Editorial
Moving Forward as a Growing Platform of Geriatric Medicine and Gerontologic Research

Frailty: Its Scope and Implications for Geriatricians

Invited Review
Pharmacological Interventions for Treatment of Sarcopenia: Current Status of Drug Development for Sarcopenia

Review Article
Exercise, the Gut Microbiome, and Frailty

Original Articles
Fracture Experiences and Long-Term Care Initiation among Older Population: Analysis of Korean National Health Insurance Service-Senior Cohort Study
Femoral Intertrochanteric Fractures of the Patients in the Emergency Department due to Minor Falls: Special Consideration in the Middle-old to Oldest-old Patients
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Efficacy and Safety of X-incision with Inversed Morcellation in Holmium Laser Enucleation of the Prostate: Comparison to Conventional Morcellation

Letters to the Editor
What is the Optimal Tool to Measure Gait Speed in a Clinical Setting?
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 research 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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Moving Forward as a Growing Platform of Geriatric Medicine and Gerontologic Research

Jae-Young Lim

Department of Rehabilitation Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seoul, Korea

For the past 20 years, *Annals of Geriatric Medicine and Research* (AGMR) has played a significant role in the development of academic research in the field of geriatric medicine as the official journal of the Korean Geriatrics Society. The number of cross-reference and total citations has markedly increased since AGMR was listed in the Emerging Sources Citation Index database in March 2018. As the name AGMR implies, the journal’s comprehensive aim and scope cover not only clinical studies of geriatric medicine but basic science, pre-clinical, and translational studies in the field of gerontology. Notably, AGMR also offers future perspectives on geriatric issues and emerging research needs in Asian countries faced with a rapidly growing aging population.

We are excited to announce that the Korean Society for Gerontology, an academic group of representative scientists in aging research, has endorsed AGMR as their official journal. The Korean Society for Gerontology was founded in 1989 by scientists and researchers with an interest and enthusiasm to understand the fundamental principles of the life phenomenon of aging and contribute to the healthy lives of aging people. It has become a professional academic organization representing aging research in Korea. The society, which celebrates its 30th anniversary this year, is making great efforts to strengthen their members’ research capabilities and expand exchanges at various levels with international academic organizations—all to make a leap forward in aging research. In a previous issue, cellular NAD⁺ levels were highlighted as a key determinant of mitochondrial quality in aging and degenerative diseases as reported by Hwang and Hwang.¹ This distinguished review article regarding mitochondrial biogenesis is a good example of gerontologic basic research featured in AGMR. In the current issue, Kwak and Kwon² have presented the current status of drug development in sarcopenia. The field of drug development for sarcopenia is a new arena of future medical and biological research among health care professionals and scientists. The endorsement as the official journal of the two leading academic societies in geriatric medicine and gerontologic research is expected to expand the readership of AGMR and to promote quantitative and qualitative growth of the academic contents of the journal. More qualified research outcomes and products will be targeted for publication in AGMR. Editorial experts from the two societies will contribute to the development of the journal by participating in editorial and reviewer boards.

A second exciting development is the launch of the new journal website. Overall, the design and visualization of the website was improved to make it more user-friendly. Now, it is easier to browse through the website and find articles quickly by sorting via article category. In addition, the function of browsing through the articles has been enhanced so that the readers can see the current status of the articles being read and cited at a glance with the metric information of the journal such as journal hits, downloads, and cross-reference citations. At the same time, we have also launched a mobile-friendly application version, which enables users to communicate with each other using social network services. It will be intriguing to see what the journal has created and where the future will reach.

It is our hope that AGMR will move forward as a growing platform for academic needs of professionals and researchers in geriatrics and gerontology and will aid in dissemination of knowledge across communities.

CONFLICT OF INTEREST DISCLOSURES

The author claims no conflicts of interest.

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Frailty: Its Scope and Implications for Geriatricians

Chang Won Won

Department of Family Medicine, College of Medicine, Kyung Hee University, Seoul, Korea

With the aging of population, more older adults become frail and many become dependent or bedridden. Frailty is defined as a status of vulnerability to endogenous and exogenous stressors that increase the risk of negative health-related outcomes. Frailty is usually caused by the interaction between progressive age-related decline in physiologic systems and chronic diseases, leading to decreased functional reserve capacities.1) Frailty is generally considered a transition between successful aging and disability.2)

What is the Scope of Managing Frailty for Geriatricians?

Disease to function-oriented focus: Frailty is a status of decreased functional reserve capacities.1) Thus, frailty does not fit into the traditional medical hierarchy of ‘health and disease’. Addressing frailty means a shift away from the disease-centered paradigm toward a focus on function.3)

Comprehensive approach: Frailty includes social and psychological components in addition to physical dysfunction.4) A longitudinal study showed that social frailty, defined as living alone, lack of social contacts, and lack of social support, was associated with the use of nursing care and contact numbers of health care professionals.5) Cognitive dysfunction predicts physical frailty; moreover, physical frailty and cognitive impairment affect each other, resulting in worse outcomes.5) Therefore, screening for frailty requires comprehensive geriatric assessment. Hearing impairment and visual disability are also risk factors for frailty.5)

Multimorbid, complex status: Frailty is frequently associated with a multimorbid status. In the Cardiovascular Health Study, 9.7% of older adults with multiple morbidities were frail, while 67.7% of frail older adults had multiple morbidities.5) To address frailty, a ‘complex systems’ approach is needed to address multidimensional processes and ‘complex relation of biological and non-biological factors’ on which frailty is based.5)

Implications for chronic diseases: Frailty is an important consideration for geriatricians in the clinical setting, particularly with respect to treatment goals for chronic disease in older patients.9) For example, guidelines from the European Society of Hypertension and the European Society of Cardiology recommend leaving decisions regarding antihypertensive therapy in frail older patients to the treating physician and considering treatment based on monitoring of the clinical effects of treatment and individual tolerability.10) The American Geriatrics Society consensus panels recommend glycated hemoglobin levels between 7.5% and 8.0%, particularly in individuals aged > 80 years who are at a high risk for frailty, comorbid conditions, and polypharmacy.11) The decision to treat primary hypercholesterolemia with statins in Older adults aged 80 or more must be individualized and frailty status must be considered to decide on it as frailty may exacerbate adverse effects of statins.12)

Why is Frailty Important to Geriatricians?

The management of frailty is the area in which the art of geriatrics is best practiced. Frailty has replaced the traditional concept of ‘chronological age’ with the more accurate and individually tailored ‘biological age’.1) In other words, frailty shed light on individualized care. Frail older adults are vulnerable and complicated, with care needs requiring skill and experience.

For this reason, frailty is a giant geriatric syndrome important to geriatricians; in this domain, the real value of geriatrics is shining brightly. Geriatricians differ from other specialists by providing specialized care for frail older adults. Geriatricians should champion the care of complex, vulnerable, and complex frail older adults.

Research and Implications

The Korean Frailty and Aging Cohort Study (KFACS), funded by the Ministry of Health, has been ongoing since December 2015. The KFACS is a multicenter, longitudinal study, with a baseline...
survey conducted in 2016–2017 and a 2-year follow-up survey underway. The KFACS aims to identify risk factors for adverse outcomes associated with frailty and preventative measures in community-dwelling older adults.

The final goal of the research is to increase knowledge for the diagnosis and management of frailty for implementation in clinical practice to reduce disability and dependency of frail older adults. KFACS data revealed discrepancies in the prevalence of frailty scales. Additionally, the risk of frailty was associated with limited contact with friends, anorexia, long sleep latency or long sleeping duration, high sodium intake, and low self-rating of health. The KFACS dataset and laboratory findings are available to extramural researchers.

CONFLICT OF INTEREST DISCLOSURES

The author claims no conflicts of interest.

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Pharmacological Interventions for Treatment of Sarcopenia: Current Status of Drug Development for Sarcopenia

Ju Yeon Kwak1, Ki-Sun Kwon1,2

1Aging Research Center, Korea Research Institute of Bioscience and Biotechnology, Daedeon, Korea
2Department of Functional Genomics, KRIIBB School of Bioscience, University of Science and Technology, Daedeon, Korea

Sarcopenia, the loss of skeletal muscle mass and function with age, was first recognized as a disease in the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) (M62.84) and has recently attracted attention as aged populations increase. However, the diagnostic criteria for sarcopenia remain controversial and there are as yet no US Food and Drug Administration-approved medications for sarcopenia. Given that both intrinsic and extrinsic factors contribute to sarcopenia onset and development, understanding the mechanism of sarcopenia is important for the development of therapeutic strategies. In this review, we described a variety of drugs for sarcopenia under investigation, including myostatin/ActR2 signaling inhibitors, exercise mimetics, anabolic hormones, and natural compounds. However, the combination of non-drug therapies with exercise and nutritional supplements are also needed as more easily accessible intervention strategies against sarcopenia rather than pharmacological treatments alone. Many approaches to develop therapeutic methods to overcome sarcopenia may lead to healthy aging.

