performed cholecystectomy using a three-port method for the LC. We then performed a choledochotomy approximately 1 cm in length in the center of the anterior or wall of the CBD using endo scissors. A flexible choledochoscope (Olympus, Tokyo, Japan) was inserted through this incision and any CBD stones were retrieved using saline irrigation, a wire basket (Olympus), and lithotripsy with a laser (Olympus). Subsequently, total stone removal was confirmed using a flexible choledochoscope from the distal CBD to the right and left hepatic ducts. The CBD incision was repaired by T-tube insertion, internal drainage, or primary suturing using polydioxanone 4-0 or 5-0 sutures (Ethicon Inc., Somerville, NJ, USA).

**Statistical Analysis**

Data are expressed as mean ± standard deviation. The patients were divided into two groups based on age: < 80 years (group A) and ≥ 80 years (group B). For statistical analyses, comparisons between groups were performed using Student t-tests for continuous data and chi-square or Fisher exact tests for categorical data. Logistic regression analysis was used to identify the factors associated with the risk of postoperative complications following LCBDE. Data were analyzed using PASW Statistics for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA). Differences were considered statistically significant at p < 0.05.

**RESULTS**

**Patient Demographics and Disease Characteristics**

A total of 363 patients underwent LCBDE during the study period, including 240 patients < 80 years (group A; mean age 65.6 ± 12.8 years) and 123 patients ≥ 80 years of age (group B; mean age 83.9 ± 3.5 years).

We compared the demographic data and disease characteristics
between groups A and B (Table 1). The BMI was lower in group B than that in group A (21.7 ± 3.2 kg/m\(^2\) vs. 23.0 ± 3.6 kg/m\(^2\), p = 0.001). Compared to group A, group B had higher rates of Charlson Comorbidity Index ≥ 5 (43.1% vs. 7.1%, p < 0.001), ASA physical status classification > grade III (54.5% vs. 23.3%, p < 0.001) and a higher proportion of patients with multiple stones (69.1% vs. 57.1%, p = 0.031). The rates of myocardial infarction and chronic renal disease were significantly higher in group B—13.0% (p = 0.014) and 3.3% (p = 0.047), respectively—than in group A. However, the other demographic and disease characteristics did not differ significantly between the two groups, including sex ratio, previous abdominal surgery, previous gastrectomy, CBD diameter, maximum stone size, hypertension, diabetes, chronic obstructive pulmonary disease, cerebrovascular accident, dementia, liver disease, and preoperative ICU management (Table 1).

**Surgical Outcomes**

We compared surgical outcomes between groups A and B (Table 2). The methods of CBD repair (primary repair, internal drainage, or T-tube insertion) did not differ significantly (p = 0.420). While the operation time tended to be shorter in group B, the difference was not statistically significant (109.2 ± 45.1 minutes vs. 120.2 ± 58.0 minutes, p = 0.066). The estimated blood loss and open conversion rates did not differ significantly (p = 0.0268 and p = 1.000, respectively). The CBD stone clearance rate also did not differ significantly between the two groups (93.5% vs. 97.1%, p = 0.160). However, the postoperative hospital stay was significantly longer in group B compared to that in group A (7.6 ± 6.1 days vs. 6.2 ± 3.9 days, p = 0.013).

**Postoperative Complications**

The total postoperative complications did not differ significantly between the groups (13.8% in group A vs. 20.3% in group B, p = 0.130) (Table 3). One case of minor bile leakage and wound infection occurred in each group. The Clavien-Dindo classification grade II cases, including dysuria, hemobilia, ileus, intra-abdominal hematoma, pancreatitis, pneumonia, and UTI, also did not differ significantly between the groups. In addition, the rate of major

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**Table 1.** Comparison of patient demographics and disease characteristics between younger than 80 years old (A) and the 80 years old and older group (B)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n = 363)</th>
<th>Group A (n = 240)</th>
<th>Group B (n = 123)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>71.8 ± 13.7</td>
<td>65.6 ± 12.8</td>
<td>83.9 ± 3.5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Sex, female</td>
<td>186 (51.2)</td>
<td>118 (49.2)</td>
<td>68 (55.3)</td>
<td>0.318</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>22.6 ± 3.6</td>
<td>23.0 ± 3.6</td>
<td>21.7 ± 3.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Charlson Comorbidity Index ≥ 5</td>
<td>70 (19.3)</td>
<td>17 (7.1)</td>
<td>53 (43.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ASA PS classification ≥ grade III</td>
<td>123 (33.9)</td>
<td>56 (23.3)</td>
<td>67 (54.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Previous abdominal surgery</td>
<td>109 (30.0)</td>
<td>67 (27.9)</td>
<td>42 (34.1)</td>
<td>0.228</td>
</tr>
<tr>
<td>Previous gastrectomy</td>
<td>61 (16.8)</td>
<td>35 (14.6)</td>
<td>26 (21.1)</td>
<td>0.138</td>
</tr>
<tr>
<td>CBD diameter (mm)</td>
<td>13.7 ± 5.3</td>
<td>13.5 ± 5.3</td>
<td>14.3 ± 5.1</td>
<td>0.134</td>
</tr>
<tr>
<td>Number of stone</td>
<td></td>
<td></td>
<td></td>
<td>0.031</td>
</tr>
<tr>
<td>Single</td>
<td>141 (38.8)</td>
<td>103 (42.9)</td>
<td>38 (30.9)</td>
<td></td>
</tr>
<tr>
<td>Multiple</td>
<td>222 (61.2)</td>
<td>137 (57.1)</td>
<td>85 (69.1)</td>
<td></td>
</tr>
<tr>
<td>Maximum stone size (mm)</td>
<td>12.3 ± 6.5</td>
<td>12.2 ± 6.3</td>
<td>14.2 ± 6.9</td>
<td>0.749</td>
</tr>
<tr>
<td>Initial total bilirubin (mg/dL)</td>
<td>2.9 ± 3.1</td>
<td>3.1 ± 3.4</td>
<td>2.5 ± 2.3</td>
<td>0.044</td>
</tr>
<tr>
<td>Past history</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>157 (43.3)</td>
<td>96 (40.0)</td>
<td>61 (49.6)</td>
<td>0.093</td>
</tr>
<tr>
<td>DM</td>
<td>69 (19.0)</td>
<td>50 (20.8)</td>
<td>19 (15.4)</td>
<td>0.259</td>
</tr>
<tr>
<td>COPD</td>
<td>38 (10.5)</td>
<td>23 (9.6)</td>
<td>15 (12.2)</td>
<td>0.471</td>
</tr>
<tr>
<td>MI</td>
<td>29 (8.0)</td>
<td>13 (5.4)</td>
<td>16 (13.0)</td>
<td>0.014</td>
</tr>
<tr>
<td>CRF</td>
<td>5 (1.4)</td>
<td>1 (0.4)</td>
<td>4 (3.3)</td>
<td>0.047</td>
</tr>
<tr>
<td>CVA</td>
<td>38 (10.5)</td>
<td>25 (10.4)</td>
<td>13 (10.6)</td>
<td>1.000</td>
</tr>
<tr>
<td>Dementia</td>
<td>14 (3.9)</td>
<td>8 (3.3)</td>
<td>6 (4.9)</td>
<td>0.566</td>
</tr>
<tr>
<td>Liver disease</td>
<td>10 (2.8)</td>
<td>7 (2.9)</td>
<td>2 (1.6)</td>
<td>0.724</td>
</tr>
<tr>
<td>Preop ICU management</td>
<td>10 (2.8)</td>
<td>6 (2.5)</td>
<td>4 (3.3)</td>
<td>0.739</td>
</tr>
</tbody>
</table>

Values are presented as mean ± standard deviation or number (%). BMI, body mass index; ASA PS, American Society of Anesthesiologists physical status; CBD, common bile duct; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; CRF, chronic renal disease; CVA, cerebrovascular accident; ICU, intensive care unit.
complications also did not differ significantly between groups (8.9% vs. 6.7%, p = 0.526) (Table 2). Major bile leakage (Clavien-Dindo classification grade IIIa) occurred in seven cases (5.7%) in group B and in five cases (2.1%) in group A, while acute renal failure (Clavien-Dindo grade IV) occurred in one patient in group B.

### Risk Factors for Postoperative Complications

The influence of sex, age, ASA score, surgical history, CBD diameter, stone size, stone number, preoperative bilirubin level, Charlson Comorbidity Index, and preoperative ICU management of postoperative complications after LCBDE are summarized in Table 4. A multivariate regression model included factors associated with overall postoperative complications at a p < 0.15 significance level.
as determined by univariate analysis. In univariate analysis, age ≥ 80 years was not an independent factor for postoperative complications (odds ratio [OR] = 1.60; 95% confidence interval [CI], 0.903–2.837; p = 0.837). In multiple logistic regression analysis, Charlson Comorbidity Index ≥ 5 (OR = 2.307; 95% CI, 1.162–4.579; p = 0.017) and operation time ≥ 2 hours (OR = 3.204; 95% CI, 1.802–5.695, p < 0.001) were independent factors associated with postoperative complications.

### Causes of Endoscopic Procedure Failure

The causes of endoscopic procedure failure are listed in **Table 5**. ERCP cannulation and stone removal failure did not differ significantly between the two groups (p = 0.874). Among patients who did not undergo ERCP, significantly more cases received one-stage treatment in group A (10.4% vs. 2.4%, p = 0.006), while group B had a higher proportion of patients at high risk for ERCP (27.6% vs. 17.1%, p = 0.021).

### DISCUSSION

As the number of older patients increases in an aging society, several studies have demonstrated the safety and feasibility of LCBDE in patients aged ≥ 70 years. However, no previous study has investigated the safety of LCBDE in patients aged ≥ 80 years. There-
fore, this study aimed to determine the safety of LCBDE and investigate the risk factors for postoperative complications by comparing the patient demographics, LCBDE results, and clinical factors affecting surgical outcomes between patients aged ≥ 80 years and < 80 years.

Choledocholithiasis is one of the most common causes of acute abdominal pain; moreover, the proportion of older patients with choledocholithiasis is increasing. While LC is a basic treatment for gallstones, various methods for CBD stones are used in clinical practice. One-stage treatment includes LCBDE with stone removal plus LC, while two-stage treatment includes ERCP with EST or endoscopic retrograde pancreatic drainage plus LC. Despite these various treatment methods, an accurate consensus on the treatment of choledocholithiasis has not been established.

The results of a meta-analysis showed no differences between one- and two-stage treatment in overall morbidity (OR = 0.91; 95% CI, 0.66–0.24; p = 0.54) or mortality (OR = 0.36; 95% CI, 0.08–1.58; p = 0.18). The CBD stone clearance rate was higher in the two-stage treatment compared to that in the one-stage treatment (OR = 0.63; 95% CI, 1.16–2.28; p = 0.005), while the hospital stay was shorter for one-stage treatment (mean difference, -2.46 days; 95% CI, -3.67 to -1.24; p < 0.0001). A meta-analysis reported a clearance rate of CBD stones after LCBDE of approximately 89.5%–100%. In addition, Hua et al. reported a stone clearance rate of 99%. These results are similar to the stone clearance rate of 95.9% in the present study, with no difference between groups A and B (97.1% vs. 93.5%, p = 0.160).

ERCP plus LC is a two-stage treatment; in these cases, LC can be a relatively simple surgery after endoscopic treatment. However, severe complications such as hemorrhage, pancreatitis, and duodenal injury can occur following ERCP and EST. Recently, Hua et al. reported a significantly greater number of patients with severe complications after two-stage treatment (Clavien-Dindo classification, > grade III: 10.7% vs. 0%, p = 0.004); however, the overall morbidity was comparable between the one- and two-stage treatment groups (23.8% vs. 22.6%, p = 1.000). Therefore, one-stage treatment may be necessary in certain cases, such as those conducted in high-risk patients with ERCP, those surgeries conducted by inexperienced endoscopists, or those conducted among patients who do not agree to undergo endoscopic treatment. However, LCBDE is more difficult than LC; it must be performed by an experienced surgeon, and the operation time is longer than that of LC.

Several studies have reported a higher incidence of postoperative complications in older patients. Kim et al. observed that as frailty increased, postoperative mortality (OR = 2.05, p < 0.001) and hospital stay (OR = 1.42, p = 0.001) increased after general surgery, while the risk of complications did not. Another study on postoperative complications in older patients > 80 years reported that preoperative ASA physical status classification ≥ 3 and longer operation time were dependent factors related to severe postoperative complications requiring ICU or transfer for complication management. Similar to our results showed a prolonged hospital stay in group B than in group A (7.5 ± 6.1 days vs. 6.2 ± 3.9 days, p = 0.013). However, the rates of postoperative complications (20.3% vs. 13.8%, p = 0.130) or major complications (8.9% vs. 6.7%, p = 0.526) did not differ significantly between the groups. We also identified risk factors for postoperative complications after LCBDE. Liu et al. showed that surgeon experience was the most important factor for bile leakage (OR = 4.228; 95% CI, 1.300–13.438; p = 0.03). Hua et al. observed a significantly higher rate of bile leakage for slender CBD (< 8 mm vs. ≥ 8 mm: risk ratio = 9.87; 95% CI, 1.89–51.6; p = 0.007). In this study, the bile leakage rates did not differ between the two groups (5.7% vs. 2.1%, p = 0.116). However, multivariate analysis in the present study showed that Charlson Comorbidity Index ≥ 5 (OR = 2.307; 95% CI, 1.162–4.579; p = 0.017) and operation time ≥ 2 hours (OR = 3.204; 95% CI, 1.802–5.695; p < 0.001) were important risk factors for postoperative complications, while age ≥ 80 years was not (OR = 1.600; 95% CI, 0.903–2.837; p = 0.037). These results suggested that surgeons should carefully evaluate comorbidities and be cognizant of the operation time when operating on older patients.

We also investigated the differences in the causes of endoscopic failure according to age group (Table 5). The most common cause of ERCP failure was altered surgical anatomy (69/363; 19.0%). More patients were at high risk for ERCP in group B than in group A, and older patients tended to receive one-stage treatment. In addition, poor cooperation with ERCP was more common in group B (17.1%). A study comparing the results of LCBDE without ERCP and after failure of endoscopic stone removal reported no significant differences in the length of hospital stay, operation time, or number of complications. Thus, one-stage treatment without attempting ERCP may be non-inferior. Analysis of the group of patients who did not undergo ERCP in this study showed that one-stage treatment was more common in younger patients (10.4% vs. 2.4%, p = 0.006), likely due to avoiding ERCP because post-ERCP pancreatitis is more likely to occur in younger patients. Previous studies have demonstrated that primary repair is safe and should be an alternative to T-tube drainage and internal drainage during LCBDE.
performed cholecotomty repair using the continuous primary repair method (198/363; 54.5%). The CBD drainage rates, such as T-tube or internal drainage, did not differ significantly between the two groups (p = 0.420).

This study had some limitations. First, since this was a single-institution retrospective study, the generalizability of the results to other populations is limited. However, it is important to note the safety of LCBDE in the oldest old patients aged ≥ 80 years. Second, the number of patients in the older group was only about half that in the younger group; therefore, the risk of bias was high. Finally, although an operation time of 2 hours or more was an independent risk factor for postoperative complications, there is a limit to applying these results in clinical practice as the operation time cannot be precisely predicted before surgery. However, these findings provide a basis for surgeons to be aware of operative time. Further research is needed to develop a method to predict operative time before surgery.

In conclusion, LCBDE can be safely performed in the oldest old patients aged ≥ 80 years. However, LCBDE should be carefully considered in patients with several comorbid diseases and those expected to have longer operative times.

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CONFLICT OF INTEREST
The researchers claim no conflicts of interest.

FUNDING
None.

AUTHOR CONTRIBUTION
Conceptualization, JIM; Data curation, HJY, JIM; Investigation and methodology, HJY, JIM, SJL, ISC; Supervision, JIM, SJL, ISC; Writing-original draft, HJY, JIM; Writing-review & editing, HJY, JIM, SJL, ISC.

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INTRODUCTION

The prevalence of overt and subclinical hypothyroidism and metabolic syndrome (MS) is increasing worldwide owing to aging and increasing obesity. Thirty percent of the individuals treated with levothyroxine (LT4) are > 70 years of age.\(^1\) However, elevated thyroid-stimulating hormone (TSH) levels caused by aging may be due to the adaptation of the thyroid axis or a deficit of thyroid hormones. Therefore, treatment recommendations should be specific to this particular age group, and the treatment effectiveness should be monitored.