Key Words: Sarcopenia, Skeletal muscle, Aging, Diagnosis, Drug

INTRODUCTION

Sarcopenia is the decline in skeletal muscle mass and function with age.1 Muscle mass and strength peak in early adulthood, followed by a gradual decline after 40 years of age,2 with a more substantial decline from the fifth decade onwards.3 Sarcopenia has been considered a consequence of normal aging; however, research on sarcopenia has supported its recognition as a disease entity, with a new disease code in the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) (M62.84) established in October 2016.4

Currently, the suggested clinical diagnostic criteria for sarcopenia are based on low muscle mass and function (strength or performance)5 although an international consensus is needed regarding the specific criteria and cut-offs. The technologies used to estimate muscle mass include magnetic resonance imaging, computed tomography, dual-energy X-ray absorptiometry scans, and bioelectrical impedance analysis. The parameters to test muscle strength and performance are handgrip strength and gait speed, respectively. The European Working Group on Sarcopenia in Older People (EWGSOP) classifies sarcopenia into three conceptual stages based on the severity of the condition: presarcopenia is characterized by low muscle mass only without influence on muscle function. Sarcopenia is characterized by low muscle mass with low muscle function (either muscle strength or physical performance). Finally, severe sarcopenia is characterized by low muscle mass with low of the muscle function (both muscle strength or physical performance). The Asian Working Group for Sarcopenia (AWGS) also adopted this algorithm.6 In 2019, the updated EWGSOP2 classified sarcopenia into ‘probable’, ‘confirmed’, or ‘severe’. EWGSOP2 elevated low muscle strength as a primary indicator of probable sarcopenia instead of low muscle mass and defined confirmed sarcopenia depending on the presence of accompanying low muscle mass.7

Research in the economic costs associated with sarcopenia indicates that the direct expenditure was approximately $18.5 billion...
($10.8 billion in men and $7.7 billion in women) in the United States in 2000, comprising approximately 1.5% of the country’s total health expenditure. The EWGSOP reported that the prevalence of sarcopenia among individuals 60-70 years of age was 5%-13% and increased to 50% in those over 80 years of age depending on the definition and method for identifying sarcopenia. Saropenia is the most significant cause of disability and frailty in the elderly, which lead to a poor quality of life. In addition, sarcopenia is associated with other diseases such as diabetes, non-alcoholic fatty liver disease, and cardiovascular disease including hypertension and arterial stiffness. Therefore, the management of sarcopenia is important for healthy aging. However, despite development efforts, to date, there remain no US Food and Drug Administration (FDA)-approved drugs for the treatment of sarcopenia (Table 1)

As the population of adults aged over 60 years worldwide is predicted to expand to 2 billion by 2050, there is corresponding interest in the development of diagnostic tools and drugs for sarcopenia to improve the quality of life and reduce healthcare costs.

**MOLECULAR TARGETS FOR PHARMACOLOGICAL INTERVENTION**

The etiologies of sarcopenia are not fully understood. An imbalance between muscle protein synthesis and degradation may cause the onset of sarcopenia and various mechanisms are potentially involved in the pathogenesis of sarcopenia. Both intrinsic factors within skeletal muscle (e.g., inflammation, apoptosis, autophagy, mitochondria, neuromuscular junction, and calcium metabolism) and extrinsic factors in systemic environments (e.g., endocrine, nutritional status, and immobility) contribute to defective myogenesis, muscle atrophy, and weakness. Therefore, understanding the mechanisms in sarcopenia is essential to identify molecular targets for pharmacological treatment.

**MYOSTATIN**

Myostatin is the most intensively studied molecular target for mus-

<table>
<thead>
<tr>
<th>Company name</th>
<th>Drug name</th>
<th>Collaborator</th>
<th>Target</th>
<th>Remark</th>
</tr>
</thead>
<tbody>
<tr>
<td>Novartis AG</td>
<td>Bimagrumab (antibody)</td>
<td>MorphoSys AG</td>
<td>Activin receptor type 2B</td>
<td>Thigh muscle volume increased by week 2 and was sustained throughout the treatment period (June 2017, phase 2).</td>
</tr>
<tr>
<td>Regeneron Pharmaceuticals Inc.</td>
<td>Trevogrumab (antibody)</td>
<td>Sanofi S.A.</td>
<td>Myostatin</td>
<td>Primary endpoint of phase 2: percent change in total lean body mass.</td>
</tr>
<tr>
<td>Biophytis SAS</td>
<td>Sarconeos (natural active ingredients)</td>
<td>NA</td>
<td>Proto-oncogene protein c-MAS-1, MAS receptor</td>
<td>Meaningful activity in animal models of muscular dystrophies. Good tolerability profile and no serious adverse events (phase 1).</td>
</tr>
<tr>
<td>ARMGO Pharma Inc.</td>
<td>ARM-210 (small molecule)</td>
<td>Servier</td>
<td>Ryanodine receptor</td>
<td>Treatment of Becker and limb-girdle muscular dystrophies as well as cachexia.</td>
</tr>
<tr>
<td>Immusoft Corporation</td>
<td>NA (cell therapy)</td>
<td>Bellicum Pharmaceuticals</td>
<td>Enzyme/protein replacement therapy</td>
<td>Immune system programming technology.</td>
</tr>
<tr>
<td>Neurontune AG</td>
<td>NT-1654 (fragment of neural agrin)</td>
<td>NA</td>
<td>NA</td>
<td>Low-density lipoprotein receptor-related protein 4, acetylcholine. NT-1654 accelerated muscle reinnervation after nerve crush.</td>
</tr>
<tr>
<td>AAVogen Inc.</td>
<td>AVGN7 (gene therapy)</td>
<td>NA</td>
<td>Activin receptors</td>
<td>Gene expression inhibitors. AVGN7 contains a gene called SMAD7, which stops gene expression for muscle wasting.</td>
</tr>
<tr>
<td>Amgen Inc.</td>
<td>ATA 842 (antibody)</td>
<td>NA</td>
<td>Myostatin, activin</td>
<td>ATA 842 demonstrated increased muscle mass and muscle strength in the treatment of young and old mice for 4 weeks.</td>
</tr>
<tr>
<td>Vibe Pharmaceuticals LLC</td>
<td>VB-102 (protein)</td>
<td>NA</td>
<td>NA</td>
<td>The drug can potentially regenerate muscle and bones.</td>
</tr>
<tr>
<td>BioViva</td>
<td>AAV gene therapy</td>
<td>NA</td>
<td>Myostatin</td>
<td>Obtained from a natural source and has potential in the modulation of myostatin expression.</td>
</tr>
<tr>
<td>Teijin Pharma Ltd.</td>
<td>TEI-SARM2</td>
<td>NA</td>
<td>Androgen receptor</td>
<td>Selective androgen receptor modulator.</td>
</tr>
</tbody>
</table>

cle-wasting disease. Also known as growth differentiation factor-8 (GDF-8), myostatin is a member of the transforming growth factor β (TGF-β) superfamily. Myostatin is predominantly expressed in cells of skeletal muscle lineage and inhibits muscle cell growth and differentiation through binding with its receptor complex activin type 2B (ACVR2B), resulting in activation of Smad signaling. The loss of myostatin function induces muscle hypertrophy in children and improved muscle function in animal models.

In addition, myostatin haploinsufficiency prevents not only aging-related declines in muscle function and but also enhances the longevity of mice. Therefore, the targeting of myostatin has been proposed as a primary strategy for pharmacological interventions in muscle-wasting diseases.

The first human trial tested the myostatin inhibitor Stamulumab (MYO-029) developed by Wyeth Pharmaceuticals with Cambridge Antibody Technology Group. Stamulumab is a recombinant human antibody that neutralizes the activity of myostatin protein by preventing myostatin from binding to ACVR2B. Phase 2 clinical trials were conducted in muscular dystrophy patients but development was discontinued due to the lack of efficacy on muscle strength. Landogrozumab (LY-2495655) is a humanized monoclonal antibody developed by Eli Lilly & Company that also neutralizes the activity of the myostatin protein. Phase 2 clinical trials have been performed in patients with sarcopenia (completed in December 2013), elective total hip replacement (completed in February 2014), and cancer cachexia (completed in January 2016), and are still under review. Increased appendicular lean body mass was reported with LY-2495655 treatment in patients aged 75 years or older who had fallen in the past year. After hip fracture surgery, LY-2495655 treatment induced increased appendicular lean body mass and decreased fat mass; however, the appendicular lean body mass did not reach the superiority threshold at week 12.