MS is characterized by a combination of insulin resistance (IR), dyslipidemia, arterial hypertension (HT), and central obesity. Body mass index (BMI) is widely used to assess the presence of geriatric syndromes such as sarcopenia and malnutrition.\(^2\)\(^,\)\(^3\) Therefore, we used BMI for MS diagnosis in this study as it is more practical in geriatric medicine and is included in the World Health Organization (WHO) and American Association of Clinical (AACE) criteria.\(^4\)\(^,\)\(^5\) Both MS and hypothyroidism promote atherosclerosis. Therefore, the cardiovascular (CV) risk increases in the presence of both conditions. The Framingham Risk Score calculates the CV risk and can predict the occurrence of CV events.\(^6\)\(^,\)\(^7\) LT4 replacement therapy may reduce the risk of MS and atherosclerosis by decreas-

Predictability of Metabolic Syndrome Diagnosed by Body Mass Index for Cardiovascular Risk in Older Patients Treated with Levothyroxine

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Division of Geriatrics, Department of Internal Medicine, Faculty of Medicine, Ege University, Izmir, Turkey

Background: We investigated the prevalence and metabolic features of two definitions of metabolic syndrome (MS) between older patients with chronic thyroiditis treated with levothyroxine (LT4) and controls. We also assessed the ability of both criteria to predict cardiovascular (CV) risk. Methods: This cross-sectional, retrospective study included individuals aged ≥60 years who attended a geriatric outpatient clinic between January 2015 and December 2018. The LT4 treatment group was classified as having high or low CV risk based on the Framingham score. Results: This study enrolled 111 patients with chronic thyroiditis treated with LT4 and 131 patients without thyroid disease as the control group. The prevalence of MS according to the World Health Organization (WHO) criteria and American Association of Clinical (AACE) criteria was similar in the LT4 treatment (21.6% and 26.1%, respectively) and the control (30.5% and 34.4%, respectively) groups (p>0.05). While the prevalence of MS and CV risk did not differ significantly between the control and LT4 treatment groups, the prevalence of MS with both definitions was higher among individuals with high CV risk in the LT4 treatment group (p<0.05). For the prediction of CV risk, the sensitivity and specificity of the AACE criteria were higher than those of the WHO criteria in the LT4 treatment group. Conclusions: The prevalence of MS in euthyroid patients treated with LT4 was similar to that of patients without thyroid disease. When the LT4 treatment group was classified based on CV risk, MS was more common in those with a high CV risk.

Key Words: Hypothyroidism, Metabolic syndrome, Body mass index, Heart disease risk factors, Aged, Thyroxine

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ing cholesterol levels. However, literature on the prevalence of MS in older patients as assessed using different criteria is scarce, and the predictability of both MS definitions for CV risk has not been studied in older patients treated with LT4. Therefore, we investigated the prevalence and metabolic features of the two definitions of MS in older patients with chronic thyroiditis treated with LT4 and compared them with controls without chronic thyroiditis. We also investigated the ability of both criteria to identify individuals with LT4 treatment at a high CV risk based on the Framingham Risk Score.

MATERIALS AND METHODS

Subjects
This observational, cross-sectional, retrospective study assessed 1396 patients (589 and 807 patients with and without thyroid disease, respectively) who attended the geriatric outpatient clinic at the Medical Faculty Hospital between January 2015 and December 2018. Among patients with thyroid-related disorders, this study selected individuals diagnosed with chronic thyroiditis confirmed by thyroid ultrasonography and/or anti-thyroid peroxidase (anti-TPO) antibodies, as well as euthyroid patients treated with LT4 for at least 6 weeks. The exclusion criteria for the LT4 treatment group, inclusion criteria for the control group, and number of patients are shown in Fig. 1. Finally, this study enrolled 111 of 589 patients who met the inclusion criteria. Of the 807 patients, we enrolled 131 patients who did not have thyroid diseases in the sex-matched control group. Overall, this study enrolled a total of 242 patients. Their baseline demographic information, such as age; sex; physical data, including body height and body weight; and systolic and diastolic blood pressure, were recorded. Histories of smoking status, diabetes mellitus (DM), dyslipidemia, HT, and laboratory measurements were obtained from electronic medical records.

The study was conducted in accordance with the ethical principles stated in the “Declaration of Helsinki” and approved by the Ege University Human Research Ethics Committee along with the permission for the use of patient data for publication purposes (Reference number/Protocol No. 18-11.1T/1). Informed consent was not obtained from participants as this was a retrospective chart review. This study complied the ethical guidelines for authorship and publishing in the Annals of Geriatric Medicine and Research.

Laboratory Measurements
Hospital laboratory values measured in the same month were recorded, including levels of serum TG (mg/dL), total cholesterol (TC; mg/dL), high-density lipoprotein cholesterol (HDL-C; mg/dL), FG (mg/dL), glycated hemoglobin (HbA1c; %, mmol/mol), anti-TPO antibody (IU/mL), TSH (mIU/L), and FT4 (ng/dL). All measurements were performed using routine laboratory methods.
Definitions

The diagnostic criteria for MS are shown in Table 1. Given the type of research design, our ability to evaluate waist circumference (WC) and perform oral glucose tolerance tests (OGTTs) was low. Both the waist-to-hip ratio and OGTT results were not available in our study. Therefore, the diagnosis of MS according to WHO criteria was limited to the use of BMI > 30 kg/m², impaired fasting glucose (IFG), or type 2 DM based on FG and HbA1c levels only, as shown in Table 1.

IFG was defined as a glucose concentration ≥ 110 mg/dL (6.1 mmol/L) according to the WHO criteria. BMI was calculated by dividing weight in kilograms by the square of height in meters. The study participants were classified into three categories according to their BMI: normal weight (≥ 24 kg/m²), overweight (> 24 and < 30 kg/m²), and obese (> 30 kg/m²). IR was calculated using the Homeostatic Model Assessment for IR (HOMA-IR) and was defined as a HOMA index > 2.5.

CV risk was calculated using the Framingham Risk Score. Patient sex, age, TC level, HDL-C level, use of medication for HT, known vascular disease, DM, systolic blood pressure, and smoking status were used to calculate the risk value of CV. A Framingham Risk Score ≥ 20% or having a diagnosis of DM was chosen as the threshold for high CV risk.

Statistical Analysis

The results are expressed as mean ± standard deviation and parenteral minimum and maximum values, unless otherwise indicated. The prevalence of various metabolic and CV risk factors for different MS definitions was calculated using 2 × 2 contingency tables. Logistic regression analysis was performed to determine which MS criteria best predicted CV risk. Sensitivity, specificity, and area under the receiver operating characteristic (ROC) curves were used to evaluate the ability of different MS diagnostic criteria to correctly identify individuals with a high risk of CV. Two-sided p-values < 0.05 were considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics for Windows (version 25.0; IBM, Armonk, NY, USA).

Sample Size Calculation

We conducted a post hoc power analysis in G*Power 3.1 to determine whether the study sample size was adequate. With a sample size of 111 for the prediction of CV risk, an effect size of 0.7, and a margin of error of 0.05, the calculated representation power was calculated as 0.96.

RESULTS

This study enrolled 242 patients, including 111 patients treated with LT4 (the LT4 treatment group) and 131 patients without thyroid disease (the control group). The sex distribution did not differ significantly between the LT4 treatment and control groups. Patients in the LT4 treatment group were younger than those in the control group. In addition, the LT4 treatment group had a lower BMI than that in the control group. The anti-TPO antibodies and levothyroxine replacement doses were 370.9 ± 42.8 IU/mL (10–1360) and 68.6 ± 31.8 μg (12.5–200), respectively, in the LT4

---

Table 1. The criteria selected for clinical diagnosis of metabolic syndrome

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Required</td>
<td>IGT, IFG, T2DM or</td>
<td>IGT or IFG</td>
</tr>
<tr>
<td>Low insulin sensitivity†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>And ≥ 2 of abnormalities with</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>BMI &gt; 30 kg/m² and/or</td>
<td>BMI ≥ 25 kg/m² or</td>
</tr>
<tr>
<td></td>
<td>Waist-to-hip ratio§</td>
<td>Waist ≥ 102 cm (male); ≥ 88 cm (female)§</td>
</tr>
<tr>
<td>Lipids§</td>
<td>TG ≥ 150 mg/dl (1.7 mmol/L) and/or</td>
<td>TG ≥ 150 mg/dl (1.7 mmol/L) and</td>
</tr>
<tr>
<td></td>
<td>HDL-C &lt; 35 mg/dl (0.9 mmol/L) (male); &lt; 40 mg/dl (1.0 mmol/L) (female)</td>
<td>HDL-C &lt; 40 mg/dl (1.0 mmol/L) (male); &lt; 50 mg/dl (1.3 mmol/L) (female)</td>
</tr>
<tr>
<td>Blood pressure§</td>
<td>≥ 140/90 mmHg</td>
<td>≥ 130/85 mmHg</td>
</tr>
<tr>
<td>Other</td>
<td>Microalbuminuria</td>
<td>Other features of IR†</td>
</tr>
</tbody>
</table>

WHO, World Health Organization; AACE, American Association of Clinical Endocrinologists; T2DM, type 2 diabetes mellitus; WC, waist circumference; TG, triglycerides; IGT, impaired glucose tolerance; IFG, impaired fasting glucose; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; IR, insulin resistance.

†Lipids includes patients on drugs for elevated triglycerides for elevated triglycerides.

§Blood pressure includes taking antihypertensive medication.

‡Other features of IR: family history of T2DM, sedentary lifestyle, advancing age, and ethnic groups susceptible to T2DM.

†Data for LT4 treatment group.

The criteria is not available in this study.
treatment group. Forty-eight percent of patients in the LT4 treatment group had thyroid nodules. Thirty-five percent and 28.8% of the LT4 treatment group were on drug treatment for hyperlipidemia and DM, respectively, while nearly half of the participants were on drug treatment for HT (49.5%). The prevalence of CV risk and MS according to the WHO and AACE criteria were similar in both groups (p > 0.05). The characteristics of the patients according to the presence of thyroid disease are shown in Table 2.

We classified the LT4 treatment group into two: low CV risk (71 patients, 64%) and high CV risk (40 patients, 36%). The mean age and BMI were similar between the groups (65.7 ± 5.7 vs. 68.7 ± 6.8, p = 0.12, and 28 ± 4.4 vs. 29.3 ± 4.9, p = 0.365, respectively). As regards laboratory test results, only the mean HbA1c and FG levels were higher in the high CV risk group compared to those in the low CV risk group (p < 0.001). A similar situation was observed for the IFG (p < 0.001). However, the same relationship was not observed for IR (p > 0.05). The diagnosis of MS defined by WHO and AACE was higher in the LT4 treatment group with high CV risk than in those with low CV risk (p < 0.001). BMI and TG, the MS criteria that were not included among the CV risk criteria, were not identified as significantly associated with the prediction of CV risk in univariate logistic regression analysis. The characteristics of the LT4 treatment group according to CV risk are shown in Table 3.

All individuals in the LT4 treatment group with MS according to the WHO criteria were also diagnosed with MS, as defined by AACE in the LT4 treatment group. Hypertriglyceridemia and overweight status were extremely common components in both MS criteria, whereas the occurrence of low HDL-C was low in both criteria. HT is more prevalent in patients with MS according to the WHO Health Organization criteria. The prevalence of the MS components is presented in Table 4.

The sensitivity and specificity of the AACE criteria were higher than those of the WHO criteria. The ability of both criteria to identify participants with high CV risk is shown in Table 5.

### DISCUSSION

In clinical practice, thyroid dysfunction is common among older individuals. Thyroid metabolism has a bidirectional relationship with metabolic syndrome. However, the prevalence of MS is low among euthyroid patients with or without LT4 treatment. We observed no significant difference in the prevalence of MS and CV risk between the LT4 treatment and control groups. However, the prevalence of MS was significantly higher among individuals with high CV risk in the LT4 treatment group. To predict CV risk, the

### Table 2. Characteristics of the study population

<table>
<thead>
<tr>
<th>Variable</th>
<th>LT4 treatment group (n = 111)</th>
<th>Control group (n = 131)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>66.8 ± 6.2 (60–91)</td>
<td>70.8 ± 5.7 (64–91)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Sex, female</td>
<td>99 (89.2)</td>
<td>105 (80.2)</td>
<td>0.540</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.5 ± 4.6 (18–48)</td>
<td>30.5 ± 4.4 (16.7–39)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Body composition</td>
<td></td>
<td></td>
<td>0.001*</td>
</tr>
<tr>
<td>Normal</td>
<td>19 (17.1)</td>
<td>10 (7.6)</td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>51 (45.9)</td>
<td>43 (32.8)</td>
<td></td>
</tr>
<tr>
<td>Obese</td>
<td>41 (36.9)</td>
<td>78 (59.5)</td>
<td></td>
</tr>
<tr>
<td>TSH level (mIU/L)</td>
<td>2.2 ± 1.2 (0.5–4.9)</td>
<td>1.9 ± 0.9 (0.5–5)</td>
<td>0.221</td>
</tr>
<tr>
<td>FT4 level (μg/dL)</td>
<td>1.2 ± 0.2 (0.8–2.2)</td>
<td>1.2 ± 0.2 (0.9–1.73)</td>
<td>0.799</td>
</tr>
<tr>
<td>Fasting glucose level (mg/dL)</td>
<td>102.7 ± 23.9 (73–234)</td>
<td>109.2 ± 28.4 (67–255)</td>
<td>0.142</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.7 ± 0.9 (4.6–11.2)</td>
<td>6.0 ± 0.9 (4.6–10.8)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Triglycerides level (mg/dL)</td>
<td>142.9 ± 64.9 (43–383)</td>
<td>135.3 ± 68.4 (43–420)</td>
<td>0.152</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>32 (28.8)</td>
<td>42 (32.1)</td>
<td>0.587</td>
</tr>
<tr>
<td>Hypertension</td>
<td>55 (49.5)</td>
<td>91 (69.5)</td>
<td>0.002*</td>
</tr>
<tr>
<td>Hyperlipidemia treatment</td>
<td>39 (35.1)</td>
<td>15 (11.5)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>IFG</td>
<td>37 (33.3)</td>
<td>52 (39.7)</td>
<td>0.306</td>
</tr>
<tr>
<td>WHO criteria of MS</td>
<td>24 (21.6)</td>
<td>40 (30.5)</td>
<td>0.117</td>
</tr>
<tr>
<td>AACE criteria of MS</td>
<td>29 (26.1)</td>
<td>45 (34.4)</td>
<td>0.166</td>
</tr>
<tr>
<td>CV risk</td>
<td>40 (36)</td>
<td>42 (32.1)</td>
<td>0.515</td>
</tr>
</tbody>
</table>

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

LT4, levothyroxine; BMI, body mass index; TSH, thyroid stimulating hormone; FT4, free thyroxine; IFG, impaired fasting glucose; WHO, World Health Organization; AACE, American Association of Clinical Endocrinologists; MS, metabolic syndrome; CV, cardiovascular.