Regeneron Pharmaceuticals Inc. has developed the myostatin antibody Trevogrumab (REGN1033) in collaboration with Sanofi. Phase 2 clinical trials in sarcopenia patients were completed in February 2015 and the evaluations of its efficacy on muscle mass and function are ongoing.

Acceleron Pharma developed ramaccept (ACE-031) a decoy form of ACVR2B. Although the FDA awarded orphan status to this drug for muscular dystrophy and reviewed it in 2010, the development of ACE-031 was discontinued due to concerns about safety including minor nosebleeds, gum bleeding, and/or small dilated blood vessels within the skin (completed on June 2011). Alternatively, Acceleron Pharma is developing ACE-083 as a newer form of ACE-031. ACE-083 is designed for facioscapulohumeral muscular dystrophy (FSHD) and Charcot-Marie-Tooth disease (CMT) based on a modified form of human follistatin. Follistatin inhibits muscle growth signaling by binding to activins A and B and myostatin as well as other ligands in the family except for BMP9/10. The results of phase 1 of clinical trials of ACE-083 reported in 2018 included increased muscle volume as the ACE-083 dose increased. Phase 2 clinical trials are ongoing to test its safety, tolerability, pharmacokinetics, and pharmacodynamics in patients with FSHD and CMT.

**ACTIVIN RECEPTOR**

In addition to ligands such as myostatin and activins, receptor ACVR2B has also been targeted for the development of drugs for sarcopenia. An ACVR2B antibody, which blocks the signaling pathway, was reported to induce muscle hypertrophy. Novartis Institutes for BioMedical Research has developed a human monoclonal antibody, bimagrumab (BYM-338), in collaboration with MorphoSys AG. BYM-338 binds to both ACVR2A and ACVR2B and acts competitively with its ligands. In August 2013, the FDA granted breakthrough therapy designation to BYM-338 for sporadic inclusion body myositis, the most common idiopathic inflammatory myopathy that is characterized by progressive pathological muscle weakness and atrophy. BYM-338 promotes differentiation of primary human skeletal myoblasts and prevents the inhibition of differentiation induced by myostatin or activin A. BYM-338 also inhibits myostatin- or activin A-induced atrophy, thus sparing the myosin heavy chain from degradation. BYM-338 significantly increases skeletal muscle mass in mice, beyond the sole inhibition of myostatin. BYM-338 is administered by intravenous infusion. Phase 2/3 clinical trials of BYM-338 in patients with sporadic inclusion body myositis were completed in January 2016. However, no significant effects were observed in any objective measurements related to muscle strength or physical function. Phase 2 clinical trials of BYM-338 were also conducted in patients with hip fracture recovery or sarcopenia. In older adults with sarcopenia, BYM-338 increased muscle mass and strength and also improved mobility in those with slow walking speed. Although the aforementioned study was the first to evaluate a type II activin receptor antagonist in older individuals with sarcopenia, it had some limitations. For example, the use of a gait speed cutoff of 1.0 m/s rather than the more common 0.8 m/s limited the number of participants in the study whose gait speed improved with bimagrumab. Moreover, the lack of introductory sessions before the gait speed or 6-minute walk tests probably led to a pervasive learning effect in the performance test results. Physical activity was not monitored, so there were also limits in understanding how exercise might interact with the drug in this population. In December 2018, Novartis discontinued development of BYM-338 for hip fracture...
recovery and sarcopenia.

Although there are currently no clear drug candidates as most of the compounds in development have had very limited efficacy in larger clinical trials, many smaller clinical trials have demonstrated that the inhibition of myostatin/ACVR2 signaling may improve muscle mass in patients with muscle wasting. As positive effects on muscle wasting through exercise training and nutritional supplementation have been reported, hybrid therapies combining myostatin inhibitors with other approaches such as exercise and nutritional therapy could be more effective in the treatment of muscle wasting.

EXERCISE MIMETICS

Numerous studies have examined the positive effects of exercise on patients with sarcopenia. Exercise has consistently demonstrated improved muscle strength and function, with inconsistent effects on improving muscle mass. However, as most patients with sarcopenia have problems with physical activity, there is a limit to the ability of exercise to overcome sarcopenia. Thus, exercise mimetics (exercise pills) are a potential therapeutic strategy for sarcopenia that produce the effects of exercise without exercise. The peroxisome proliferator-activated receptor beta or delta (PPARβ/δ) agonist GW1516 and exercise training synergistically increased oxidative myofibers and running endurance in adult mice. Moreover, 4 weeks of AMP-activated protein kinase (AMPK) agonist AICAR treatment alone enhanced running endurance by 44% even in sedentary mice. In addition, PPARδ or AMPK activates robust transcription that re-programs the metabolic skeletal muscle genome. These results demonstrate that the AMPK-PPARδ pathway can be targeted by orally active drugs to enhance training adaptation or increase endurance without exercise.

Metformin has also examined under drug repurposing for the prevention of sarcopenia with prediabetes through activation of AMPK. Metformin is commonly prescribed for the treatment of type 2 diabetes. The effects of metformin on muscle are still uncertain and its exact mechanism of action is a matter of debate. However, metformin extended the lifespan and health span with improved physical performance in model systems. Thus, metformin has been studied as a potential pharmacological intervention to delay aging and the incidence of age-related diseases as well as sarcopenia. Although most potential exercise mimetics including AMPK agonists are still in pre-clinical stages due to side effects, the development of exercise mimetics is urgently needed and should be continued for patients on bedrest or with severe sarcopenia patients with loss of physical activity.

HORMONES

Decreased circulating levels of several anabolic hormones with aging may contribute to changes in muscle mass and function in older individuals. Therefore, hormonal manipulation has investigated as the basis of many of the therapies for sarcopenia. In phase 2 clinical trials by GTx Inc., treatment with selective androgen receptor modulator (SARM) enobosarm (also known as ostarine, MK-2866) induced dose-dependent increases in total lean body mass with improvements in physical function in older individuals. Moreover, its side effects were similar to those of the placebo, indicating that it is safer than steroids. Another phase 2 clinical trial of the SARM MK-0773 (also known as PF-05314882) also increased lean body mass in women with sarcopenia, without evidence of androgenization. Physical performance also tended to increase, although the difference was not statistically significant. Several patients in the treatment group experienced elevated transaminase levels that resolved after discontinuing the study. Despite growing evidence linking age-related hormonal changes to the development of sarcopenia, it is still too early to determine the clinical efficacy of hormonal supplementation for the management of sarcopenia.

NATURAL COMPOUNDS

Since sarcopenia is an age-related disease, natural compounds with anti-aging effects have been assessed for anti-sarcopenic properties. Ursolic acid, a pentacyclic triterpenoid enriched in apples, reduced muscle atrophy and stimulated muscle hypertrophy in mice by enhancing skeletal muscle insulin/IGF-1 signaling and inhibiting atrophy-associated mRNA expression. Furthermore, the effects were accompanied by reductions in adiposity and levels of fasting blood glucose, and plasma cholesterol and triglycerides.

Tomatidine improves muscular strength and decreases adiposity. Tomatidine, abundant in unripe green tomatoes, is a metabolite of α-tomatine. Supplementation with tomatidine in old mice significantly reduced age-dependent declines in skeletal muscle mass, strength, and quality.

Both ursolic acid and tomatidine generate hundreds of small positive and negative changes in mRNA levels in aged skeletal muscle, with remarkably similar mRNA expression signatures. Ursolic acid and tomatidine in aged skeletal muscle reportedly repressed a subset of the mRNAs positively regulated by activating transcription factor 4 (ATF4), a basic leucine zipper (bZIP) transcription factor subunit regulating oxidative and other stress responses.
High-energy skeletal muscle tissue relies upon mitochondria for energy production and contractile function; however, mitochondrial function declines with aging. The association between sarcopenia and mitochondria may also inform new and effective treatments for sarcopenia. Mitophagy plays a significant role in mitochondrial quality control in muscles; therefore, mitophagy-inducing agents may have anti-sarcopenic functions. Urolithin A is a metabolically transformed compound from a group of natural compounds, ellagitannins (ETs), which are found in pomegranates, as well as nuts and berries. Urolithin A has been shown to induce mitophagy and prolong lifespan in C. elegans and increase muscle function in rodents.

The results of studies in model animals suggest that supplementation with these natural compounds may ameliorate sarcopenia in older individuals, especially when clinically assessed with other medical treatment options.

CONCLUSION

According to reports from the FDA in 2017, many patients with sarcopenia are uncertain if their symptoms worsen due to sarcopenia or as a natural result of aging. Therefore, older individuals should recognize sarcopenia as a disease to prevent or treat. As a new disease code for sarcopenia was established in ICD-10-CM (M62.84) in October 2016, other countries will also soon accept sarcopenia as a disease entity.

As a result of sarcopenia, patients have difficulty in performing basic physical tasks such as standing and walking long distances. Moreover, balance problems, falling, fatigue, and muscle pain, along with comorbid conditions such as arthritis, make them inactive. In addition to physical limitations, patients with sarcopenia experience emotional impacts such as fear of injury and embarrassment of their physical limitations, limited social interactions and feelings of isolation, and difficulties caring for themselves and living independently. Therefore, the development of preventive and therapeutic strategies against sarcopenia is imperative for healthy aging. Future large-scale clinical trials are essential to develop precision medicine reflecting individual patient characteristics since the cause and clinical features vary between patients. Comprehensive strategies together with pharmacological and non-pharmacological intervention including exercise, physical therapy, dietetic regulation, lifestyle modification, and emotional support may be more effective against sarcopenia.

CONFLICT OF INTEREST DISCLOSURES

The researchers claim no conflicts of interest.

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INTRODUCTION

Previous studies have reported a direct link between disease and disability without adequately accounting for disability in the absence of disease. The concept of frailty was proposed to describe this condition. Frailty is defined as a clinical state in which an individual is vulnerable to imbalanced homeostasis when exposed to a stressor event. Frailty can occur as a consequence of a cumulative decline in a range of physiological conditions. Although frailty is not a specific disease, it is a concept that encompasses clinical signs such as loss of weight, leisure time activity, gait speed, grip strength, and exhaustion. Healthy aging refers to aging without such aging-related deficits. It is obvious that exercise is a crucial tool to achieve healthy aging. The ultimate aim of exercise is to prevent aging-related deficits, leading to healthy aging. However, aging is also related to the gut microbiome. It is becoming increasingly clear that the composition of the gut microbiome changes with age. Novel methods are being introduced that can lead to healthy aging through regulation of the composition of the gut microbiome. Recent studies have shown that healthy centenarians have different gut microbiome characteristics compared to those of average older adults. However, whether regulation of the gut microbiome through exercise training can lead to healthy aging is currently unclear. Therefore, in this review, we investigated whether alterations of the gut microbiome through exercise training can lead to healthy aging. The overview of study is shown in Fig. 1.

Exercise, the Gut Microbiome, and Frailty

Hyung Eun Shin¹, Seong Eun Kwak¹, Ji-Hyun Lee¹, Didi Zhang¹, Jun Hyun Bae¹, Wook Song¹,²,³

¹Health and Exercise Science Laboratory, Seoul National University, Seoul, Korea
²Institute of Sport Science, Seoul National University, Seoul, Korea
³Institute on Aging, Seoul National University, Seoul, Korea

Corresponding Author:
Wook Song, PhD
Institute of Sport Science, Seoul National University, 1, Gwanak-ro, Gwanak-gu, Seoul 08826, Korea
E-mail: songw3@snu.ac.kr
ORCID: https://orcid.org/0000-0002-8825-6259

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General Concepts of the Gut Microbiome

The gut microbiome is an essential part of our body. It is involved in the regulation of various host metabolic pathways, leading to interactive host-microbiota metabolic signaling that connects the gut, muscle, and brain. The host and its microbiota interact to produce gut microbiome-derived metabolites that contribute to the metabolic phenotype of the host. The microbiome of the human gut includes at least 1,000 microbial species and approximately $10^{14}$ micro-organisms. The human microbiome is presumed to encode approximately $4 \times 10^6$ genes, approximately 150 times that in the human genome. Recent studies have defined a host as a super-organism in which eukaryotic and prokaryotic cells co-exist. The gut microbiome is formed on the basis of the interaction of environmental factors, including lifestyle, the presence of disease, etc. The microbiome may be altered by external and internal stimuli such as stress, diet, and antibiotic use.

Although the general characteristics of the gut microbiome in healthy people are not yet completely defined, the gut microbiomes of people with disease (e.g., metabolic syndrome, physical frailty, cognitive dysfunction, etc.) show a gradual change toward an imbalanced composition compared to those in healthy people. These imbalanced microbiome characteristics may contribute to disease onset and may play a role in a vicious cycle. The gut microbiome coexists with the host in a symbiotic relationship and contributes to immune regulation and homeostasis. Therefore, unbalanced gut microbiomes as a result of aging need to be prevented through exercise training and dietary habits. We investigated whether exercise training can balance the gut microbiome and contribute to healthy aging in the older population, with a focus on the relationship between the gut and muscle and the brain.

Gut Microbiome and Exercise

Exercise can significantly alter the composition of the gut microbiome, although the mechanism by which this occurs remains unclear. Some studies have assessed the effects of exercise as a treatment on metabolic disorders in mice with diabetes. When db/db (type 2 diabetes [T2D]) and db/+ (control) mice were made to exercise at a low intensity, the proportion of Bifidobacterium spp. increased in the db/+ mice that exercised. In another study, wild-type mice were subjected to voluntary wheel running for 12 weeks. After the exercise intervention, the Bacteroidetes:Firmicutes ratio increased, preventing diet-induced obesity. In addition, 4-week-old C57BL/6J mice that were made to exercise on a treadmill had an increased relative abundance of Butyricimonas and Akkermansia. The other effects of exercise on the gut microbiome composition of mice are summarized in Table 1.

It is obvious that exercise is associated with alterations in the composition of the gut microbiome. However, human studies have not investigated whether the gut microbiome is regulated by exercise. Allen et al. showed that exercise can induce compositional and functional alterations in the human gut microbiome. Specifically, exercise increased the fecal concentration of short-chain fatty acids.
acids (SCFAs) in lean participants. Studies have also compared gut microbiomes between athletes and non-athletes. When compared with sedentary controls, Rugby Union players had increased levels of fecal metabolites such as SCFAs that are related to enhanced muscle turnover. In addition, comparisons of the gut microbiomes of professional and amateur cyclists revealed a higher abundance of *Methanobrevibacter smithii* in professional cyclists. The other effects of exercise on the composition of the gut microbiome in humans are summarized in Table 2.

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<th>Table 1. Effects of exercise on the gut microbiome in mice</th>
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BMI, body mass index; HRR, heart rate reserve; SCFAs, short-chain fatty acids.

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<th>Table 2. Effects of exercise on the gut microbiomes in humans</th>
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BMI, body mass index; HRR, heart rate reserve; SCFAs, short-chain fatty acids.
Gut Microbiome in Aging

Age-related changes in the composition and diversity of the gut microbiome aggravate the immune system to regulate inflammatory responses. Collapse of the immune system causes age-related diseases. The gut microbiome is related to the immune system in that both vary in composition with age. Although the gut microbiota of humans is determined to some extent at birth, the composition continually changes throughout life according to the external environment. This age-dependent gut microbiome is closely correlated with host inflammation and pathophysiology as the host ages. The gut physiology induced by this altered gut microbiome can cause host sensitivity to microbiota, leading to chronic and severe inflammatory responses.

Furthermore, these inflammatory responses can result in diseases such as cachexia, frailty, cancer, fatty liver disease, metabolic syndrome, T2D, and neurodegenerative diseases. The gut microbiomes of older people are entirely different from those of younger adults. With increasing age, the diversity of the gut microbiome decreases, with reduced numbers of Bifidobacteria, Faecalibacterium, Firmicutes, Faecalibacterium prausnitzii, Clostridium cluster XIV, and Blautia coccoides-Eubacterium rectal. However, inter-individual variations among individuals of the same age also exist because of various environmental factors. In particular, the abundance of certain key species in older adults decreases, whereas the abundance of subdominant species increases. Also, the Firmicutes:Bacteroidetes ratio decreases in older individuals. In one study, the gut microbiomes of older individuals exhibited a predominance of Bacteroidetes compared to those of younger individuals. Bacteroidetes comprising Bacteroides, Alistipes, and Parabacteroides genera were the dominant core microbiota among older people. These results clearly show that the gut microbiome changes with age. Therefore, we investigated how alterations in the gut microbiome could affect organs including the skeletal muscle and brain.

Gut-Muscle Axis

Gut microbiome and physical frailty
Physical frailty is common in the older population and is negatively correlated with health indicators. Although the mechanism of physical frailty is not yet fully understood, the core components of physical frailty are strength, gait, body composition, and fatigue. Physical frailty, including weak muscle strength, slow gait speed, and poor balance, can lead to disability in performing activities of daily living. Physical frailty is significantly associated with metabolic risk factors, independent of muscle loss. Recent studies have clarified the relationship between physical frailty and the gut microbiome. Van Tongeren et al. evaluated the relationship between the gut microbiome diversity and frailty scores in the older population. Their results showed that the proportion of Lactobacilli, Bacteroides/Prevotella, and Faecalibacterium prausnitzii was significantly decreased, whereas the proportion of Enterobacteriaceae was significantly increased in older individuals with high frailty scores. Claesson et al. also observed an association between the gut microbiome diversity and the Functional Independence Measure, the Barthel index (daily routine activity scale), and nutrition. Their results demonstrated a correlation between decreased gut microbiome diversity and increased frailty with high levels of inflammatory markers.