*p<0.05.
Table 3. The characteristics of the LT4 treatment group according to CV risk

<table>
<thead>
<tr>
<th>Variable</th>
<th>Low CV risk (n = 71)</th>
<th>High CV risk (n = 40)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>28.0 ± 4.4</td>
<td>29.3 ± 4.9</td>
<td>0.365</td>
</tr>
<tr>
<td>Body composition</td>
<td></td>
<td></td>
<td>0.327</td>
</tr>
<tr>
<td>Normal</td>
<td>15 (78.9)</td>
<td>4 (21.1)</td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>31 (60.8)</td>
<td>20 (39.2)</td>
<td></td>
</tr>
<tr>
<td>Obese</td>
<td>25 (61.0)</td>
<td>16 (39.0)</td>
<td></td>
</tr>
<tr>
<td>TSH level (mIU/L)</td>
<td>2.1 ± 1.2</td>
<td>2.3 ± 1.1</td>
<td>0.293</td>
</tr>
<tr>
<td>FT4 level (μg/dL)</td>
<td>1.2 ± 0.2</td>
<td>1.28 ± 0.2</td>
<td>0.169</td>
</tr>
<tr>
<td>Anti-TPO antibodies (IU/mL)</td>
<td>406.1 ± 476.7</td>
<td>308.5 ± 400.4</td>
<td>0.341</td>
</tr>
<tr>
<td>Levothyroxine replacement dose (μg)</td>
<td>69.6 ± 31.6</td>
<td>66.9 ± 32.5</td>
<td>0.466</td>
</tr>
<tr>
<td>Fasting glucose level (mg/dL)</td>
<td>94.8 ± 8.4</td>
<td>116.8 ± 34.0</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.4 ± 0.3</td>
<td>6.3 ± 1.3</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>HbA1c (mmol/mol)</td>
<td>36</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Triglycerides level (mg/dL)</td>
<td>140.0 ± 63.0</td>
<td>148.2 ± 68.8</td>
<td>0.539</td>
</tr>
<tr>
<td>IFG</td>
<td>4 (5.6)</td>
<td>33 (82.5)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>High triglycerides</td>
<td>34 (47.8)</td>
<td>12 (33.3)</td>
<td>0.660</td>
</tr>
<tr>
<td>WHO criteria of MS</td>
<td>4 (5.6)</td>
<td>20 (50.0)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>AACE criteria of MS</td>
<td>4 (5.6)</td>
<td>25 (62.5)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>HOMA-IR index ≥ 2.5</td>
<td>31 (43.7)</td>
<td>24 (60.0)</td>
<td>0.098</td>
</tr>
</tbody>
</table>

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

CV risk was calculated by the Framingham Risk Score.

CV, cardiovascular; BMI, body mass index; TSH, thyroid stimulating hormone; FT4, free thyroxine; TPO, thyroid peroxidase; IFG, impaired fasting glucose; WHO, World Health Organization; AACE, American Association of Clinical Endocrinologists; MS, metabolic syndrome; HOMA-IR, homeostatic model assessment for insulin resistance.

*p<0.05.

Table 4. Prevalence of MS components among LT4 treatment group with MS

<table>
<thead>
<tr>
<th></th>
<th>MS Positive criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HT&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>WHO (1998)</td>
<td>24 (21.6)</td>
</tr>
<tr>
<td>AACE (2003)</td>
<td>29 (26.1)</td>
</tr>
</tbody>
</table>

Values are presented as number (%).

MS, metabolic syndrome; HT, hypertension; HDL-C, high density lipoprotein cholesterol; TG, triglycerides; IR, insulin resistance; T2DM, type 2 diabetes mellitus; WHO, World Health Organization; AACE, American Association of Clinical Endocrinologists; HOMA, homeostatic model assessment.

<sup>a</sup>Patients taking antihypertensive treatment.

<sup>b</sup>Body mass index (BMI) ≥ 25 kg/m².

<sup>c</sup>HDL-C < 35 mg/dL (male) and < 40 mg/dL (female) of WHO, HDL-C < 40 mg/dL (male) and < 50 mg/dL (female) of AACE.

<sup>d</sup>Triglycerides ≥ 150 mg/dL or drug treatment for elevated triglycerides.

<sup>e</sup>Homeostatic model assessment (HOMA) index ≥ 2.5 (hyperinsulinemic euglycemic clamp not available).

<sup>f</sup>Patients taking hypoglycemic drug treatment.

Table 5. Ability of diagnostic criteria of metabolic syndrome to identify patients treated with LT4 with high CV risk

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>AUC (95% CI)</th>
<th>Significance (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO (1998)</td>
<td>0.83</td>
<td>0.77</td>
<td>0.722 (0.615–0.829)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>AACE (2003)</td>
<td>0.86</td>
<td>0.82</td>
<td>0.784 (0.685–0.883)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

CV, cardiovascular; AUC, area under the receiver operating characteristic curve; CI, confidence interval; WHO, World Health Organization; AACE, American Association of Clinical Endocrinologists.
sensitivity and specificity of the AACE criteria were higher than those of the WHO criteria in the LT4 treatment group.

Hypothyroidism is one of the most significant causes of obesity. However, using LT4 treatment to treat obesity is not recommended in patients without overt hypothyroidism. In addition, LT4 treatment does not have clinical benefits in older persons with subclinical hypothyroidism, and no specific trial in obese older people has yet been performed. More than three-quarters of patients in the LT4 treatment group were overweight or obese, although they were receiving adequate LT4 treatment. A recent study reported a lower BMI in obese LT4 users aged > 65 years compared to obese LT4 users aged < 65 years. Thus, age and body composition are the main predictive factors of LT4 requirement in obesity, and the risk of LT4 over-replacement decreases with aging and higher BMI in hypothyroidism.

A recent study reported the relationship between subclinical hypothyroidism and the development of MS only in young men. Another study including only older people showed the opposite finding and that the prevalence of MS was higher in women with subclinical hypothyroidism compared to that in men. Most participants in our study were postmenopausal women. The prevalence of MS may have been high owing to the possible effects of estrogen withdrawal.

Thyroid hormones play an important role in energy homeostasis and glycolipid metabolism. Changes in these hormones are risk factors for CV diseases. In our study, half of the LT4 treatment group had IR and nearly one-third had DM. When patients with LT4 treatment were classified into groups according to CV risk status (high or low risk), HbA1c levels and FG levels were higher in the high CV risk group compared to those in the low CV risk group, whereas BMI and HOMA-IR index were similar. HbA1c and FG levels correlated with a higher CV risk in the LT4 treatment group than was the HOMA-IR index. Hypothyroidism is associated with a higher risk of cardiac mortality in the general population. Huang et al. indicated that older adults with hypothyroidism who used LT4 treatment had a lower CV disease mortality risk than those who did not include patients taking antihypertensive medication LT4 treatment. In this study, no additional evidence on the presence of DM was reported. Mele et al. showed that LT4 users in euthyroid obese group had healthier lipid profile than no-users, and they had similar IR and FG to no-users. Thus, despite the CV mortality risk being decreased with LT4 treatment due to its impact on lipid profile, DM still remains a risk factor for CV mortality in patients with hypothyroidism.

Thyroid gland dysfunction contributes to components of MS, including weight gain, lipid disorders, and HT. Among studies that have investigated the relationship between thyroid dysfunction and MS, most assessed thyroid function in MS or in euthyroid populations or in those with subclinical hypothyroidism. These studies showed that the presence of MS was associated with a significantly increased risk of developing subclinical hypothyroidism and that individuals with higher TSH levels had an increased risk of MS. However, neither the prevalence of MS nor appropriate MS criteria have been investigated in older patients who are biochemically euthyroid but are receiving LT4 monotherapy. In our study, the prevalence of MS in the LT4 group was similar to that in the control group. The prevalence of MS in the general population varies widely based on ethnicity, sex, age, and presence of comorbidities. Additionally, the prevalence of MS is influenced by the increasing prevalence of obesity, and DM also affects the prevalence of MS. A study that assessed MS in older adults using four criteria—the WHO, US National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP-III), International Diabetes Federation (IDF), and Joint Interim Statement (JIS) criteria—showed a high prevalence of MS for all definitions. A cross-sectional study of 742 individuals aged > 20 years in Iran reported that the WHO definition, compared to the AACE, identified more patients with MS (41.8% vs. 30.7%). In addition, neither criterion showed significantly superior diagnostic value for health-related quality of life, although the AACE definition had higher adjusted odds ratios for reporting poor health-related quality of life. A cohort study of 1,187 Dutch older persons aged > 65 years showed a prevalence of MS of 34.2% using the NCEP-ATP-III criteria. We analyzed the TC/HDL ratio to determine the CV risk and found that TC/HDL ratio increased with higher serum TSH levels. Consequently, the prevalence of MS in older individuals and the appropriate criteria for MS in older adults are not clear.

Compared with the WHO criteria, the HDL threshold was higher in the AACE criteria (< 40 mg/dL for males and < 50 mg/dL for females). HDL cholesterol is known as the cardiotoxic cholesterol. Therefore, the WHO cut-off (< 35 mg/dL for males and < 40 mg/dL for females) may underestimate the CV risk in our group of euthyroid patients undergoing LT4 treatment. In addition, the AACE criteria of MS uses a lower BMI threshold than that in the WHO definition. Therefore, compared to the WHO criteria, the AACE one may identify more individuals with increased CV risk. Previous findings showed that the WC/BMI-based definitions of MS were associated with a higher risk of CV compared to IR-based definitions. In our study, the sensitivity and specificity of the AACE criteria for the prediction of CV risk were higher than those of the WHO criteria. The prevalence of hypothyroidism is increasing among older patients worldwide. CV risk was further increased in the presence...
of MS in these patients. The implementation of comprehensive geriatric assessment including the evaluation of MS should be undertaken. The use of BMI for the assessment of MS provides an easy and quick evaluation as it does not require additional measurements. The AACE criteria were superior to the WHO criteria in the prediction of CV risk in older patients undergoing LT4 treatment.

This study had several limitations. First, we retrospectively analyzed only 111 patients with chronic thyroiditis. A randomized controlled trial is needed to assess the relationship between MS and the degree of Framingham CV risk. In addition, we did not consider other MS criteria in the present study as waist circumference data were not available.

ACKNOWLEDGMENTS

We would like to thank M.D. Prof. Selahattin Fehmi Akçiçek and M.D. Bahattin Gökdemir for critically revising the article for important intellectual content.

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

None.

AUTHOR CONTRIBUTIONS

Conceptualization: FÖKK, SS, FS; Data curation and Formal analysis: FÖKK, FS; Investigation and Methodology: FÖKK, SS, FS; Project administration: FÖKK, FS; Supervisions: FÖKK, SS, FS; Writing-original draft: FÖKK, SS, FS; Writing-review & editing: FÖKK, SS, FS.

REFERENCES


Optimal Cut-Off Points of 4-meter Gait Speed to Discriminate Functional Exercise Capacity and Health Status in Older patients with Chronic Obstructive Pulmonary Disease

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Background: Gait speed, a vital sign of health and functional capacity, is commonly used to measure mobility. Although studies have assessed gait speed in older adults and individuals with chronic obstructive pulmonary disease (COPD) separately, few have evaluated gait speed in older adults with COPD. Therefore, the primary objective of our study was to determine the threshold point for the 4-meter gait speed test (4MGS) to better discriminate between functional exercise capacity and health status in older patients with COPD. The second objective was to determine possible predictors of gait speed.

Methods: In this cross-sectional study, we assessed participants' pulmonary function, dyspnea, health status (COPD Assessment Test [CAT]), gait speed (4MGS), functional exercise capacity (6-minute walk test [6MWT]), and physical activity.

Results: Forty-five older patients with COPD participated in this study. The predicted 6MWT and CAT scores were independent and significant determinants of the 4MGS score, explaining 54% of the variance (p<0.001). We identified gait speeds of 0.96 m/s and 1.04 m/s as thresholds to predict abnormal functional exercise capacity (sensitivity 85% and specificity 56%) and impaired health status (sensitivity 90% and specificity 69%), respectively (p<0.05).

Conclusion: Our findings demonstrated that gait speed can discriminate between abnormal functional exercise capacity and impaired health status in older patients with COPD. Moreover, functional exercise capacity and health status are predictors of gait speed.

Key Words: Chronic obstructive pulmonary disease, Gait, Exercise, Health status

INTRODUCTION

Chronic obstructive pulmonary disease (COPD), a major global burden, is an inflammatory lung disease that causes respiratory difficulties and airflow limitations.¹ Age and COPD prevalence are directly related, making COPD a prominent health problem among older adults.² Age-related anatomical and physiological changes in the cardiorespiratory system result in high mortality in this population.³ COPD at older ages further impairs physical well-being and leads to functional disability.⁴

Low gait speed is also a serious risk factor for cardiovascular and all-cause mortality in community-dwelling older individuals.⁵⁻⁷ Additionally, gait speed is a marker of functional exercise capacity in both patients with COPD and older adults.⁵,⁷ Gait requires complex integration and interaction between motor, sensory, and cognitive systems.⁹ Gait speed, the vital sign of health and functional capacity, is commonly used to measure mobility.⁹ Lower gait speed is an indicator of impairment, especially in chronic respiratory diseases.¹⁰ The 4-meter gait speed test (4MGS) is a valid and reliable test to assess gait speed in patients with COPD.¹¹ Although studies have assessed gait speed in patients with COPD and older adults separately, few have assessed the combina-
tion of these factors. Determining the optimal cut-off scores and predictors of 4MGS will contribute to literature and is important for understanding the possible effects of both aging and COPD. Moreover, despite the importance of gait speed in older adults with COPD, literature on the threshold points for gait speed to discriminate between functional exercise capacity and health status is also lacking. Therefore, the main purpose of the present study was to determine the cut-off point for the 4MGS to better discriminate between functional exercise capacity and health status in older patients with COPD. The second purpose was to determine possible predictors of gait speed in this patient population.

MATERIAL AND METHODS

Study Design and Participants
This cross-sectional study included 45 older patients (aged ≥ 60 years) with COPD. An experienced specialist diagnosed COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. Patients who (1) were clinically stable, (2) were not receiving any antibiotic treatment, and (3) had followed the same medication regimen for at least 3 weeks were included in the study. We excluded clinically unstable patients or those with musculoskeletal, neurological, or cardiovascular diseases that could hinder assessments.

This study complied the ethical guidelines for authorship and publishing in the Annals of Geriatric Medicine and Research. The study protocol was approved by Selcuk University, Faculty of Health Sciences Ethics Committee (No. 2021/857). The study adhered to the principles of the Declaration of Helsinki, and all participants provided written informed consent. This study complied with the ethical guidelines for authorship and publishing in the Annals of Geriatric Medicine and Research.

Outcome Measures
According to the European Respiratory Society (ERS) and American Thoracic Society (ATS) guidelines, we used a spirometer (Quark-SPIRO; COSMED, Roma, Italy) to evaluate pulmonary function, including forced vital capacity (FVC), forced expiratory volume in 1 second (FEV₁), and FEV₁/FVC.

We used the modified Medical Research Council (mMRC) Dyspnea Scale to assess dyspnea during certain daily activities. This self-administered tool measures the level of difficulty attributable to dyspnea in daily life. The scale has five expressions covering the entire range of dyspnea from no limitations (level 0) to full capacity insufficiency (level 4).

We used the COPD Assessment Test (CAT) to assess symptoms and effect of COPD on the health-related well-being of individuals. This reliable and valid tool has eight items, and the score for each range from 0 to 5 (maximum total score = 40), with higher scores indicating higher symptom burden. The GOLD guidelines define a CAT score ≥ 10 as “impaired health.”

We used the 4MGS to evaluate gait speed. Using floor marking tape, an 8-m-long hallway was divided into three zones: acceleration (2 m), testing (4 m), and deceleration (2 m) zones. The participants were asked to walk at their usual speed along the hallway, and the examiner recorded the total time from the start to the endpoint using a stopwatch. To calculate gait speed, the walking distance was divided by time.

We used the 6-minute walk test (6MWT) to assess functional exercise capacity, as indicated in the ERS and ATS guidelines. Each participant performed two 6MWTs with a minimum rest of 30 minutes. In each of the two tests, as the participants walked more, the value was recorded and expected walking percentage values were calculated. We recorded the longer of the two walking distances and calculated the percentage of predicted (%pred) values. The functional capacity of the participants was categorized as normal (≥ 82%pred) or abnormal (< 82%pred).

None of the participants had COPD requiring oxygen therapy during the tests.

We used the International Physical Activity Questionnaire Short Form (IPAQ-SF) to evaluate physical activity level in terms of gait and vigorous-to-moderate activities. We assessed the scale score by multiplying each activity duration by its known metabolic equivalents (METs).

Sample Size
We determined the minimum required sample size for multiple linear regression analysis using G*Power software (version 3.1.9.7; Heinrich Heine University, Düsseldorf, Germany) based on the results of a previous study, in which the 6MWT scores were a significant indicator of 4MGS scores in patients with COPD (R² = 0.19). The results showed that at least 37 participants were required for eight determinants in the model (age, body mass index [BMI], predicted FEV₁, mMRC score, CAT score, 6MWT distance, predicted 6MWT, and IPAQ-SF) (a probability level of 0.05, an anticipated effect size of 0.234, and a statistical power level of 80%).

Statistical Analysis
We used IBM SPSS Statistics for Windows (version 25.0; IBM Corp., Armonk, NY, USA) to analyze the data. Histograms and Shapiro-Wilk tests were used to check for normality. Values are expressed as median (interquartile range) and mean ± standard deviation for continuous variables and as numbers for categorical variables.
To examine correlations between 4MGS and other variables, we used Pearson product-moment correlation coefficients. In addition, we applied stepwise multiple linear regression analysis to identify variables with the largest effect on 4MGS. We also created a regression equation for this study.

We applied receiver operating characteristic (ROC) curve analysis to assess the discriminative value of 4MGS for abnormal functional exercise capacity (6MWT predicted < 82%) and impaired health status (CAT score ≥ 10).\textsuperscript{25} p-values < 0.05 were considered statistically significant.

**RESULTS**

This study included 45 older adult patients with COPD (mean age, 70.15 ± 7.66 years). Among all the patients, 84.4% were male. The participant characteristics are listed in Table 1.

4MGS was significantly correlated with predicted FEV\textsubscript{1} (r = 0.513), mMRC score (r = -0.586), CAT score (r = -0.630), 6MWT distance (r = 0.675), predicted 6MWT (r = 0.709), and IPAQ-SF score (r = 0.510) (p < 0.001; Table 2).

The results of the stepwise multiple regression analysis revealed predicted 6MWT and CAT score as independent and significant determinants of 4MGS, explaining 54% of the variance (p < 0.001) (Table 3). The regression equation formula was as follows: 4MGS = 0.791 + (0.005 × 6MWT predicted) + (-0.008 × CAT score).

4MGS had a discriminative value for abnormal functional exercise capacity, with an area under the curve (AUC) of 0.71 (p = 0.030, 95% confidence interval 0.56–0.86). The 4MGS cut-off of 0.96 m/s had an 85% sensitivity and 56% specificity to predict abnormal functional exercise capacity (Fig. 1A).

4MGS had a discriminative value for impaired health status, with an AUC of 0.79 (p = 0.006, 95% confidence interval 0.65–0.93). The 4MGS cut-off of 1.04 m/s had a 90% sensitivity and 69% specificity for determining impaired health status in the sample (Fig. 1B).

Table 1. Characteristic features of the patients (n=45)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>70.15 ± 7.66</td>
</tr>
<tr>
<td>Sex, male (%)</td>
<td>84.4</td>
</tr>
<tr>
<td>BMI (kg/m\textsuperscript{2})</td>
<td>28.12 ± 5.74</td>
</tr>
<tr>
<td>Smoking (pack-year)</td>
<td>48.59 ± 38.47</td>
</tr>
<tr>
<td>GOLD stage</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>4</td>
</tr>
<tr>
<td>II</td>
<td>27</td>
</tr>
<tr>
<td>III</td>
<td>11</td>
</tr>
<tr>
<td>IV</td>
<td>3</td>
</tr>
<tr>
<td>Pulmonary function test</td>
<td></td>
</tr>
<tr>
<td>(%)</td>
<td>60.75 ± 9.06</td>
</tr>
<tr>
<td>FEV\textsubscript{1} (%pred)</td>
<td>56.42 ± 16.93</td>
</tr>
<tr>
<td>FVC (%pred)</td>
<td>71.11 ± 15.83</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>28 (62.2)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>17 (37.7)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>13 (28.8)</td>
</tr>
<tr>
<td>Asthma</td>
<td>3 (6.6)</td>
</tr>
<tr>
<td>CAT score (0–40)</td>
<td>20.77 ± 10.39</td>
</tr>
<tr>
<td>mMRC score (0–4)</td>
<td>0.513</td>
</tr>
<tr>
<td>6MWT distance (m)</td>
<td>291.12 ± 147.11</td>
</tr>
<tr>
<td>6MWT (%pred)</td>
<td>60.56 ± 7.02</td>
</tr>
<tr>
<td>4-meter gait speed (m/s)</td>
<td>0.94 ± 0.28</td>
</tr>
<tr>
<td>IPAQ-SF (MET min/wk)</td>
<td>198.00 (0–676.50)</td>
</tr>
</tbody>
</table>

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

Table 2. Correlations between other outcomes and 4-meter gait speed (n=45)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pearson correlation coefficient (r)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>-0.244</td>
<td>0.107</td>
</tr>
<tr>
<td>BMI (kg/m\textsuperscript{2})</td>
<td>0.056</td>
<td>0.715</td>
</tr>
<tr>
<td>FEV\textsubscript{1} (%pred)</td>
<td>0.513</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>mMRC score (0–4)</td>
<td>-0.586</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>CAT score (0–40)</td>
<td>-0.63</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>6MWT distance (m)</td>
<td>0.675</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>6MWT (%pred)</td>
<td>0.709</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>IPAQ-SF (MET min/wk)</td>
<td>0.51</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

BMI, body mass index; FEV\textsubscript{1}, forced expiratory volume in 1 second; mMRC, Modified Medical Research Council; CAT, COPD Assessment Test; 6MWT, 6-minute walk test; IPAQ-SF, International Physical Activity Questionnaire-Short Form; MET, metabolic equivalent.

*p<0.05.

Table 3. Stepwise multiple linear regression model of 4-meter gait speed

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE</th>
<th>Beta</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>0.791</td>
<td>0.145</td>
<td></td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>6MWT (%pred)</td>
<td>0.005</td>
<td>0.001</td>
<td>0.517</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>CAT score (0–40)</td>
<td>-0.008</td>
<td>0.004</td>
<td>-0.308</td>
<td>0.023*</td>
</tr>
</tbody>
</table>

Summary of model: R=0.75, R\textsuperscript{2}=0.56, adjusted R\textsuperscript{2}=0.54 (p<0.001).

B, unstandardized regression coefficient; SE, standard error; CAT, COPD Assessment Test; 6MWT, 6-minute walk test.

*p<0.05.

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The leading finding of the study demonstrated that gait speeds of 0.96 m/s and 1.04 m/s were thresholds predicting abnormal functional exercise capacity and impaired health status, respectively. In addition, our results indicated that health status and functional exercise capacity were significant predictors of gait speed, explaining 54% of the variance in this population.

4MGS is a valid and reliable tool for patients with COPD, while gait speed is commonly considered a vital sign in the literature. Moreover, in chronic lung disease, mainly COPD, gait speed is related to pulmonary function, physical activity, dyspnea, functional exercise capacity, quality of life, and self-efficacy. Consistent with the literature, we observed correlations between gait speed and pulmonary function, dyspnea, health status, functional exercise capacity, and physical activity.

6MWT provides an objective evaluation of functional exercise capacity and is commonly used to assess patients with moderate to severe pulmonary diseases. Changes in 6MWT distance and other derived measurements can be used to determine treatment outcomes and predict mortality and morbidity in chronic respiratory diseases. Gait speed is a determinant of functional capacity in COPD. Our results demonstrated that functional exercise capacity is a factor influencing gait speed in older patients with COPD. These findings indicate that gait speed may be impaired in exercise-intolerant older patients with COPD.

COPD is related to impaired health status. The effect of COPD on patient health status can be assessed using the CAT. The CAT score is a determinant of functional exercise capacity, higher risk of exacerbation, and frailty in patients with COPD. We found that CAT was a determinant of 4MGS, indicating that impaired health status can cause a limitation in gait speed in this population. Improving patient health status can lead to increased gait speed.

Different 4MGS cut-off scores have been reported in the literature. Karpman et al. reported 0.8 m/s as a cut-off gait speed to predict abnormal exercise capacity in patients with COPD. Another study in the same population reported that a maximum gait speed of 1.27 m/s discriminated intact exercise capacity. A study of cardiac patients suggested a gait speed of 0.7 m/s as the cut-off to predict abnormal exercise capacity. Additionally, individuals with walking speeds > 1 m/s were independent in activities of daily living (ADL), less likely to be hospitalized, and less likely to have an adverse event. Our findings showed that gait speeds of 0.96 m/s and 1.04 m/s were indicators of abnormal functional exercise capacity (sensitivity 85%, specificity 56%) and impaired health status (sensitivity 90%, specificity 69%), respectively, in older patients with COPD. The diversity in reported cut-off values may be because of differences in methodologies and sample populations. Differences in test administration strategies and reference values

**DISCUSSION**

Fig. 1. Receiver operating characteristic (ROC) curves for 4-meter gait speed cut-off point to discriminate functional exercise capacity and health status in older with chronic obstructive pulmonary disease. (A) 6MWT <82%pred and ≥82%pred (cut-off point 0.96 m/s; sensitivity 85%; specificity 56%; AUC=0.71, 95% CI 0.56–0.86; p=0.03). (B) CAT score ≥10 and <10 (cut-off point 1.04 m/s; sensitivity 90%; specificity 69%; AUC=0.79, 95% CI 0.65–0.93; p=0.006). 6MWT, 6-minute walk test; AUC, area under the ROC curve; CI, confidence interval; CAT, COPD Assessment Test.
might be the underlying causes of discrepancies in the reported cut-off values.

This study had several limitations. First, although the study sample size was larger than the minimum required, most participants were in GOLD classes II and III. Thus, our findings cannot be generalized to all levels of COPD severity. The second limitation was the absence of an age- and sex-matched healthy control group. The inclusion of a control group in this study could provide a deeper and wider perspective. Third, we referred to values reported by Enright and Sherrill as the reference values for 6MWT were not validated in the Turkish population.

In conclusion, our findings indicated that gait speed could discriminate between impaired health status and abnormal functional exercise capacity in older patients with COPD. Moreover, functional exercise capacity and health status were independent determining factors for gait speed in this population.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST
The researchers claim no conflicts of interest.

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None.

AUTHOR CONTRIBUTIONS
Conceptualization: IO, MIK, NZ, CK, AE; Data curation and Formal analysis: IO, MIK, NZ; Investigation and Methodology: IO, MIK, CK, AE; Project administration: IO, AE; Supervision: IO, MIK, NZ, CK, AE; Writing-original draft: IO, MIK, CK, AE; Writing-review and editing: IO, MIK, NZ, CK, AE.

REFERENCES


Possible Sarcopenia and Its Association with Nutritional Status, Dietary Intakes, Physical Activity and Health-Related Quality of Life among Older Stroke Survivors

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Background: Screening for sarcopenia in the stroke population is an emerging concept in research and clinical practice. Therefore, this cross-sectional study aimed to assess the prevalence of possible sarcopenia and its associated factors among older stroke survivors who visited the neurology and rehabilitation departments of three public hospitals in Malaysia. Methods: We acquired data on sociodemographic characteristics, clinical profiles, malnutrition risk, dietary intake, physical activity level, and health-related quality of life. Possible sarcopenia was diagnosed in individuals with decreased calf circumference and low handgrip strength, as proposed by the Asia Working Group for Sarcopenia (2019). Finally, we performed descriptive analysis and binary logistic regression. Results: Among 196 older adults with stroke (mean ± standard deviation of age: 67.60 ± 5.70 years), 42.3% had possible sarcopenia, with a higher prevalence in the more advanced age group (≥70 years). In univariable analysis, possible sarcopenia was significantly associated with anthropometric indices, malnutrition risk, nutrient intake, physical activity level, and health-related quality of life. In multivariable analysis, body mass index (adjusted odds ratio [AOR]=0.57; 95% confidence interval [CI], 0.43–0.75) was the only factor associated with possible sarcopenia among individuals aged ≥70 years. Recurrent stroke (AOR=3.48; 95% CI, 1.02–11.92), body mass index (AOR=0.64; 95% CI, 0.54–0.76), and EQ-5D index (AOR=0.15; 95% CI, 0.03–0.78) were significantly associated with possible sarcopenia in the 60–69-year age group. Conclusion: The prevalence of possible sarcopenia among community-dwelling older stroke survivors was high. Therefore, we recommend routine screening for possible sarcopenia to ensure early nutritional and exercise intervention.

Key Words: Stroke, Sarcopenia, Older adult, Malnutrition, Diet

INTRODUCTION

The aging process places older adults at higher risks of malnutrition and stroke. Approximately three-quarters of strokes occur in people aged > 65 years.¹ Strokes in older adult patients are generally more severe and have poorer prognosis and clinical outcomes than those in younger patients.² The assessment for sarcopenia among the stroke population is a recently emerging concept in research and clinical practices. Sarcopenia is defined as “a progressive and generalized skeletal muscle disorder associated with increased likelihood of adverse outcomes including falls, fractures, physical disability and mortality.”³ Although sarcopenia is primarily related to the aging process, it may be accelerated in the presence of physical inactivity; malnutrition; and specific diseases such as stroke,

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endocrine diseases, and malignant tumors. To date, only few studies have investigated the prevalence of sarcopenia in the stroke population. Studies in the United States and Japan reported a prevalence of sarcopenia after stroke ranging from 14% to 54%. Other studies reported a sarcopenia prevalence of up to 54% among older Japanese patients undergoing rehabilitation in ward. Sarcopenia was significantly associated with worse recovery activities of daily living, dysphagia, and a lower rate of home discharge. An individual is diagnosed with sarcopenia if he or she has low appendicular skeletal muscle mass (ASM) and muscle strength or low physical performance. However, ASM measurement requires expensive devices such as magnetic resonance imaging, computed tomography, dual-energy X-ray absorptiometry, and bioelectrical impedance analysis. Acknowledging the difficulties of installing advanced diagnostic equipment in the primary health care or community setting, the Asian Working Group for Sarcopenia (AWGS) in 2019 proposed the terminology “possible sarcopenia” to identify the early signs of sarcopenia and allow prompt health education, nutritional strategies, and exercise interventions. The AWGS suggested using either calf circumference (CC) or the Strength, Assistance with walking, Rise from a chair, Climb stairs and Falls (SARC-F) or SARC-CalF to identify individuals with possible sarcopenia. Possible sarcopenia was diagnosed based on handgrip strength (HGS) or 5-time chair stand test results.

Other than age, sarcopenia is also significantly associated with other factors such as household status, lifestyle, physical inactivity, poor nutritional and dental status, and diseases; however, evidence is limited in the stroke population. To the best of our knowledge, no published findings are available regarding possible sarcopenia in the community-dwelling older stroke population in Malaysia. Thus, the objectives of this study were to assess the prevalence of possible sarcopenia among older stroke survivors attending outpatient clinics and to determine the factors associated with possible sarcopenia among different age groups.

MATERIALS AND METHODS

Study Design and Setting
This cross-sectional study was performed in three public hospitals with the highest stroke cases in 2015–2016 in the East Coast region of Peninsular Malaysia from May to August 2019. The statistics of stroke cases discharged from public hospital registries were obtained from the Health Informatics Centre, Ministry of Health Malaysia. A clinical dietitian applied convenience sampling to screen and recruit all patients with stroke attending the neurology and rehabilitation departments. The same clinical dietitian performed the survey by rotating between the three hospitals to minimize evaluation errors.

Participants
This study included older adults with stroke (age ≥ 60 years) diagnosed with stroke as confirmed by a medical doctor and able to communicate in Bahasa Melayu. Patients with contracture deformity, amputation, or severe organ failures were excluded. A proxy respondent who was the primary caregiver (spouse, parent, child, or sibling) was recruited if the respondent presented with severe language, vision, or cognitive impairments. Older adults with stroke and their caregivers were approached during the awaiting hours in the outpatient clinics.

Sample Size
A previous study reported a 14% prevalence of sarcopenia among middle-aged and older stroke adults. Based on the single proportion formula, a 95% confidence interval (CI), and a 10% non-response rate, a total of 206 respondents were required in this study.

Definition of possible sarcopenia
We diagnosed possible sarcopenia as the presence of decreased CC (males: < 34 cm, females: < 33 cm) and low HGS (males: < 28 kg, females: < 18 kg). CC was measured using a measuring tape with the participant in the seated or supine position with the non-paretic knee bent at 90°. For patients with bilateral stroke, the CC of both sides were measured, and the maximum values were reported. HGS was measured using a Takei Digital Grip Strength Dynamometer (Model T.K.K.5401; Takei Scientific Instruments, Niigata, Japan) with the participant in the standing or seated position with a fully extended elbow. Each hand (left and right) was tested twice, with a 60-second rest in between measurements. All readings were recorded in kilograms (kg) and the maximum mean HGS of either left or right hand was reported.

Independent Variables and Measurements

Sociodemographic and clinical profiles
The independent variables included sociodemographic profiles, clinical characteristics, anthropometric measurements, dietary intake, physical activity (PA) levels, and health-related quality of life. We extracted data on participant comorbidities including hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, and ischemic heart disease from their medical records based on the
Malaysian Clinical Practice Guidelines. We also asked the participants whether they frequently faced problems (Yes or No) such as chewing, swallowing, loss of appetite, speech, memory, sleeping at night, and paresis of the dominant arm.