Studies have shown that the gut microbiome is related to senescence. One study suggested that healthy gut microbiome characteristics, such as a high biodiversity, a high representation of SCFA producers, a representation of bacteria with beneficial metabolic activity, and a low representation of pathogens, are strongly correlated with a prolonged lifespan. Healthy centenarians show remarkable gut microbiome characteristics compared with healthy older individuals. The gut microbiome of older adults who stay healthy is similar to that of young people aged 30–50 years. These studies are important because they indicate that positive changes in the gut microbiome through lifestyle habits may lead to improved healthy aging. In one study, individuals in a village with a high percentage of longevity were recruited to participate in gut microbiome research. The author studied eight centenarians (100–108 years of age), eight individuals aged 85–99 years residing in the same village, and eight older residents aged 80–92 years from other urbanized villages. Their results showed decreased ratios of Faecalibacterium and Akkermansia, increased ratios of Escherichia group and Methanobrevibacter, and altered ratios of Bacteroidetes in the gut microbiome of centenarians. Another cohort study of individuals ranging from young children to semi-supercentenarians (105–109 years of age) investigated the overall changes in the gut microbiome profile with age. The results indicated that the characteristics of the gut microbiome tended to significantly change with age. Notably, in adults over 95 years of age, the ratios of Faecalibacterium, Roseburia, Coprococcus, and Blautia were decreased, whereas those of Enterobacteriaceae were increased.

To determine the changes in the gut microbiomes of semi-supercentenarians, Biagi et al. conducted a study including young adults (30 years old), older adults (65–75 years), centenarians (99–104 years), and semi-supercentenarians (105–109 years old). Their results demonstrated that the composition of the gut microbiome had a positive effect on the host’s immune system; in that study, the proportions of Christensenellaceae, Akkermansia, and Bifidobacterium were significantly increased, although the gut microbiomes of
centenarians and semi-supercentenarians had characteristics common to those of older populations.49) More specifically, Akkermansia and Bifidobacterium are well-known health-related genera that can promote immune regulation, prevent inflammation, and maintain healthy metabolic homeostasis.33) Future studies are needed to provide clear evidence that specific bacterial taxa can prolong life by maintaining metabolic homeostasis in older individuals.

Although age-related alterations in the gut microbiome have been studied extensively, the functional ability of the gut microbiome is not yet fully understood. One pilot study reported that the gut microbiome of centenarians showed increased proteolytic ability.37) Although the abundance of genes related to carbohydrate metabolism markedly decreased, the abundance of genes associated with the metabolism of aromatic amino acids (e.g., tryptophan and phenylalanine) and other amino acids (lysine, valine) that are closely related to aging increased.7) That pilot study demonstrated the need for more studies to confirm the potential functional capabilities of the gut microbiome.7)

Gut microbiome and sarcopenia
Frailty and sarcopenia are overlapping concepts that are common in older adults.46) In particular, sarcopenia is a syndrome characterized by a lower muscle mass, quality, and strength.36) Although there are numerous causes of sarcopenia, gut microbiota can affect skeletal muscle homeostasis through microbiota-induced metabolites, suggesting a possible biological basis toward the onset of sarcopenia.37) Adequate control of the gut microbiome is required to prevent sarcopenia because the gut microbiome may be involved in the physiopathological mechanism of sarcopenia. The gut microbiome plays a crucial role in determining skeletal muscle mass, muscle structure, and muscle function.20,38) Mice with sarcopenia have gut microbiome characteristics distinct from those of normal mice.26,39) SCFA producers, such as Faecalibacterium, Clostridium XIVa, and Butyricoccus, are positively correlated with skeletal muscle mass. The microbiome can also contribute to muscle anabolism.9) The circulation of SCFA byproducts of the gut microbiome, especially butyrate, in the body can positively influence skeletal muscle mass and function by regulating insulin sensitivity and inflammatory signals.40) Furthermore, imbalances in the gut microbiome arise with age, which can cause a syndrome called ‘leaky gut’, in which gut microbiota can pass into the blood and promote inflammation. The activation of inflammation can inhibit the synthesis of skeletal muscle.40) A previous study analyzing the serum microbiomes of younger (20–35 years) and older (60–75 years) participants revealed a higher abundance of Bacteroidetes phylum than that in older participants. The increase in Bacteroidetes was positively related to the levels of insulin-like growth factor 1 (IGF-1), which can act as an anabolic agent.41) In contrast, inflammatory biomarkers such as interleukin 6 (IL-6) and tumor necrosis factor (TNF)-alpha are negatively correlated with the abundance of Bacteroidetes.41)

Effect of exercise on the gut-muscle axis
As mentioned earlier, the proportions of bacteria that produce SCFAs are high in the gut microbiomes of centenarians. Older individuals with frailty show reduced representation of SCFA producers (e.g., Faecalibacterium prausnitizii).43) As exercise training can increase the representation of SCFA producers,15) alteration of gut microbiomes, especially SCFA producers, by exercise may improve physical frailty. Previous studies have shown that moderate-intensity exercise can lead to significant changes in the gut microbiome. For example, the representation of the Butyricimonas, Prevotella, and Akkermansia taxa increase. This can increase biodiversity and promote metabolic activity.16,43) In addition, adult women with active lifestyles have higher rates of several health-promoting bacteria (Akkermansia, Faecalibacterium, and Roseburia) than do age-matched women.46) A recent study reported that athletes are more likely to express bacterial genes associated with SCFA-producing bacteria and carbohydrate amino acid metabolism compared with the general population.34) This may contribute to higher concentrations of acetate, butyrate, and propionate in athletes.15) These preliminary studies suggest that exercise training may prevent physical frailty by increasing SCFA producers in the gut microbiome.

Among the byproducts of the gut microbiome, SCFAs have been the most studied. They mainly act on skeletal muscle and mitochondria by promoting insulin sensitivity, inflammation regulation, and anabolism.5,46) SCFAs produced by the gut microbiome (e.g., Faecalibacterium, Butyricimonas, etc.) can enter systemic circulation and be absorbed into skeletal muscle. Free fatty acid receptors 2 and 3 (FFAR-2 and FFAR-3) can promote insulin sensitivity and regulate glucose uptake.47) SCFAs can also activate mitochondrial biosynthesis regulator NAD-dependent deacetylase sirtuin-1 (SIRT1) receptors.49) The most intriguing mediator among SCFAs is butyrate, which affects the activity of several regulatory pathways (e.g., UCP2-AMPK-ACC and PGC1-alpha) and improves ATP production and myofiber metabolism efficiency.40) Treatment with probiotics, including the major SCFA producer Faecalibacterium prausnitizii, was also effective in reducing systemic inflammation in mice and promoting assimilation to produce healthy muscles.40)
to attract attention. Cognitive frailty is defined as a syndrome in older individuals with physical frailty and cognitive dysfunction. Cognitive dysfunction can cause neurodegenerative disorders such as Alzheimer disease (AD) and Parkinson disease. Recent studies have reported a strong association between imbalance in the gut microbiome and cognitive dysfunction (e.g., dementia). In particular, gut microbiomes known to be harmful to the host can accelerate the onset of dementia. Studies have focused on microbial byproducts in blood or brain tissue to investigate the potential role of the gut microbiome in the development of dementia. The percentages of mannitol, succinic acid, and 3,4-dihydroxybenzeneacetic acid, which are byproducts of microorganisms, are higher in patients with AD, who have different gut micro-organisms compared to those in normal controls. In addition, lipopolysaccharide (LPS) derived from Gram-negative bacteria has been recently reported in the hippocampal and neocortex tissues of patients with AD. An imbalance of the gut microbiome in these patients can cause the accumulation of by-products in brain tissue. The amount of Clostridium difficile in patients with dementia was significantly higher than that in patients without dementia. According to the 16S rRNA microbial profile, the gut microbiome diversity is significantly lower in people with Clostridium clustering. Cyanobacteria within the gut microbiota can synthesize neurotoxins such as saxitoxin and alpha-anatoxin. Moreover, Citrobacter, Escherichia coli, Klebsiella, Mycobacteria, Pseudomonas, Streptococcus, Streptomyces, Staphylococcus, Salmonella, and Bacillus spp. in the gut microbiota can synthesize amyloid peptides. These peptides can be transmitted and accumulate in the brain, resulting in cognitive dysfunction or dementia. Also, reduction of Bifidobacteria and Eubacterium rectale is associated with biomarkers of AD. These results suggest that the gut microbiome may be an essential factor in the pathogenesis of dementia, although the apparent causal relationship between the gut microbiome and neurodegeneration has not yet been elucidated. In one study, comparison of the gut microbiomes of amyloid-positive patients, amyloid-negative patients, and control individuals revealed a low ratio of Eubacterium rectale and a high proportion of Escherichia/Shigella in amyloid-positive patients. Differences in gut microbiomes play a role in controlling amyloid accumulation in the brain through immune regulation. Although the gut microbiome and dementia are highly related, there is limited research on the association of mild cognitive impairment (MCI) with the gut microbiome. Additionally, the relative proportions of microorganisms of the gut microbiota, such as Bifidobacterium, Butyricicoccus, and Clostridium XIVb, were negatively correlated with the presence of cognitive dysfunction in patients with Parkinson disease.