Anthropometric measurements
Anthropometric measurements included weight, height, mid-upper arm circumference, and waist circumference. Weight was measured to the nearest 0.1 kg using a Seca Model 803 digital weighing scale (Seca, Hamburg, Germany). Height was assessed using a stadiometer Seca 206 (Seca, Hamburg, Germany) to the nearest 0.1 cm. The height of participants with balance and gait problems was estimated using knee height and prediction equations derived in a previous study on the Malaysian older adult population. Body mass index (BMI) was also calculated. Waist circumference was measured using a measuring tape placed at the midpoint between the lower margin of the least palpable rib and the top of the iliac crest. Mid-upper arm circumference was measured on the non-paralytic arm using a measuring tape from the midpoint on the triceps between the process acromion and olecranon process.

Malnutrition risk
We screened the participants for malnutrition risk based on the Malnutrition Risk Screening Tool-Hospital (MRST-H) validated in the older adult Malaysian population. The MRST-H contains five items. Three items are related to financial dependency, feeding dependency, and significant unintentional weight loss. The other two items in the MRST-H involve anthropometric measurements to assess muscle wasting/malnutrition based on sex-specific cut-off points for mid-upper arm circumference (MUAC) and CC. A score is allocated to each question with a positive answer (answering yes) or an MUAC and CC below the cut-off points. An individual is classified as having high malnutrition risk if he or she has scores 2 or above. The MRST-H scale has an excellent overall discriminatory accuracy in discriminating malnourished groups, with an area under the curve (AUC) of 0.84 when validated against the Subjective Global Assessment.

Dietary intake
A clinical dietitian assessed the dietary intake of the participants using the 7-day Dietary History Questionnaire through face-to-face interviews. The participants were asked to recall all food and beverages consumed for the past 7 days. Dietary analysis was conducted using the Nutritionist Pro nutrition analysis software (Axxya Systems, Redmond, WA, USA) to calculate the daily mean intakes of energy, protein, carbohydrate, fat, vitamin A, vitamin C, potassium, calcium, and iron. The energy and protein intakes were presented in kcal/kg ideal body weight (IBW)/day to prevent over- or underestimation of nutrient intake. We calculated IBW for older adults by multiplying a BMI of 25 kg/m² by the participants’ actual height squared. Adequate energy and protein intakes were defined as the consumption of at least 25 kcal/kg IBW/day and 1.0 g/kg IBW/day, respectively.

PA levels
The weekly PA levels were assessed using the short Malay version of the International Physical Activity Questionnaire (IPAQ). The IPAQ comprises seven items with four activity domains (vigorous, moderate, walking, and sitting). Each participant was asked to report the amount of time (in minutes) and the number of days (per week) spent on each activity domain. The participants were classified as achieving the recommended PA if they had total metabolic equivalents of task values-minutes per week of 600 or above (equivalent to moderate-to-vigorous activity levels).

Health-related quality of life
The health-related quality of life of participants was assessed using the Malay version of the EuroQoL-5 Dimensions-5 Levels (EQ-5D-5L) questionnaire validated in the Malaysian population. The participants were asked to rate their health on the day of evaluation based on a 5-point scale, indicating increasing severity of problems (1 = no problems, 2 = slight problems, 3 = moderate problems, 4 = severe problems, and 5 = extreme problems). The EQ-5D-5L description system contains five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Based on the rating of the five main dimensions of the descriptive system, we generated an EQ-5D summary index based on the equation proposed by Shafie et al. for the Malaysian population. The EQ-5D summary index ranged from 0 (death) to 1 (full health), with negative values representing states worse than death. The participants were also asked to self-rate their “health today” based on a scale of 0–100 (from worst to best score) using the EQ-visual analogue scale (VAS).

Ethics Approval
We performed all methods in this study in accordance with relevant guidelines and regulations. The Medical Research and Ethics Committee in the Ministry of Health, Malaysia (No. NMRR-19-4024-47231 (IIR)) and the UniSZA Human Research Ethics Committee approved the study protocol before commencing the study (No. UniSZA/UKHREC/2019/102). Written informed consent was obtained from cognitively intact older adults with stroke or from a proxy if the participants had severe aphasia or hearing, vision, or cognitive issues. Also, this study complied the ethical
guidelines for authorship and publishing in the Annals of Geriatric Medicine and Research.

**Statistical Analysis**

Continuous variables are presented as either mean ± standard deviation or median (interquartile range) based on the normality of data. Categorical variables are presented as frequencies and percentages. We performed binary logistic regression to examine factors associated with possible sarcopenia in different age groups (60–69 years and ≥ 70 years) because age is a well-known factor for sarcopenia. We included factors with a p-value of < 0.25 in univariable analysis and of clinical importance (sex and protein intake per kg IBW per day) in multivariable logistic regression. Variables with small cells (≤ 5) were excluded from multivariable logistic regression. The magnitudes of the associations are presented as adjusted odds ratio (AOR) with 95% CI. Interactions and multicollinearity between variables were also checked. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA), with a p-value of < 0.05 considered statistically significant.

**RESULTS**

A total of 448 patients with stroke was screened, and 237 of them were excluded based on the selection criteria. A total of 211 respondents completed the survey; however, we included only 196 respondents in the data analysis because 15 of them had unknown cases. The mean age of the participants was 67.60 ± 5.70 years. Two-thirds of the participants (66.3%) were aged 60–69 years; the remaining participants were aged ≥ 70 years. Approximately half of the participants were in the chronic phase of stroke (> 6 months from stroke onset). More than half of the participants were males (51.1%), married (73.0%), of Malay origin (86.7%), and not working (96.9%). Primary education levels were reported by 43.4% of the participants. The stroke cases were predominantly ischemic stroke (84.7%) and first-ever stroke (78.1%). Hyperlipidemia (95.9%) was the leading comorbidity, followed by hypertension (94.4%), diabetes mellitus (55.6%), ischemic heart disease (13.8%), and atrial fibrillation (7.1%). Most participants were non-smokers (63.8%), whereas 33.1% were ex-smokers and 3.1% were active smokers at the time of the survey. The prevalence of

| Table 1. Comparison of sociodemographic, clinical, nutritional status, lifestyle practices and health-related quality of life between different age groups (n=196) |
|-----------------|-----------------|-----------------|-----------------|
| Variable         | 60-69 y (n = 130) | ≥ 70 y (n = 66) | p-value<sup>d</sup> |
| Sex              |                  |                  |                  |
| Female           | 60 (46.2)        | 28 (42.4)        | 0.651            |
| Male             | 70 (53.8)        | 38 (57.6)        |                  |
| Ethnicity        |                  |                  |                  |
| Malay            | 113 (86.9)       | 57 (86.4)        | 1.000            |
| Chinese and Indian | 17 (13.1)    | 9 (13.6)         |                  |
| Marital status   |                  |                  |                  |
| Married          | 100 (76.9)       | 43 (65.2)        | 0.090            |
| Single/divorced/widowed | 30 (23.1) | 23 (34.8)       |                  |
| Education levels |                  |                  |                  |
| Never attended school | 10 (7.7)    | 9 (13.6)         | <0.001           |
| Primary          | 46 (35.4)        | 39 (59.1)        |                  |
| Secondary and above | 74 (56.9)   | 18 (27.3)        |                  |
| Types of strokes |                  |                  |                  |
| Ischemic         | 106 (81.5)       | 60 (90.9)        | 0.096            |
| Hemorrhagic      | 24 (18.5)        | 6 (9.1)          |                  |
| Position of stroke |                |                  |                  |
| Left             | 64 (49.2)        | 31 (47.0)        | 0.827            |
| Right            | 58 (44.6)        | 32 (48.5)        |                  |
| Bilateral/unspecific | 8 (6.1)    | 3 (4.5)          |                  |
| Stroke episode   |                  |                  |                  |
| First            | 103 (79.2)       | 50 (75.8)        | 0.588            |
| Recurrent        | 27 (20.8)        | 16 (24.2)        |                  |
| Stroke duration  |                  |                  |                  |

(Continued to the next page)
### Table 1. Continued

<table>
<thead>
<tr>
<th>Variable</th>
<th>60-69 y (n = 130)</th>
<th>≥ 70 y (n = 66)</th>
<th>p-value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early subacute (0–3 mo)</td>
<td>42 (32.3)</td>
<td>21 (31.8)</td>
<td>0.893</td>
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<tr>
<td>Late subacute (4–6 mo)</td>
<td>18 (13.8)</td>
<td>11 (16.7)</td>
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</tr>
<tr>
<td>Chronic (&gt; 6 mo)</td>
<td>70 (53.8)</td>
<td>34 (51.5)</td>
<td></td>
</tr>
<tr>
<td>Presence of comorbidities (yes)</td>
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<tr>
<td>Hypertension</td>
<td>123 (94.6)</td>
<td>62 (93.9)</td>
<td>1.000&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>Diabetes mellitus</td>
<td>74 (56.9)</td>
<td>35 (53.0)</td>
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<tr>
<td>Hyperlipidemia</td>
<td>124 (95.4)</td>
<td>64 (97.0)</td>
<td>0.720&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>Ischemic heart disease</td>
<td>15 (11.5)</td>
<td>12 (18.2)</td>
<td>0.272</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>6 (4.6)</td>
<td>8 (12.1)</td>
<td>0.076&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoke</td>
<td>83 (63.8)</td>
<td>37 (56.1)</td>
<td>0.352</td>
</tr>
<tr>
<td>Ex-smoker/Smoking</td>
<td>47 (36.2)</td>
<td>29 (43.9)</td>
<td></td>
</tr>
<tr>
<td>Physical activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Achieved</td>
<td>37 (28.5)</td>
<td>19 (28.8)</td>
<td>1</td>
</tr>
<tr>
<td>Not achieved</td>
<td>93 (71.5)</td>
<td>47 (71.2)</td>
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</tr>
<tr>
<td>Adequacy of energy intake</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>No (&lt; 25 kcal/kg IBW)</td>
<td>60 (46.2)</td>
<td>39 (59.1)</td>
<td>0.098</td>
</tr>
<tr>
<td>Yes (≥ 25 kcal/kg IBW)</td>
<td>70 (53.8)</td>
<td>27 (40.9)</td>
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<tr>
<td>Adequacy of protein intake</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No (&lt; 1.0 g/kg IBW)</td>
<td>76 (58.5)</td>
<td>42 (63.6)</td>
<td>0.538</td>
</tr>
<tr>
<td>Yes (≥ 1.0 g/kg IBW)</td>
<td>54 (41.5)</td>
<td>24 (36.4)</td>
<td></td>
</tr>
<tr>
<td>Nutrient intake</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbohydrate (g/day)</td>
<td>211.56 ± 53.87</td>
<td>197.00 ± 51.36</td>
<td>0.071&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Fat (g/day)</td>
<td>50.24 ± 14.39</td>
<td>45.43 ± 13.26</td>
<td>0.024&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Vitamin A (µg/day)</td>
<td>663.73 ± 507.77</td>
<td>657.67 ± 576.29</td>
<td>0.880&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Vitamin C (mg/day)</td>
<td>103.97 ± 59.85</td>
<td>93.12 ± 58.62</td>
<td>0.229&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Potassium (mg/day)</td>
<td>1303.54 ± 422.92</td>
<td>1248.49 ± 414.31</td>
<td>0.387&lt;sup&gt;d&lt;/sup&gt;</td>
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<tr>
<td>Calcium (mg/day)</td>
<td>567.20 ± 369.47</td>
<td>543.03 ± 320.58</td>
<td>0.650&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Iron (mg/day)</td>
<td>12.24 ± 5.71</td>
<td>11.01 ± 4.24</td>
<td>0.010&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>At risk of malnutrition</td>
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<td></td>
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<tr>
<td>Yes</td>
<td>57 (43.8)</td>
<td>30 (45.5)</td>
<td>0.88</td>
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<tr>
<td>No</td>
<td>73 (56.2)</td>
<td>36 (54.5)</td>
<td></td>
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<tr>
<td>Possible sarcopenia</td>
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<td></td>
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<tr>
<td>Yes</td>
<td>41 (31.5)</td>
<td>42 (63.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No</td>
<td>89 (68.5)</td>
<td>24 (36.4)</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td>24.53 ± 4.71</td>
<td>23.08 ± 4.38</td>
<td>0.039&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>86.22 ± 11.83</td>
<td>84.91 ± 10.53</td>
<td>0.448&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>EQ-5D index</td>
<td>0.69 ± 0.47</td>
<td>0.54 ± 0.57</td>
<td>0.030&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>VAS</td>
<td>60.00 ± 20.00</td>
<td>60.00 ± 20.00</td>
<td>0.817&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Presence of difficulties (yes)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chewing has difficulty</td>
<td>9 (6.9)</td>
<td>9 (13.6)</td>
<td>0.189</td>
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<tr>
<td>Swallowing has difficulty</td>
<td>12 (9.2)</td>
<td>11 (16.7)</td>
<td>0.159</td>
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<tr>
<td>Loss of appetite</td>
<td>9 (6.9)</td>
<td>7 (10.6)</td>
<td>0.413</td>
</tr>
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<td>Memory has difficulty</td>
<td>10 (7.7)</td>
<td>8 (12.1)</td>
<td>0.433</td>
</tr>
<tr>
<td>Speech has difficulty</td>
<td>12 (9.2)</td>
<td>4 (6.1)</td>
<td>0.585</td>
</tr>
<tr>
<td>Sleeping has difficulty</td>
<td>24 (18.5)</td>
<td>13 (19.7)</td>
<td>0.848</td>
</tr>
<tr>
<td>Paresis of dominant arm has difficulty</td>
<td>69 (53.1)</td>
<td>31 (47.0)</td>
<td>0.452</td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation or number (%). Vitamins A and C, Iron, EQ-5D, and VAS data are expressed as median±interquartile range. BMI, body mass index; WC, waist circumference; VAS, visual analogue scale; BW, body weight; IBW, ideal body weight.

Ideal body weight at BMI 25 kg/m<sup>2</sup> was used.

<sup>a</sup> Chi-square test, <sup>b</sup> independent t-test, <sup>c</sup>Fisher exact test, <sup>d</sup>Mann-Whitney U test.

Significant level p<0.05.
possible sarcopenia was 42.3% among the older adults with stroke.

Table 1 shows that the prevalence of possible sarcopenia was significantly higher in the advanced age group (≥70 years) than in the 60–69-year age group (63.6% vs. 31.5%). Additionally, the advanced age group had significantly lower educational level (59.1% vs. 35.4% had achieved primary education level), fat (45.43 ± 13.26 vs. 50.24 ± 14.39 g/day) and iron (11.01 (4.24) vs. 12.24 (5.71) mg/day) intakes, BMI (23.08 ± 4.38 vs. 24.53 ± 4.71 kg/m²), and ED-5D index (0.54 (0.57) vs. 0.69 (0.47)) than their counterparts. Inadequate energy (59.1% vs. 46.2%) and protein (63.6% vs. 58.5%) intakes, high malnutrition risk (45.5% vs. 43.8%), and physical inactivity (71.2% vs. 71.5%) were common, with no significant differences between the two age groups. The two groups also did not differ significantly in the presence of difficulties in chewing, swallowing, loss of appetite, memory, speech, sleeping, and paresis of the dominant arm.

Table 2 compares the anthropometric measurements and possible sarcopenia status by sex. Individuals without possible sarcopenia had significantly higher MUAC, CC, WC, BMI, and HGS than those with possible sarcopenia regardless of sex.

Table 3 compares the characteristics of individuals with and without possible sarcopenia according to age group. The 60–69-year age group showed a higher prevalence of possible sarcopenia among individuals who failed to meet the PA and energy recommendations; had lower CHO and fat intake; had high malnutrition risk; had lower BMI, WC and HRQoL values (EQ-5D index and VAS); and had frequent problems with chewing, swallowing, loss of appetite and speech. Meanwhile, the advanced age group showed a significantly higher prevalence of possible sarcopenia among individuals who failed to meet the PA and energy recommendations; had lower CHO intake; had high malnutrition risk; had lower BMI, WC, and EQ-5D index values; and were ex- or active smokers.