Effect of exercise on gut-brain axis
Although studies have elucidated a relationship between gut health and the brain, the mechanisms by which the exercise-induced gut environment can influence cognitive function remain unknown. Exercise may have a significant effect on cognitive function by altering the gut microbiome because of its strong relationship with cognitive function; thus, exercise may result in positive changes in the gut environment.

The gut-brain axis is a bidirectional communication channel that is regulated by hormones, immunity, and nerve signals. A well-known characteristic of SCFAs is the prevention of obesity by increasing the expressions of glucagon-like peptide 1 and peptide YY, which can induce satiety. In addition, sodium butyrate treatment is effective in increasing the expression of brain-derived neurotrophic factor (BDNF), which acts as an antidepressant. Taken together, an increase in the number of SCFA-producing bacteria resulting from exercise seems to have a potentially significant and beneficial effect on the gut-brain axis.

Exercise affects the gut-brain axis by controlling vagus nerve tension. The vagus nerve affects anti-inflammatory immune regulation and the imbalance of modified vagal activity. The hypothalamic-pituitary-adrenal (HPA) axis is typically affected in patients with depression and inflammatory bowel disease (IBD). Although the potential effects of extrinsic vagal nerve stimulation (VNS) on neuroimmunomodulation are poorly studied, VNS may be effective in controlling conditions such as depression, IBD, etc. that are difficult to treat. The effect of the vagus nerve on the gut microbiome during exercise requires study. However, steady aerobic exercise can lead to a decrease in the resting heart rate and an increase in the input of the vagus nerve to the sinus node. Increased parasympathetic nerve stimulation can last for a long time. Regular aerobic exercise can have the same effect as VNS to induce a potential rise in the cholinergic anti-inflammatory pathway. Although research is lacking, exercise-induced activation of the vagus nerve in the gut microbiome may prevent brain disease.

DISCUSSION
With the gradual development of social and economic environments, sedentary lifestyles are associated with metabolic syndromes, such as obesity, diabetes, etc., that can promote aging. These imbalances can be improved through exercise training to maintain homeostasis. Many mechanisms are involved in the beneficial effects of exercise training on health. Exercise training can activate anti-inflammatory responses, promote the HPA axis, and enforce neuromuscular function. Recently, physical activity has been proposed to alter gut micro-organisms. In addition, exer-
Exercise can promote a healthy state by improving the gut microbiome. However, little is known about the effect of increased physical activity through exercise training on the gut microbiome. Exercise training may lead to positive changes in the gut microbiome. However, the direct or indirect mechanisms by which exercise training does so remain uncertain. It is difficult to elucidate the long-term effects of exercise because the gut microbiota is influenced by several genetic and environmental factors. For this reason, previous studies have primarily sought to demonstrate the correlation between the gut microbiome and physical function. These studies have shown that the gut microbiome has distinct characteristics. This led to the hypothesis that improvements in physical function through exercise training could also be associated with the gut microbiome. On the basis of the effects of exercise that addressed in this review paper, exercise may be a feasible method for preventing or delaying aging.

With age, the gut microbiome becomes imbalanced, which can lead to age-related diseases such as physical frailty and cognitive dysfunction. These geriatric diseases can be effectively controlled by exercise. We examined whether the changes to the gut microbiome resulting from exercise training could have a positive effect on these diseases. Previous studies have reported changes in the diversity of the gut microbiome and specific bacterial groups with exercise training. Therefore, it is important to study alterations in the gut microbiome according to the type and intensity of exercise. However, to our knowledge, no studies have determined which exercise types (e.g., resistance or aerobic exercise) are more effective in influencing the gut microbiome. In previous animal studies, alterations in the gut microbiome through exercise training have been studied mainly in aerobic exercise such as a voluntary running wheel, treadmill, etc. because of the limitations of resistance training. Previous studies categorized aerobic exercise as low-, medium-, and high-intensity to investigate changes in the gut microbiome. However, direct comparison of exercise intensity to determine the most appropriate intensity has not yet been reported. Thus, studies are required to determine the most appropriate exercise intensity to prevent age-related brain and metabolic diseases through the gut microbiome.

CONCLUSION

By interacting with the host, the gut microbiome has an enormous impact on the entire body. Recent studies have consistently reported that the gut microbiome is related to geriatric diseases. As the gut microbiome is changed in the older individuals with altered physiology, it is necessary to determine whether the gut microbiome is involved in the improvement of physical function by exercise and whether exercise training can prevent geriatric diseases in future studies.

CONFLICT OF INTEREST DISCLOSURES

The researchers claim no conflicts of interest.

ACKNOWLEDGEMENTS

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Fracture Experiences and Long-Term Care Initiation among Older Population: Analysis of Korean National Health Insurance Service-Senior Cohort Study

Hye-jin Kim1, Soong-nang Jang1, Ja-kyung Lee1, Yong-Chan Ha2

1Red Cross College of Nursing, Chung-Ang University, Seoul, Korea
2Department of Orthopaedic Surgery, Chung-Ang University College of Medicine, Seoul, Korea

Background: Long-term care is a burden on individuals, families, and society. It is important to find ways to delay the onset of disability to lessen the burden of long-term care in aging societies. Fracture is one of the risk factors that affect physical functions and make older people dependent. This study aimed to examine how much more often older adults who experienced fractures initiated long-term care compared to those who did not, and whether the risk of entering long-term care differed significantly by fracture site.

Methods: The analyses included insurants aged 65 years and over from the Korean National Health Insurance Service-senior cohort study (2002–2013). Cox proportional hazard models were used to calculate the hazard ratios of the first certification of initiation of long-term care after fracture, by fracture site, and for multiple recurrent fractures.

Results: The incidence rate of initial long-term care beneficiaries was approximately 2.5 times higher when older people had experienced fractures; these individuals entered long-term care beneficiary status 3 years earlier compared to those who had no fracture events. Lower extremity fracture and multiple recurrent fractures more than doubled the risk for long-term care.

Conclusion: Additional attention to fracture sites in prevention and rehabilitation settings is warranted to reduce disability and the related long-term care burden.

Key Words: Fractures, Long-term care, Survival analysis, Frail elderly

INTRODUCTION

Healthy aging policies must be established to maintain the health status of older adults and delay the initiation of long-term care (LTC) for as long as possible. Functional decline is one of the main factors for entering LTC; however, a preceding factor for healthy aging is the resilience of disease or injuries inducing disability.1 Fractures significantly affect normal functioning in older adults. It is especially difficult to recover from fractures after surgery and treatment. A vicious cycle begins, as hip fractures increase a patient’s dependency, leading to even more falls.2,3 In addition, limb injuries caused by fractures reduce social activity, productivity, and subsequently, cognitive stimulation to increase the risk of dementia and compromise life expectancy and quality of life.4,5 Injuries, including fractures and dementia, independently increase the demand for LTC and also tend to be associated with one another or occur at the same time.6,7 This synergistic association may lead to a sudden need for LTC.

A study in Germany predicted that disability and increased dependency caused by extremity injuries would increase the incidence of initiation of LTC among older adults.8 The incidence rate of LTC is 2.5 times higher in older adults with extremity injuries and even higher for both lower and upper extremity and severe injuries.9 However, we do not know the net long-term effect of fracture on care needs among the older population. It is particularly important to elaborate on the impact of geriatric fall-related inju-
ries because fractures account for a high proportion of deaths from injuries. Assessing the long-term health effects and care needs of geriatric fractures will help focus interventions on fractures and fall prevention in older populations. However, few studies have assessed the impact of fracture on LTC initiation. Since fracture experience is a life event that can have a sustained influence on body integration, balance, strength, and pain in older individuals, the present study investigated whether the long-term health (or functional) effect of fractures was linked to future dependency.