Table 4 shows that in univariable analysis, both age groups shared similar factors related to possible sarcopenia. Participants who failed to meet the PA or energy recommendations were three times more likely to have possible sarcopenia. Similarly, participants with high malnutrition risk were 4–9 times more likely to have possible sarcopenia. In contrast, increasing CHO intake, BMI, WC, and EQ-5D index were associated with lower odds of having possible sarcopenia in both age groups. Moreover, every increase in fat intake and VAS score was associated with a lower risk of possible sarcopenia in the 60–69-year age group. Ex-smokers and smokers were five times more likely to have possible sarcopenia in the advanced age group. Multivariable analysis showed that recurrent stroke (AOR = 3.48; 95% CI, 1.02–11.92), BMI (AOR = 0.64; 95% CI, 0.54–0.76), and EQ-5D index (AOR = 0.15; 95% CI, 0.03–0.78) remained significant in the 60–69-year age group after adjusting for confounding variables. Meanwhile, only BMI (AOR = 0.57; 95% CI, 0.43–0.75) remained significant in the advanced age group.

DISCUSSION

The results of this study revealed a few important findings. First, the prevalence of possible sarcopenia among older stroke survivors was high, at 42.3%, and was higher in the advanced age group (≥70 years) than in the 60–69-year age group. Second, a higher BMI was significantly associated with a lower risk of possible sarcopenia regardless of age. Participants in the younger age group (60–69 years) with recurrent stroke were more likely to have possible sarcopenia. Conversely, a higher EQ-5D index in this age group was significantly associated with a lower risk of having possible sarcopenia.

The prevalence of possible sarcopenia in the Malaysian stroke population was high and deserves attention from healthcare professionals for further evaluation and treatment. Other Asian studies in Japan and Korea reported the prevalence of sarcopenia diag-

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**Table 2. Comparison of the anthropometric measurements and possible sarcopenia status within females and males**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Female Without possible sarcopenia (n = 52)</th>
<th>Possible sarcopenia (n = 36)</th>
<th>p-value&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Male Without possible sarcopenia (n = 61)</th>
<th>Possible sarcopenia (n = 47)</th>
<th>p-value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>MUAC (cm)</td>
<td>28.99 ± 3.29</td>
<td>25.49 ± 3.41</td>
<td>&lt;0.001</td>
<td>30.07 ± 2.37</td>
<td>25.11 ± 2.87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CC (cm)</td>
<td>33.98 ± 3.16</td>
<td>28.84 ± 3.04</td>
<td>&lt;0.001</td>
<td>36.02 ± 2.58</td>
<td>29.51 ± 2.44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>89.02 ± 10.56</td>
<td>80.93 ± 12.05</td>
<td>0.001</td>
<td>92.07 ± 10.19</td>
<td>77.75 ± 5.66</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td>26.47 ± 4.62</td>
<td>20.83 ± 3.74</td>
<td>&lt;0.001</td>
<td>26.42 ± 3.64</td>
<td>20.59 ± 2.27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HGS (kg)</td>
<td>17.35 ± 5.80</td>
<td>11.52 ± 4.90</td>
<td>&lt;0.001</td>
<td>27.32 ± 7.77</td>
<td>18.01 ± 7.71</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation.

MUAC, mid-upper arm circumference; CC, calf circumference; WC, waist circumference; BMI, body mass index; HGS, handgrip strength.

<sup>a</sup>Independent t-test.

Significant level p<0.05.
<table>
<thead>
<tr>
<th>Variable</th>
<th>60-69 y (n = 130)</th>
<th>Age group</th>
<th>p-value</th>
<th>60-69 y (n = 130)</th>
<th>Age group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Without possible sarcopenia (n = 89)</td>
<td>Possi</td>
<td>Male</td>
<td>60-69 y (n = 130)</td>
<td>Age group</td>
<td>p-value</td>
</tr>
<tr>
<td></td>
<td>60-69 y (n = 130)</td>
<td>ble sarcopenia (n = 41)</td>
<td>49 (55.1)</td>
<td>21 (51.2)</td>
<td>0.709</td>
<td>12 (50.0)</td>
</tr>
</tbody>
</table>

Ethnicity                      | Malay             | 76 (85.4) | 37 (90.2) | 0.580 | 20 (83.3) | 37 (88.1) | 0.713 |
| Chinese and Indian             | 13 (14.6) | 4 (9.8) | 4 (16.7) | 0.009 | 10 (41.7) | 29 (69.0) | 0.039 |
| Marital status                 | Married           | 70 (78.7) | 30 (73.2) | 0.508 | 12 (50.0) | 31 (73.8) | 0.064 |
| Single/divorced/widowed        | 19 (21.3) | 11 (26.8) | 12 (50.0) | 11 (26.2) | 0.079 |
| Education levels               | Never attended school | 6 (6.7) | 4 (9.8) | 0.805 | 4 (16.7) | 5 (11.9) | 0.816 |
| Primary                       | 31 (34.8) | 15 (36.6) | 13 (54.2) | 26 (61.9) |
| Secondary and above            | 52 (58.4) | 22 (53.7) | 7 (29.2) | 11 (26.2) |
| Types of strokes               | Ischemic          | 76 (85.4) | 30 (73.2) | 0.143 | 24 (100.0) | 36 (85.7) | 0.079 |
| Hemorrhagic                    | 13 (14.6) | 11 (26.8) | 0 (0.0) | 6 (14.3) |
| Position of stroke             | Left              | 40 (44.9) | 24 (58.5) | 0.245 | 15 (62.5) | 16 (38.1) | 0.121 |
| Right                         | 42 (47.2) | 16 (39.0) | 9 (37.5) | 23 (54.8) |
| Bilateral/unspecified          | 7 (7.9) | 1 (2.4) | 0 (0.0) | 3 (7.1) |
| Stroke episode                 | First             | 74 (83.1) | 29 (70.7) | 0.161 | 19 (79.2) | 31 (73.8) | 0.768 |
| Recurrent                     | 15 (16.9) | 12 (29.3) | 5 (20.8) | 11 (26.2) |
| Stroke duration                | Early subacute (0–3 mo) | 29 (32.6) | 13 (31.7) | 0.933 | 11 (45.8) | 10 (23.8) | 0.199 |
| Late subacute (4–6 mo)         | 13 (14.6) | 3 (12.2) | 3 (12.5) | 8 (19.0) |
| Chronic ( > 6 mo)              | 47 (52.8) | 23 (56.1) | 10 (41.7) | 24 (57.1) |
| Presence of comorbidities (yes) | Hypertension       | 83 (93.3) | 40 (97.6) | 0.431 | 24 (100) | 38 (90.5) | 0.288 |
| Diabetes mellitus              | 52 (58.4) | 22 (53.7) | 13 (54.2) | 22 (52.4) | 1.000 |
| Hyperlipidemia                 | 87 (97.8) | 37 (90.2) | 23 (95.8) | 41 (97.6) | 1.000 |
| Ischemic heart disease         | 10 (11.2) | 5 (12.2) | 4 (16.7) | 8 (19.0) | 1.000 |
| Atrial fibrillation            | 5 (5.6) | 1 (2.4) | 5 (20.8) | 3 (7.1) | 0.128 |
| Smoking status                 | Never smoke       | 55 (61.8) | 28 (68.3) | 0.557 | 19 (79.2) | 18 (42.9) | 0.005 |
| Ex-smoker/smoking              | 34 (38.2) | 13 (31.7) | 5 (20.8) | 24 (57.1) |
| Physical activity              | Achieved          | 31 (34.8) | 6 (14.6) | 0.021 | 11 (45.8) | 8 (19.0) | 0.027 |
| Not achieved                   | 58 (65.2) | 35 (85.4) | 13 (54.2) | 34 (81.0) |
| Adequacy of energy intake      | < 25 kcal/kg IBW/day | 34 (38.2) | 26 (63.4) | 0.009 | 10 (41.7) | 29 (69.0) | 0.039 |
| ≥ 25 kcal/kg IBW/day           | 55 (61.8) | 15 (36.6) | 14 (58.3) | 13 (31.0) |

(Continued to the next page)
Table 3. Continued

<table>
<thead>
<tr>
<th>Variable</th>
<th>60-69 y (n = 130)</th>
<th>≥ 70 y (n = 66)</th>
<th>p-value(^{a})</th>
<th>Without possible sarcopenia (n = 89)</th>
<th>Possible sarcopenia (n = 41)</th>
<th>p-value(^{a})</th>
<th>Without possible sarcopenia (n = 24)</th>
<th>Possible sarcopenia (n = 42)</th>
<th>p-value(^{a})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequacy of protein intake</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1.0 g/kg IBW/day</td>
<td>47 (47.2)</td>
<td>29 (70.7)</td>
<td>0.059</td>
<td>13 (54.2)</td>
<td>29 (69.0)</td>
<td>0.290</td>
<td></td>
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<tr>
<td>≥ 1.0 g/kg IBW/day</td>
<td>42 (52.8)</td>
<td>12 (29.3)</td>
<td>0.064</td>
<td>11 (45.8)</td>
<td>13 (31.0)</td>
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<td></td>
</tr>
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<td>Nutrient intake</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbohydrate (g/day)</td>
<td>224.77 ± 50.89</td>
<td>182.88 ± 49.29</td>
<td>&lt; 0.001(^{b})</td>
<td>225.34 ± 59.83</td>
<td>180.81 ± 37.89</td>
<td>0.002(^{c})</td>
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<tr>
<td>Fat (g/day)</td>
<td>52.05 ± 14.69</td>
<td>46.32 ± 13.04</td>
<td>0.034(^{d})</td>
<td>46.97 ± 11.98</td>
<td>44.55 ± 14.01</td>
<td>0.480(^{e})</td>
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<tr>
<td>Vitamin A (µg/day)</td>
<td>726.83 ± 334.55</td>
<td>812.07 ± 398.37</td>
<td>0.207(^{c})</td>
<td>735.00 ± 397.26</td>
<td>704.06 ± 429.94</td>
<td>0.774(^{f})</td>
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<tr>
<td>Vitamin C (mg/day)</td>
<td>102.75 ± 60.49</td>
<td>106.60 ± 59.10</td>
<td>0.735(^{g})</td>
<td>96.48 ± 65.02</td>
<td>91.20 ± 55.37</td>
<td>0.728(^{h})</td>
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<tr>
<td>Potassium (mg/day)</td>
<td>1300.28 ± 373.58</td>
<td>1310.62 ± 519.36</td>
<td>0.909(^{i})</td>
<td>1336.82 ± 406.98</td>
<td>1198.01 ± 414.78</td>
<td>0.193(^{j})</td>
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<tr>
<td>Calcium (mg/day)</td>
<td>640.72 ± 277.88</td>
<td>686.67 ± 373.64</td>
<td>0.435(^{k})</td>
<td>617.55 ± 348.62</td>
<td>636.11 ± 329.59</td>
<td>0.830(^{l})</td>
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<tr>
<td>Iron (mg/day)</td>
<td>13.45 ± 4.33</td>
<td>12.42 ± 4.84</td>
<td>0.225(^{m})</td>
<td>11.70 ± 3.61</td>
<td>11.48 ± 4.73</td>
<td>0.842(^{n})</td>
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<td>At risk of malnutrition</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>25 (28.1)</td>
<td>32 (78.0)</td>
<td>&lt; 0.001</td>
<td>6 (25.0)</td>
<td>24 (57.1)</td>
<td>0.020</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>64 (71.9)</td>
<td>9 (22.0)</td>
<td>0.001</td>
<td>18 (75.0)</td>
<td>18 (42.9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>26.40 ± 4.10</td>
<td>20.46 ± 3.14</td>
<td>&lt; 0.001(^{o})</td>
<td>26.78 ± 4.20</td>
<td>20.97 ± 2.83</td>
<td>&lt; 0.001(^{p})</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>WC (cm)</td>
<td>90.04 ± 10.58</td>
<td>77.92 ± 10.09</td>
<td>&lt; 0.001(^{q})</td>
<td>92.98 ± 9.73</td>
<td>80.30 ± 7.93</td>
<td>&lt; 0.001(^{r})</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>EQ-SD index</td>
<td>0.66 ± 0.27</td>
<td>0.40 ± 0.36</td>
<td>&lt; 0.001(^{s})</td>
<td>0.62 ± 0.33</td>
<td>0.41 ± 0.30</td>
<td>0.012(^{t})</td>
<td></td>
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<tr>
<td>VAS</td>
<td>60.00 ± 20.00</td>
<td>50.00 ± 13.00</td>
<td>&lt; 0.001(^{u})</td>
<td>60.00 ± 29.00</td>
<td>52.50 ± 13.00</td>
<td>0.215(^{v})</td>
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<tr>
<td>Presence of difficulties (yes)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Chewing</td>
<td>2 (2.2)</td>
<td>7 (17.1)</td>
<td>0.004(^{w})</td>
<td>2 (8.3)</td>
<td>7 (16.7)</td>
<td>0.469(^{x})</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Swallowing</td>
<td>2 (2.2)</td>
<td>10 (24.4)</td>
<td>&lt; 0.001(^{y})</td>
<td>3 (12.5)</td>
<td>8 (19.0)</td>
<td>0.733(^{z})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>2 (2.2)</td>
<td>7 (17.1)</td>
<td>0.004(^{a})</td>
<td>2 (8.3)</td>
<td>5 (11.9)</td>
<td>1.000(^{b})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Memory</td>
<td>6 (6.7)</td>
<td>4 (9.8)</td>
<td>0.724(^{c})</td>
<td>1 (4.2)</td>
<td>7 (16.7)</td>
<td>0.241(^{d})</td>
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<tr>
<td>Speech</td>
<td>4 (4.5)</td>
<td>8 (19.5)</td>
<td>0.010(^{e})</td>
<td>1 (4.2)</td>
<td>3 (7.1)</td>
<td>1.000(^{f})</td>
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<td></td>
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<td>Sleeping</td>
<td>16 (18.0)</td>
<td>8 (19.5)</td>
<td>1</td>
<td>3 (12.5)</td>
<td>10 (23.8)</td>
<td>0.345(^{g})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paresis of dominant arm</td>
<td>43 (48.3)</td>
<td>26 (63.4)</td>
<td>0.132</td>
<td>12 (50.0)</td>
<td>19 (45.2)</td>
<td>0.800</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation or number (%). VAS data are expressed as median±interquartile range. BMI, body mass index; WC, waist circumference; VAS, visual analogue scale; BW, body weight; IBW, ideal body weight. Ideal body weight at BMI 25 kg/m\(^2\) was used. \(^{a}\)Chi-square test, \(^{b}\)Fisher exact test, \(^{c}\)independent t-test, \(^{d}\)Mann-Whitney U test. Significant level p<0.05.

Diagnosis ranging from 31% to 60% among patients with stroke.\(^{6,25,26}\) Although these findings are not directly comparable, Ueshima et al.\(^{27}\) demonstrated the high diagnostic accuracy of possible sarcopenia based on its sensitivity, specificity, and F-value. Possible sarcopenia (diagnosed based on CC and HGS) predicted sarcopenia among Japanese men and women with a sensitivity of 0.71 and 0.71, specificity of 1.00 and 0.94, and F-value of 0.83 and 0.71, respectively. Due to resource constraints, we were unable to perform confirmatory diagnosis of sarcopenia following diagnostic protocols. However, the AWGS (2019) suggested the initiation of lifestyle interventions among individuals with possible sarcopenia regardless of the final diagnosis. More research is needed to explore the usefulness of using possible sarcopenia for predicting sarcopenia diagnosis in the Malaysian population.

The results of this study add to the growing body of evidence showing that the syndrome of sarcopenia is multifactorial, with relationships to age, disease, inactivity, and poor nutrition. Unsurprisingly, advanced age was significantly associated with possible sarcopenia regardless of advanced age, also consistent with previous studies of community-dwelling older adults with stroke or those admitted to the convalescent rehabilitation ward.\(^{28,29}\) Muscle tissue gradually decreases during aging, resulting in decreased muscle mass and strength.