Accurate evaluation of the impact of fracture events in older adults on the incidence rate of the first certified use of LTC services, the social impact of LTC and fracture prevention policies can be concretely visualized. This study aimed to address the following questions using Korean national cohort data based on National Insurance claim datasets of older adults: is there an impact on the incidence rate of LTC initiation according to older adults’ fracture experience and fracture sites? If yes, what is the magnitude of this impact?

MATERIALS AND METHODS

Data and Sample
We used the Korean National Health Insurance Service-senior sample cohort (NHIS-Senior) data to identify patients with fractures and determine the risk of LTC initiation in older adults. The Korean NHIS-Senior data covered a 10% random sample (n = 558,147) of 5,500,000 total insurants aged 60 years or above from 2002 to 2013. As national health insurance in Korea is mandatory, the NHIS-Senior sample is nationally representative. The cohort comprises five databases on participants’ health insurance eligibility (general characteristics; age, sex, etc.), medical treatments, medical care institutions, health examinations, and LTC utilization. As the national LTC insurance system for older adults began in 2008, the database for LTC utilization has only been established since 2008 (2008–2013), while the other four databases (health insurance eligibility, medical treatments, medical care institutions, and health examinations) were established in 2002. Since its establishment in July 2008, LTC insurance system data were collected every December during the study period. Thus, data on LTC utilization in 2008 could be unclear.

After excluding individuals who were already in LTC in 2008, 447,276 older adults were identified as study samples in 2008 who did not enroll as LTC beneficiaries. They were followed for up to 12 years (2002–2013). The follow-up period (at least 1 year to a maximum of 11 years) varied depending on the occurrence of fractures (independent variables) and onset of LTC (dependent variables). The year of study entry was 2002, and observation of fracture incidence (independent variable) was also launched in 2002. The study was reviewed and approved by the Institutional Review Board of Chung-Ang University (No. 1041078-201607-HR-145-01K).

Dependent variable
We operationally defined ‘LTC initiation’ as receiving LTC insurance benefits for the first time. Beneficiaries of the LTC insurance schemes were individuals who were entered and registered into the LTC system. When assigned to one of three levels of LTC need through screening by the Care Needs Certification Board (including needs assessment), LTC benefits can be provided to applicants aged 65 years and above or geriatric patients under 65 years of age. According to the needs assessment and committee review, LTC services are provided ranging from level 3 (the lowest degree of care) to level 1 (the highest degree of care). The care need levels were further subdivided into five levels following the 2014 revision of the LTC insurance system. We aggregated levels 1-3 as LTC initiation, considering the consistency of the level of care needs. The first certification of LTC from 2009 to 2013 was our final outcome, which was considered the LTC initiation case (1 = LTC initiation, 0 = no).

Independent variables
We defined fractures using claim data from the medical treatments database containing older adults’ inpatient and outpatient diagnoses based on the 10th revision of the International Classification of Diseases (ICD-10) codes. Geriatric fall-related fractures fell into three categories based on the affected region: upper extremity fracture (ICD-10 codes: S52.5, S52.6, S42.2, S42.3), spine fracture (S22.0, S22.1, S32.0, M48.4, M48.5), and lower extremity fracture (S72.0, S72.1) (Table 1).

The fracture was a dummy variable, taking the value 1 if the fracture first occurred from 2002 onwards regardless of the fracture frequency, until 1 year before LTC initiation and 0 otherwise (cases without LTC initiation were followed until death or censoring). Regarding LTC initiation time, as we had the information only on the year of LTC initiation, we could not clarify whether fracture occurred before LTC initiation when they occurred within the same year (for example, when LTC initiation time was 2013, the fracture experience had to be observed from 2002 to 2012). We categorized combined fracture sites if the older adults experienced multiple recurrent fractures at multiple events during the study period. ‘All fracture’ was defined as recurrent fractures in the upper or lower extremities and spine at the same time or sequentially.

We examined demographic and chronic disease variables to explain the characteristics of LTC initiation. The demographics in-
**Table 1. Categorization of fracture sites and matching ICD-10 codes**

<table>
<thead>
<tr>
<th>Categorized fracture sites</th>
<th>ICD-10 code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper extremity fracture</td>
<td></td>
</tr>
<tr>
<td>Distal radius</td>
<td>S22.5</td>
</tr>
<tr>
<td>Fracture of the distal radius</td>
<td>S22.6</td>
</tr>
<tr>
<td>Combined fracture of the distal radius</td>
<td></td>
</tr>
<tr>
<td>Humerus</td>
<td></td>
</tr>
<tr>
<td>Fracture of the proximal humerus</td>
<td>S42.2</td>
</tr>
<tr>
<td>Fracture of shaft of humerus</td>
<td>S42.3</td>
</tr>
<tr>
<td>Spine fracture</td>
<td></td>
</tr>
<tr>
<td>Fracture of the thoracic spine</td>
<td>S22.0</td>
</tr>
<tr>
<td>Multiple fractures of the thoracic spine</td>
<td>S22.1</td>
</tr>
<tr>
<td>Fracture of the lumbar spine</td>
<td>S32.0</td>
</tr>
<tr>
<td>Fatigue fracture of vertebra</td>
<td>M48.4</td>
</tr>
<tr>
<td>Collapsed vertebra</td>
<td>M48.5</td>
</tr>
<tr>
<td>Lower extremity fracture</td>
<td></td>
</tr>
<tr>
<td>Fracture of the femoral neck</td>
<td>S72.0</td>
</tr>
<tr>
<td>Femoral neck fracture</td>
<td>S72.1</td>
</tr>
</tbody>
</table>

ICD-10, International Classification of Diseases, 10th Revision.

...continued age and sex. As the age of individuals in the cohort began at 67 years, age was grouped into four categories (67-74, 75-84, 85-94, and 95+ years). Common chronic diseases were included as dummy variables, taking the value 1 if the diseases first occurred from 2002 onwards until 1 year before LTC initiation and 0 otherwise. We determined the chronic diseases used as covariates after consulting with four medical doctors specialized in orthopedic surgery, rehabilitation medicine, and geriatric medicine. The chronic diseases included hypertension (ICD-10 codes: I10-I11), diabetes (E10-E14), ischemic diseases (I20-I25), cerebral diseases (I60-I69), hypercholesterolemia (E780), atrial fibrillation (I48), heart insufficiency (I50), lung insufficiency (J44), nervous diseases (including Parkinson disease; G20-G22), gastric diseases (K0-K9), alcoholic liver disease (K70), atherosclerosis (J70), pneumonia (J12-J18), infections or parasites (A-B), external injuries (S-T, V-Y), dementia—Alzheimer disease, vascular dementia, Lewy body dementia, circumscribed brain atrophy, dementia as a side-effect of another disease, others not specified as dementia (F00/G30, F01, G31.82, G31.0, F02, F05.1, G23.1, F03), cancer (C00-C97), osteoporosis (M80, M81, M82), arthritis (osteoarthritis, rheumatoid arthritis; M15-M19, M05, M06), orthostatic hypotension (I95.1), chronic kidney disease (N18), urinary incontinence (N39.3, N39.4, N39.40, N39.41, N39.48), and depressive disorder (F32, F33).

**Statistical Analysis**

We performed descriptive statistics using frequency and percentage of the total study population. Regarding the characteristics of LTC initiation cases, person-year exposures and the incidence rate of LTC initiation per 100 person-years were calculated. Kaplan-Meier survival curves and Cox proportional hazard models were used to examine fractures and the risk of LTC initiation after adjusting for age, sex, and chronic diseases. A stratified log-rank test was used to compare LTC initiation among groups with different types of fractures by the affected sites. Fracture sites were categorized as upper extremity, lower extremity, and spine. The hazard ratios for each fracture site were calculated since fractures were recorded as multiple events. Multiple fracture sites were categorized as seven types: upper extremity fracture only, lower extremity fracture only, spine fracture only, spine fracture only, upper extremity and spine fracture, upper and lower extremity fracture, spine and lower extremity fracture, and all three fracture types. LTC initiation was available annually but there was no information on ‘day’ or ‘month’; therefore, the results were presented by yearly age. If death and LTC initiation occurred in the same year during the study period, LTC initiation was counted. Since we could not clarify whether fractures or other diseases occurred before LTC initiation when they occurred within the same year, records of fractures and other diseases were observed until 1 year prior to LTC initiation. The statistical definition for the censoring event was ‘death or no LTC initiation’ by the end of the study period, while the complete event was the ‘year of first LTC initiation’. The effects of age can affect not only dependent variables but also independent variables. The variance inflation factor (VIF) and condition index showed no age and fracture multicollinearity. Thus, we included all covariates in the Cox proportional hazard models. Analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

**RESULTS**

Table 2 shows the exposure and incidence rates of LTC initiation by the demographic and disease characteristics of the participants starting from 2009. Of the 447,276 individuals, 43% were men and 57% were women. Most (56.6%) of their ages ranged from 75 to 84 years. The fracture experience rate was 9.8%. Among chronic diseases, 21.9% of the participants had cerebral disease, 6.8% had dementia, 2.3% had nervous diseases including Parkinson disease, and 11.1% had depressive disorders. A total of 71,706 older adults entered LTC between 2009 and 2013; among them, around 64% were women and about 63% were aged 75-84 years.