Moreover, increasing BMI was significantly associated with lower odds of having possible sarcopenia regardless of advanced age, also consistent with previous studies of community-dwelling older adults with stroke or those admitted to the convalescent rehabilitation ward.\(^{27}\) Indeed, the participants with possible sarcopenia in this
study were significantly thinner (20.7 ± 3.0 vs. 26.5 ± 4.1 kg/m²) than their counterparts. Landi et al. reported a lower risk of sarcopenia among older adult individuals with BMI of > 21.0 kg/m² than the risk among those with BMI of < 21 kg/m² in nursing homes of Italy. Cheng et al. suggested that higher fat mass can have several age-rated effects on lean mass. Individuals with higher fat mass might consume higher protein, which is important for sarcopenia prevention. Our results showed that BMI was weakly to moderately correlated with total energy (r = 0.520, p < 0.001) and protein intake (r = 0.398, p < 0.001). Despite this, the accurate measurement of BMI could be challenging among older adults with stroke and hemiparesis. Additionally, older adults with stroke show more prominent body composition changes than healthy older adults. Chang et al. showed a significantly lower bone mineral content, lower lean mass, and higher trunk fat mass among older adult Taiwanese patients with stroke (stroke duration ≥ 6 months) than healthy older adults of similar age. The study postulated that stroke-induced malnutrition, accelerated protein degradation secondary to chronic inflammation, and bone loss following physical inactivity might have explained the decrease in lean body mass and bone minerals in patients with stroke. Thus, other than BMI, body composition evaluation should be integrated into routine clinical practice for older adult patients with stroke to allow more accurate nutritional screening and assessment.

Individuals with possible sarcopenia in our study also showed a significantly overall poor quality of life, consistent with previous findings. Further exploration showed that possible sarcopenia was significantly associated with the physical dimension of HRQoL, namely, mobility, self-care, and usual activities. Sarcopenia is characterized by loss of lean body mass and muscle function,
which are required for physical functioning in stroke survivors. Matsu et al. showed that sarcopenia was a predictor of activities of daily living capability in patients with stroke undergoing rehabilitation. Improvement in sarcopenia was also associated with better functional and discharge outcomes among patients with stroke undergoing rehabilitation.

Additionally, participants with recurrent stroke were more likely to have possible sarcopenia. However, this factor was only significant in the younger age group. Recurrent stroke is often more severe, fatal, and disabling than the first episode. Thus, these patients were more likely to experience severe dysphagia, hemiparesis, and cognitive impairment, which may hinder their abilities to be mobile and consume adequate food.

This study also found that individuals who failed to consume adequate energy intake were more likely to have possible sarcopenia, although the relationship lost its significance in the multivariable analysis. Other studies have demonstrated that older adults with sarcopenia consumed significantly lesser energy, protein, vitamins (vitamin B12 and vitamin D), and minerals (potassium, calcium, magnesium, and selenium) than those without sarcopenia. Our study results showed that the adequacy and quality of nutrient intake among older adult patients with stroke deserve more attention since these patients generally consumed less than the recommended values (24.20 ± 5.25 kcal/kg BW/day; 0.95 ± 0.22 g protein/kg BW/day; potassium 1285 ± 419.8 mg/day; calcium 646.5 ± 318.0 mg/day). Kakehi et al. recommended the consumption of 25–35 kcal/kg BW/day and 1.2–1.5 g/kg BW/day protein during the subacute phase (2–4 weeks after stroke onset) and subsequently more energy to match the PA level during the convalescent phase to prevent sarcopenia. The dietary inadequacy among patients with stroke might be explained by the presence of oral dysfunction such as chewing, swallowing, and speech difficulties. Thus, texture modification, appropriate use of nutritional supplements, and oral rehabilitation strategies may help achieve adequate energy and protein intakes in these patients.

Similarly, univariable analysis in this study showed that possible sarcopenia was significantly associated with physical inactivity. Physical inactivity and immobilization after stroke can decrease muscle protein synthesis and reduce leg lean mass, leading to reduced muscle strength. The International Clinical Practice Guidelines For Sarcopenia strongly recommend resistance exercise and conditionally recommend protein supplementation/protein-rich diet in sarcopenia treatment. Multimodal exercises including a combination of resistance, aerobic, walking, and balance training are also recommended. Thus, attention should be paid to increase the PA levels of older adult patients with stroke to prevent sarcopenia and its complications.

The study has some limitations. First, we could not fully clarify the causal relationship between possible sarcopenia and its associated factors due to the cross-sectional study design. Second, we did not examine important variables such as severity of stroke and degree of disability as these data were either largely missing or required a manual search in the patient records. Third, we did not report on important nutrients such as vitamin D, omega 3 fatty acids, selenium, and magnesium because they were largely absent in the Malaysian Food Composition Database. Fourth, the measurements of CC and HGS may vary according to posture, which might have affected the diagnostic accuracy. Xu et al. reported the highest HGS measured while standing with the elbow fully extended, followed by standing with the arm raised, sitting with the elbow fully extended, and sitting with the elbow flexed 90° among 764 healthy Chinese individuals. They observed no significant differences in HGS among participants sitting with either elbow flexed or fully extended. In contrast, Jeong et al. reported a significantly lower CC when standing than when sitting regardless of the measurement side among community-dwelling Korean older adults. Although the AUC values of CC did not differ significantly when measured in different postures and sides, the AUC of right CC was largest when validating against the sarcopenia criteria according to the AWGS. Fifth, we did not perform an alternative method of sarcopenia screening, namely, SARC-F and 5-time chair stand test; thus, comparison of screening results between different methods was unlikely. Previous studies have suggested that SARC-F might underestimate the prevalence of possible sarcopenia among community-dwelling healthy older adults in Asian countries. Additionally, the presence of cognitive decline might have influenced the accuracy of the results as the SARC-F is a self-report questionnaire; thus, it depends on a participant’s ability to accurately estimate their physical abilities. In contrast, Yao et al. showed that when validated against the 2019 AWGS diagnostic criteria among patients with stroke in China, the sensitivity and specificity of the sarcopenia screening tools were as follows: SARC-F (sensitivity of 94.7%; specificity of 40.0%), Ishii’s score (sensitivity of 90.1%; specificity of 36.0%), and CC alone (sensitivity of 81.8%; specificity of 90.1%). Ishii’s score was derived from a sex-specific formula that included age, HGS, and CC values. However, they used revised cut-off points for screening when validated against the diagnostic criteria. Therefore, further research is needed to confirm the diagnostic efficacy of these screening tools among patients with stroke, and the most appropriate cut-off values is highly recommended. Sixth, the presence of cognitive decline among the elderly might have influenced the accuracy of the self-reported information for dietary intake and physical activity,
although a proxy of the respondent was used to improve the response rate. Finally, the presence of possible sarcopenia before stroke was not addressed in this study because the screening of sarcopenia was not routinely conducted in the acute stroke phase and thus should be examined in future cohort studies. Despite these limitations, this is one of the very few studies in Malaysia to examine the prevalence of possible sarcopenia among stroke survivors and its association with multiple dimensions of factors. Another point warranting discussion is stroke-related sarcopenia. Sarcopenia is caused not only by aging also by various factors. Stroke-related sarcopenia is a new concept that deserves attention and future clinical studies to elucidate its pathophysiology, early identification, prevention, and treatment. Moreover, the clinical impacts and associated complications of stroke-related sarcopenia on individuals with stroke have not been thoroughly studied and understood.

In conclusion, the prevalence of possible sarcopenia among community-dwelling older stroke survivors was high at 42.3%, with a higher prevalence in the more advanced age group (≥ 70 years). Furthermore, possible sarcopenia was significantly associated with BMI, recurrent stroke, and health-related quality of life in this population. Sarcopenia is often overlooked; therefore, we highly recommend screening for possible sarcopenia to allow early nutritional and exercise interventions.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

None.

AUTHOR CONTRIBUTIONS

Conceptualization, HJW, SH, PLL, and KAI; Data curation, HJW; Funding acquisition, SH; Investigation, HJW; Methodology, HJW, SH, PLL, and KAI; Project administration, HJW; Supervision, SH, PLL, and KAI; Writing—original draft, HJW; Writing—review & editing, SH, PLL, and KAI.

REFERENCES


Prewarming for Prevention of Hypothermia in Older Patients Undergoing Hand Surgery Under Brachial Plexus Block

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Department of Anaesthesiology and Pain Medicine, Konyang University Hospital, Konyang University College of Medicine, Daejeon, Korea

Background: Older patients are more vulnerable to inadvertent perioperative hypothermia. Prewarming contributes to the prevention of inadvertent perioperative hypothermia in patients under general or neuraxial anesthesia. However, the effects of brachial plexus block (BPB) on thermoregulation and the efficacy of prewarming in the prevention of hypothermia in older patients undergoing surgery with BPB remain unclear. This study evaluated the effects of BPB on thermoregulation and the efficacy of prewarming during BPB in older patients. Methods: Patients aged ≥65 years were randomly allocated to receive either standard preoperative insulation (control group, n=20) or preanesthetic forced-air warming for 20 minutes before BPB (prewarming group, n=20). During the perioperative period, tympanic temperatures were measured. Thermal comfort scores and shivering grades were also obtained. Results: The tympanic temperatures at the end of surgery did not differ between the groups (36.9°C ± 0.5°C and 37.0°C ± 0.4°C in the control and prewarming groups, respectively; p=0.252). The maximum temperature change was significantly lower in the prewarming group compared to the control group (0.36°C ± 0.4°C and 0.65°C ± 0.3°C, respectively; p=0.013). The hypothermia incidence and severity, thermal comfort scores, and shivering grades did not differ between the groups. Conclusion: Regardless of the application of prewarming, BPB did not cause a clinically significant impairment of thermoregulation. Moreover, the efficacy of prewarming appeared to be low; thus, it may not be routinely required in patients undergoing orthopedic hand surgery under BPB.

Key Words: Hypothermia, Brachial plexus block, Temperature, Aged, Incidence
Thesis. BPB may be preferable to general anesthesia in older patients who are at a greater risk of postoperative morbidity because it is superior in terms of recovery, analgesic consumption, and respiratory complications. However, there remain no definitive guidelines for the prevention of perioperative hypothermia using interventions such as temperature monitoring and prewarming in patients undergoing surgery using peripheral nerve blocks. The effects of BPB on thermoregulation and the clinical efficacy of prewarming in older patients undergoing BPB have not been established. Therefore, this study evaluated the effects of BPB on thermoregulation and the efficacy of prewarming in older patients undergoing hand surgery with BPB by assessing perioperative core temperatures with and without active prewarming using a convective forced-air warmer.

**MATERIAL AND METHODS**

This prospective, randomized, controlled study was performed between December 2019 and February 2021 at a single university hospital. This study was approved by the Institutional Review Board of Konyang University Hospital (No. 2019-01-004) and registered with the Korea Clinical Research Information Service (https://cris.nih.go.kr/). Written informed consent was obtained from the participants and/or their legal representatives. This study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.

This study included patients aged ≥ 65 years undergoing orthopedic hand surgery under BPB and with an American Society of Anesthesiologists physical status of I–III. The exclusion criteria were preoperative core temperature ≥ 37.5°C or < 36.0°C, obesity (body mass index > 35 kg/m²), endocrine or metabolic disease (e.g., uncontrolled diabetes, hypothyroidism, etc.), history of alcohol abuse, bleeding tendency, local infection at the BPB injection site, neuropsychiatric disease, or cognitive disorder.

The patients were randomly allocated to either the control or prewarming group (1:1 ratio) using a random number table generated by an online software tool (https://www.randomizer.org). When the patient arrived at the preanesthetic holding area, an anesthesia nurse blinded to the study purpose and not involved in data collection opened a non-translucent envelope containing the patient’s group allocation.

In our institution, the ambient temperatures in the preoperative holding area and post-anesthesia care unit (PACU) were maintained at 22°C–25°C, whereas the ambient operating room temperature was maintained at 21°C–24°C.

All patients arrived at the preanesthetic holding area without premedication and having fasted for a minimum of 8 hours. In the preanesthetic holding area, the control group received standard preoperative passive insulation using a cotton blanket. The prewarming group received 20 minutes of active prewarming using a forced-air blanket (Bair Hugger Full Body Blanket Model 30000; Arizant Healthcare Inc., Eden Prairie, MN, USA) placed over the entire body and then covered with a cotton blanket. During this period, active forced-air warmers were set to 43°C (high) and adjusted to 38°C (medium) if the temperature was too warm for the patient. At the end of active warming, the forced-air blankets were removed, and the patients were covered with cotton blankets and transferred to the operating room.

Patients from both groups received the same anesthetic and surgical management by an anesthesiologist and a surgeon who were blinded to the group assignments. Under ultrasound and nerve stimulator guidance, interscalene BPB was performed using 20–25 mL 0.5% ropivacaine. The time required for interscalene BPB (from needle puncture to needle removal after injection) was recorded. After confirming anesthesia using a pin-prick test, all patients underwent orthopedic hand surgery by the same surgeon. During surgery, the patients were covered with a surgical drape over the cotton blanket, not a forced-air warmer, and received unwarmed fluids. If the patient requested sedation, a small amount (0.5–2 mg) of midazolam was administered intravenously at the anesthesiologist’s discretion. Postoperatively, all patients were transferred to the PACU and covered with a cotton blanket.

We collected data on patient characteristics such as age, sex, weight, height, American Society of Anesthesiologists (ASA) physical status, incidence and amount of administered midazolam, administered fluid, estimated blood loss, duration of anesthesia, and duration of surgery.

**Outcome Measurements**

The temperature of all patients was measured by a trained anesthesiology resident using an infrared tympanic thermometer (Thermostan IRT 4020; Braun GmbH, Kronberg, Germany)—accurate to ±0.2°C for temperatures 35.5°C–42°C and to ±0.3°C for temperatures < 35.5°C. The highest value of at least two consecutive measurements from the same ear was recorded. The tympanic temperature was measured immediately after arrival in the preanesthetic holding area, on arrival in the operating room, immediately after BPB completion, and at 15-minute intervals during surgery and in the PACU. The tympanic temperature measured immediately after arrival at the preanesthetic holding area was considered the baseline core temperature. Hypothermia was defined as a tympanic temperature < 36°C. The severity of hypothermia (mild, 35°C–35.9°C; moderate, 34°C–34.9°C; severe, ≤ 34°C) and maximum temperature change (difference between the baseline
core temperature and lowest temperature between arrival in the operating room and PACU discharge) were also recorded.

The thermal comfort of the patients was evaluated using a numeric rating scale (0 = completely uncomfortable, 10 = completely comfortable) immediately after arrival in the preanesthetic holding area (before surgery) and PACU (after surgery). After the BPB procedure and until discharge from the PACU, shivering was evaluated using a 4-point scale (0 = no shivering; 1 = intermittent, low-intensity shivering; 2 = moderate shivering; 3 = continuous, intense shivering), and the highest value was recorded.

The primary outcome was the core temperature at the end of surgery. The secondary outcomes included maximum temperature change, hypothermia incidence and severity during the perioperative period (i.e., from arrival at the preanesthetic holding area to PACU discharge), perioperative temperature changes, perioperative thermal comfort scores, and perioperative shivering grade.

Statistical Analysis
The smallest difference required to detect hypothermia-related adverse effects is 0.5°C. A sample size of 16 patients in each group was required to detect a temperature difference of 0.5°C (± 0.5°C) at the end of surgery, with a power of 0.8 and a two-sided α-value of 0.05. To compensate for potential dropouts, 20 patients were recruited into each group.

The data distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. Normally distributed variables were analyzed using the Student t-test, while non-normally distributed variables were analyzed using the Mann–Whitney U test. Changes in tympanic membrane temperature over time were assessed using repeated-measures analysis of variance with Bonferroni correction. Categorical variables were analyzed using χ² tests, χ² tests for trends (linear-by-linear associations), or Fisher exact tests, as appropriate. Statistical significance was defined as a two-sided p-value of < 0.05. Statistical analyses were performed using PASW Statistics for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA).

RESULTS
A total of 74 patients were screened and 34 were excluded (11 due to uncontrolled diabetes, eight due to a history of neuropsychiatric disease, four due to a bleeding tendency, three due to cognitive disorders, and eight who refused to participate in the study and preferred surgery under general anesthesia instead of BPB) (Fig. 1). The patient characteristics were comparable between the groups (Table 1).

The temperatures at baseline and on arrival in the operating room did not differ significantly between the groups (Table 2). The primary outcome variable, i.e., the temperature at the end of surgery, did not show a group difference (36.9°C ± 0.5°C and 37.0°C ± 0.4°C, respectively; mean difference = -0.16; 95% confidence interval [CI], -0.44 to 0.12; p = 0.252). The maximum temperature change was significantly lower in the prewarming group compared to the control group (0.36°C ± 0.4°C and 0.65°C ± 0.3°C, respectively; mean difference = 0.29; 95% CI, 0.06 to 0.50; p = 0.013). The incidence of hypothermia was lower in the prewarming group compared to the control group (2.5% vs. 7.5%; p = 0.046). The incidence of shivering was also lower in the prewarming group compared to the control group (20.0% vs. 35.0%; p = 0.031).
Table 1. Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 20)</th>
<th>Prewarming (n = 20)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>73.3 ± 7.7</td>
<td>71.1 ± 5.2</td>
<td>0.298</td>
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<tr>
<td>Sex</td>
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<td></td>
<td>0.407</td>
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<tr>
<td>Male</td>
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<tr>
<td>Female</td>
<td>15</td>
<td>18</td>
<td></td>
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<tr>
<td>Weight (kg)</td>
<td>53.3 ± 7.6</td>
<td>58.0 ± 9.2</td>
<td>0.083</td>
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<tr>
<td>Height (cm)</td>
<td>151.4 ± 9.4</td>
<td>151.9 ± 5.9</td>
<td>0.833</td>
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<td>Body mass index (kg/m²)</td>
<td>23.4 ± 4.1</td>
<td>25.1 ± 3.9</td>
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<td>II</td>
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<td>III</td>
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<td>Midazolam</td>
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<tr>
<td>Amount (mg)</td>
<td>0 (0–0.38)</td>
<td>0 (0–0.5)</td>
<td>0.799</td>
</tr>
<tr>
<td>Incidence</td>
<td>5 (25)</td>
<td>6 (30)</td>
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<td>Fluids (mL)</td>
<td>200 (150–300)</td>
<td>200 (150–200)</td>
<td>0.565</td>
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<tr>
<td>Estimated blood loss (mL)</td>
<td>10 (1–10)</td>
<td>10 (1–10)</td>
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<td>Time taken for BPB (min)</td>
<td>6.0 ± 2.8</td>
<td>4.9 ± 2.0</td>
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<tr>
<td>Duration of surgery (min)</td>
<td>50.0 ± 16.5</td>
<td>51.3 ± 15.5</td>
<td>0.806</td>
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<tr>
<td>Duration of anesthesia (min)</td>
<td>93.1 ± 28.1</td>
<td>90.0 ± 20.0</td>
<td>0.689</td>
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</table>

Values are presented as mean±standard deviation or median (interquartile range) or number (%).
ASA, American Society of Anesthesiologists; BPB, brachial plexus block.

Table 2. Perioperative patient temperature and perioperative outcomes

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 20)</th>
<th>Prewarming (n = 20)</th>
<th>Mean difference (95% CI)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Patient temperature (°C)</td>
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<tr>
<td>Baseline</td>
<td>37.0 ± 0.3</td>
<td>36.9 ± 0.3</td>
<td>0.16 (-0.03, 0.34)</td>
<td>0.100</td>
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<tr>
<td>On arrival in the OR</td>
<td>37.0 ± 0.3</td>
<td>37.0 ± 0.4</td>
<td>-0.05 (-0.27, 0.18)</td>
<td>0.693</td>
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<tr>
<td>End of surgery</td>
<td>36.9 ± 0.5</td>
<td>37.0 ± 0.4</td>
<td>-0.16 (-0.44, 0.12)</td>
<td>0.252</td>
</tr>
<tr>
<td>Maximum temperature change (°C)</td>
<td>0.65 ± 0.3</td>
<td>0.36 ± 0.4</td>
<td>0.29 (0.06, 0.50)</td>
<td>0.013</td>
</tr>
<tr>
<td>Incidence of hypothermia</td>
<td>2 (10)</td>
<td>1 (5)</td>
<td>5 (-18.4, 28.6)</td>
<td>&gt; 0.999</td>
</tr>
<tr>
<td>Severity of hypothermia</td>
<td></td>
<td></td>
<td></td>
<td>&gt; 0.999</td>
</tr>
<tr>
<td>Mild (35°C–35.9°C)</td>
<td>2 (10)</td>
<td>1 (5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate (34°C–34.9°C)</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe (≤ 34°C)</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thermal comfort score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before surgery</td>
<td>8 (5–10)</td>
<td>8 (5–10)</td>
<td>-0.4 (-2.1, 1.3)</td>
<td>0.640</td>
</tr>
<tr>
<td>After surgery</td>
<td>10 (6.3–10)</td>
<td>10 (8–10)</td>
<td>-0.8 (-2.3, 0.7)</td>
<td>0.602</td>
</tr>
<tr>
<td>Shivering grade</td>
<td></td>
<td></td>
<td></td>
<td>&gt; 0.999</td>
</tr>
<tr>
<td>Grade 0</td>
<td>20</td>
<td>19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>0</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation or number (%) or median (interquartile range).
OR, operating room; CI, confidence interval.
Thermal comfort scale: 0=completely uncomfortable, 10=completely comfortable.
Shivering grade: 0=no shivering, 1=intermittent (low-intensity) shivering, 2=moderate shivering, 3=continuous (intense) shivering.
and severity of perioperative hypothermia did not differ significantly between the groups (p > 0.05).

Fig. 2 shows the perioperative changes in tympanic membrane temperature in both groups. In the prewarming group, the tympanic temperature did not differ significantly from baseline during the entire perioperative period. In the control group, the tympanic temperature was significantly lower than the baseline temperature immediately and 15 and 45 minutes after arrival in the PACU (p < 0.001), as well as 30 and 60 minutes after arrival (p = 0.001). However, the tympanic temperature showed no group differences at any time point (all p > 0.05). Perioperative changes in tympanic membrane temperature also did not differ significantly between the groups (p = 0.353) (Fig. 2).

The perioperative thermal comfort scores and shivering grades did not differ between the groups (all p > 0.05) (Table 2).

**DISCUSSION**

This study investigated the effects of BPB on the core temperature in older patients who were vulnerable to perioperative hypothermia. We also assessed the efficacy of active prewarming in patients undergoing hand surgery with BPB by comparing the control and prewarming groups. Although the maximum temperature change differed significantly between the two groups, the mean temperature at the end of surgery was close to 37°C regardless of prewarming, with no significant difference from the baseline temperatures observed in either group. In addition, although perioperative hypothermia occurred in 10% (2/20) and 5% (1/20) of patients in the control and prewarming groups, respectively, its severity was mild in all cases. This suggests that unlike general or neuraxial anesthesia, peripheral nerve blocks, such as BPB, do not significantly affect thermoregulatory function, even in older patients. Thus, the clinical effect of active prewarming in older patients undergoing hand surgery with BPB did not appear to be significant.

Previous studies have suggested that core temperature monitoring may be unnecessary in patients undergoing surgery under peripheral nerve block because the effects of peripheral nerve block are restricted to local thermoregulatory responses. However, to our knowledge, no prospective randomized controlled trials have been conducted to validate this suggestion. Moreover, advanced age is a well-known risk factor for hypothermia under both general and regional anesthesia and, in the case of regional anesthesia, the core temperature of adult patients may decrease by 0.03°C with increasing age. Furthermore, although preventive interventions for inadvertent hypothermia are recommended for procedures exceeding 30 minutes in duration, the efficacy of prewarming in patients undergoing surgery under BPB remains uncertain. The results of the present study may shed light on these unresolved issues.

A retrospective cohort study of adult patients undergoing orthopedic surgery under BPB reported an incidence of postoperative hypothermia of 40.6%. Moreover, a lower preoperative core temperature, history of alcohol abuse, arthroscopic shoulder surgery, use of fentanyl, concomitant use of sedatives, larger amounts of intravenous fluids, and longer duration of surgery were predictors of postoperative hypothermia. Based on these results, the authors

![Fig. 2. Perioperative tympanic temperature changes. Values are mean and standard error of the mean. *p<0.05 vs. baseline temperature in each group (Bonferroni-corrected). Tympanic temperatures showed no intergroup differences at any time point (all p>0.05). BPB0 to BPB45, 0–45 minutes after brachial plexus block; PACU0 to PACU60, 0–60 minutes after arrival at post-anesthesia care unit.](image-url)
recommended temperature monitoring as a standard of care in patients undergoing surgery under BPB. However, the effects of BPB on thermoregulation could not be assessed because factors that could affect the incidence of hypothermia, such as underlying diseases (e.g., hypothyroidism, alcohol abuse), surgery type (e.g., arthroscopic shoulder surgery requiring large volumes of irrigation solution), analgesic use (e.g., fentanyl, morphine, pethidine), and sedative use (e.g., midazolam, propofol, dexmedetomidine) were not controlled. Additionally, prewarming was not performed in all patients; therefore, whether prewarming contributed to the prevention of hypothermia could not be assessed. Our study excluded patients with a history of diseases that could affect thermoregulation and the type of surgery was limited to non-arthroscopic orthopedic hand surgery. Additionally, no intraoperative analgesics were administered and only midazolam was used as an intraoperative sedative, which does not noticeably impair thermoregulation.  

In this study, the mean tympanic temperatures at the end of surgery were 36.9°C and 37°C, and the incidence of perioperative hypothermia was 10% and 5%, in the control and prewarming groups, respectively. A retrospective study of older patients undergoing arthroscopic shoulder surgery under BPB with propofol sedation reported an incidence of perioperative hypothermia of 9.2%, which was comparable to the control group in our study. In another retrospective study of older patients who underwent both BPB and general anesthesia, the mean tympanic temperature on PACU arrival was 35.3°C, and 93.1% of the patients were hypothermic. Similarly, in a prospective study of 50–80-year-old patients undergoing spinal anesthesia, the tympanic temperature on arrival at the PACU was 35.6°C, and 88% of the patients showed hypothermia. Unwarmed patients undergoing general or neuraxial anesthesia reportedly experience a decrease in core temperature of approximately 1°C–2°C. In patients under general anesthesia, the core temperature decreased by 1.6°C ± 0.3°C during the first hour after induction of anesthesia. Meanwhile, spinal anesthesia decreased the core temperature by 1.0°C ± 0.3°C during the perioperative period. In the present study, the maximum temperature changes during the perioperative period were 0.36°C ± 0.3°C and 0.65°C ± 0.3°C in the prewarming and control groups, respectively. Thus, regardless of prewarming, BPB caused less core temperature reduction than general or neuraxial anesthesia. The extent of impairment of thermoregulatory control in patients undergoing surgery under regional anesthesia is proportional to the level of blockade. Therefore, BPB, which causes nerve block in only one upper extremity, did not significantly affect thermoregulation compared to neuraxial anesthesia.

Prewarming is the best way to prevent hypothermia caused by the redistribution of body heat following anesthesia. Among prewarming methods, convective forced-air warming is the best in terms of cost, safety, and efficacy. Prewarming does not significantly increase core body temperature via thermoregulatory vasodilation; rather, it increases the heat content of the body, especially in the peripheral thermal compartment. In this study, 20 minutes of prewarming using forced air did not alter the tympanic temperature at the end of surgery or affect the incidence of hypothermia. This could be because unlike general or neuraxial anesthesia, the body heat redistribution due to BPB was not significant, even in the control group. Nevertheless, the tympanic temperature in the control group decreased between arrival and discharge from the PACU. This may reflect the effect of exposure to the cold operating room environment, unwarmed intravenous and irrigation fluids, and heat evaporation from surgical incisions rather than an internal core-to-periphery body heat redistribution. Body heat redistribution caused by general or neuraxial anesthesia manifests as a rapid decrease in core temperature (within 30 minutes to 1 hour after anesthesia induction), a phenomenon that was not observed in this study. The perioperative temperature in the prewarming group did not differ significantly from baseline, possibly because prewarming increased the overall heat content of the body.

This study has some limitations. First, the core temperature was measured using an infrared thermometer. While infrared thermometers are commonly used in patients receiving regional anesthesia because they are minimally invasive, their reliability is controversial. However, a previous study reported that infrared systems can accurately measure skin temperature as the measurement site (rather than the thermometer used) determines the accuracy and precision of temperature monitoring. Another study demonstrated the low bias of an infrared thermometer (IRT 4000; Braun GmbH) to pulmonary artery catheters, suggesting that infrared thermometers could be an alternative for perioperative core temperature measurement. Second, the present study excluded patients with a lower preoperative core temperature and pre-existing diseases that could impair thermoregulation. The efficacy of prewarming may differ in patients with various risk factors for postoperative hypothermia. However, further research is required on this topic.

In conclusion, while active prewarming at 43°C for 20 minutes resulted in a lower maximum temperature change than standard preoperative passive insulation, there was no difference in core temperature at the end of surgery. The incidence and severity of perioperative hypothermia, changes in temperature during the perioperative period, thermal comfort scores, and shivering grades were also similar to those of the standard preoperative passive in-
REFERENCES


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We would like to invite members of the Korean Geriatrics Society and anyone who are interested.

[The 42th Review Training Course]
August 21, 2022
Seoul National University Hospital Innovation Center Seo-Hwan Seo Research Hall.
71, Daehak-ro, Jongno-gu, Seoul, Republic of Korea.
For more information please contact kgskorea1968@gmail.com

[The 22th Geriatric Medicine Certification Exam]
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National Medical Center auditorium
For more information please contact kgskorea1968@gmail.com

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Those who had a medical license for over 5 years.
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c. Procedure: Confirmation of acceptance → Confirmation of mailing address → Transfer certification fee to AGMR→ Certificate is sent by mail
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Ex. September 1, 2015 - August 31, 2020

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5. Submission Completed

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For specific study designs, such as randomized control studies, studies of diagnostic accuracy, meta-analyses, observational studies, and non-randomized studies, authors are encouraged to consult the reporting guidelines relevant to their specific research design. A good source of reporting guidelines is the EQUATOR Network (https://www.equator-network.org/) and NLM (https://www.nlm.nih.gov/services/research_report_guide.html).

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The manuscript sections should be presented in the following order: Cover Letter, Title Page, Abstract and Keywords, Introduction, Materials and Methods, Results, Discussion, Acknowledgements, References, Tables, and Figure Legends. Provide only one table or figure per page. Table 1 shows the recommended maximums of manuscripts according to publication type; however, these requirements are negotiable with the editor.

**Table 1. Recommended maximums for articles submitted to AGMR**

<table>
<thead>
<tr>
<th>Type of article</th>
<th>Abstract (word)</th>
<th>Text (word)</th>
<th>Reference</th>
<th>Table &amp; figure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original article</td>
<td>Structured b)</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>
</tr>
<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>
<td>1</td>
</tr>
</tbody>
</table>

AGMR, Annals of Geriatric Medicine and Research.

a) Maximum number of words is exclusive of the abstract, references, tables, and figure legends.
b) Background, methods, results, and conclusion.

**Title Page**

The Title Page should include only the following information:

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Sample:

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A concise and factual abstract is required. The abstract should not be more than 250 words (150 words for case reports and reviews). Abstracts should include the following headings: Background, Methods, Results, and Conclusion. Author(s) should specify the number of study participants. The abstract’s conclusion should emphasize clinical relevance. Do not use vague phrases such as “We believe that . . .” or “We suppose that . . .”. Non-standard or uncommon abbreviations should be avoided, but if essential, must be defined the first time they are mentioned in the abstract. After the abstract, list 3-5 keywords to be used for indexing. The keywords are from medical subject headings (MeSH; https://www.ncbi.nlm.nih.gov/mesh). Editorials and Letters to the editor do not require an abstract. An abstract is often presented separately from the article, and therefore must be able to stand alone.

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Tables should be submitted separately from the main body of the paper, and figure legends should be typed on separate sheets.

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Other Manuscript Formats
General guidelines are same as for original articles.

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- Case Reports
  - Case reports are considered for publication only if they report rare conditions, atypical symptoms and signs, or novel diagnostic or therapeutic approaches. The manuscript is structured in the following order: Title Page, Abstract, Introduction, Case Report, Discussion, References, Tables, and Figures. The abstract should be unstructured and should be no more than 150 words, with no more than 3 keywords attached. The introduction should briefly state the background and significance of the case. The actual case report should describe the clinical presentation and the diagnostic and therapeutic measures taken. The discussion should focus on the uniqueness of the case and should not contain an extensive review of the disease or disorder. The number of references is limited to 20. The maximum word count is 1,500 words, except references, figure legends, and tables.
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- The abstract is presented in the order of background, methods, results, and conclusion.
- The keywords are from medical subject headings (MeSH) (see https://www.ncbi.nlm.nih.gov/mesh).

**References**
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- The number of references is appropriate.
- One or more articles are cited from the “Annals of Geriatric Medicine and Research”.

**Tables and Figures**
- No more than 7 tables and figures in total.
- The title and legends of tables and figures are clear and concise.

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