The incidence rate of LTC initiation was 4.6 cases per 100 persons (95% confidence interval [CI], 4.6-4.6). The incidence of LTC initiation was higher among women (5.0) than men (4.0) and increased with age. The incidence was 13 times higher among the oldest age group (over 95 years; 26.0) compared to that in old-

<table>
<thead>
<tr>
<th>Variable</th>
<th>%</th>
<th>Exposure (person-year)</th>
<th>Case of LTC initiation</th>
<th>Incidence rate per 100 person-year (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>1,561,880</td>
<td>71,706</td>
<td>4.6 (4.6–4.6)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>43.0</td>
<td>650,553</td>
<td>25,839</td>
<td>4.0 (3.9–4.0)</td>
</tr>
<tr>
<td>Female</td>
<td>57.0</td>
<td>911,327</td>
<td>45,867</td>
<td>5.0 (5.0–5.1)</td>
</tr>
<tr>
<td>Age (y)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>67–74</td>
<td>38.4</td>
<td>609,895</td>
<td>13,978</td>
<td>2.3 (2.3–2.3)</td>
</tr>
<tr>
<td>75–84</td>
<td>56.6</td>
<td>899,253</td>
<td>45,331</td>
<td>5.0 (5.0–5.1)</td>
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<tr>
<td>85–94</td>
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<td>51,990</td>
<td>12,204</td>
<td>23.5 (23.1–23.9)</td>
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<tr>
<td>95+</td>
<td>0.1</td>
<td>742</td>
<td>193</td>
<td>26.0 (26.0–29.9)</td>
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<td>Fracture</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>90.2</td>
<td>1,418,137</td>
<td>57,012</td>
<td>4.0 (4.0–4.1)</td>
</tr>
<tr>
<td>Yes</td>
<td>9.8</td>
<td>143,743</td>
<td>14,694</td>
<td>10.2 (10.1–10.4)</td>
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<tr>
<td>Fracture sites*</td>
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<tr>
<td>Upper fracture</td>
<td>3.9</td>
<td>58,921</td>
<td>6,022</td>
<td>10.2 (10.0–10.5)</td>
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<tr>
<td>Spine fracture</td>
<td>5.1</td>
<td>74,488</td>
<td>6,549</td>
<td>8.8 (8.6–9.0)</td>
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<tr>
<td>Lower fracture</td>
<td>1.7</td>
<td>15,758</td>
<td>2,863</td>
<td>18.2 (17.5–18.8)</td>
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<tr>
<td>Multiple fracture sites†</td>
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<td></td>
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<tr>
<td>Upper extremity only</td>
<td>3.3</td>
<td>51,364</td>
<td>4,668</td>
<td>9.1 (8.8–9.4)</td>
</tr>
<tr>
<td>Spine only</td>
<td>4.5</td>
<td>66,007</td>
<td>19,923</td>
<td>30.2 (29.8–30.6)</td>
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<tr>
<td>Lower extremity only</td>
<td>1.3</td>
<td>16,233</td>
<td>5,647</td>
<td>34.8 (33.9–35.7)</td>
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<tr>
<td>Upper &amp; spine fracture</td>
<td>0.4</td>
<td>5,462</td>
<td>1,709</td>
<td>31.3 (29.8–32.8)</td>
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<tr>
<td>Upper &amp; lower fracture</td>
<td>0.1</td>
<td>1,658</td>
<td>641</td>
<td>38.7 (35.8–41.7)</td>
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<td>Spine &amp; lower fracture</td>
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<td>2,582</td>
<td>946</td>
<td>36.6 (34.4–39.0)</td>
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<tr>
<td>All fractures</td>
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<td>437</td>
<td>171</td>
<td>39.1 (35.6–45.3)</td>
</tr>
<tr>
<td>No fracture</td>
<td>90.2</td>
<td>1,418,137</td>
<td>57,012</td>
<td>4.0 (4.0–4.1)</td>
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<tr>
<td>Chronic disease prevalence</td>
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<td></td>
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<tr>
<td>Cerebral disease</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>No</td>
<td>78.1</td>
<td>1,240,914</td>
<td>35,782</td>
<td>2.9 (2.9–2.9)</td>
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<td>Yes</td>
<td>21.9</td>
<td>320,966</td>
<td>35,924</td>
<td>11.1 (11.2–11.3)</td>
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<tr>
<td>Nervous disease</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>97.7</td>
<td>1,529,977</td>
<td>65,430</td>
<td>4.3 (4.2–4.3)</td>
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<tr>
<td>Yes</td>
<td>2.3</td>
<td>31,903</td>
<td>6,276</td>
<td>19.7 (19.2–20.2)</td>
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<tr>
<td>Dementia</td>
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<td></td>
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</tr>
<tr>
<td>No</td>
<td>93.2</td>
<td>1,470,367</td>
<td>51,967</td>
<td>3.5 (3.5–3.6)</td>
</tr>
<tr>
<td>Yes</td>
<td>6.8</td>
<td>91,513</td>
<td>19,739</td>
<td>21.6 (21.3–21.9)</td>
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<tr>
<td>Orthostatic hypotension</td>
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<td></td>
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<td></td>
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<tr>
<td>No</td>
<td>99.8</td>
<td>1,558,994</td>
<td>71,420</td>
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<tr>
<td>Yes</td>
<td>0.2</td>
<td>2,886</td>
<td>286</td>
<td>9.9 (8.8–11.1)</td>
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<tr>
<td>Depressive disorder</td>
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<tr>
<td>No</td>
<td>88.9</td>
<td>1,391,034</td>
<td>56,985</td>
<td>4.1 (4.1–4.1)</td>
</tr>
<tr>
<td>Yes</td>
<td>11.1</td>
<td>170,846</td>
<td>14,721</td>
<td>8.6 (8.5–8.8)</td>
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<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No</td>
<td>37.5</td>
<td>589,487</td>
<td>11,365</td>
<td>1.9 (1.9–2.0)</td>
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<tr>
<td>Yes</td>
<td>62.5</td>
<td>922,705</td>
<td>39,987</td>
<td>4.3 (4.3–4.4)</td>
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<tr>
<td>Diabetes mellitus</td>
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<td></td>
<td></td>
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<tr>
<td>No</td>
<td>66.3</td>
<td>1,043,049</td>
<td>39,623</td>
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<td>Yes</td>
<td>33.7</td>
<td>518,831</td>
<td>32,083</td>
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<td>Ischemic disease</td>
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<td></td>
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<tr>
<td>No</td>
<td>78.4</td>
<td>1,229,998</td>
<td>51,743</td>
<td>4.2 (4.2–4.2)</td>
</tr>
</tbody>
</table>
er adults (67-74 years; 2.3). Of the total cohort participants who entered LTC, around one in four cases experienced fracture (n = 14,694). The incidence of LTC initiation was 10.2 per 100 person-years, approximately 2.5 times higher among participants who experienced fractures compared to those who did not. Those who experienced upper extremity fractures entered LTC at 10.2

Table 2. Continued

<table>
<thead>
<tr>
<th>Variable</th>
<th>%</th>
<th>Exposure (person-year)</th>
<th>Case of LTC initiation</th>
<th>Incidence rate per 100 person-year (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>21.6</td>
<td>331,882</td>
<td>19,963</td>
<td>6.0 (5.9–6.1)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Yes</td>
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<td>153,327</td>
<td>7,720</td>
<td>5.0 (4.9–5.2)</td>
</tr>
<tr>
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<td>1,408,553</td>
<td>63,986</td>
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<td>96.9</td>
<td>1,517,679</td>
<td>67,785</td>
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<td>44,201</td>
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</tr>
<tr>
<td>Atrial fibrillation</td>
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<td>101,800</td>
<td>9,664</td>
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<td>Heart insufficiency</td>
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<td>Lung insufficiency</td>
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<tr>
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<td>65,427</td>
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<td>Gastric diseases</td>
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<td>4,998</td>
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<td>Osteoporosis</td>
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<td>466,043</td>
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<td>1,005,209</td>
<td>50,314</td>
<td>5.0 (5.0–5.1)</td>
</tr>
<tr>
<td>No</td>
<td>36.2</td>
<td>556,671</td>
<td>21,392</td>
<td>3.8 (3.8–3.9)</td>
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<tr>
<td>Urinary incontinence</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Yes</td>
<td>97.7</td>
<td>1,526,426</td>
<td>68,370</td>
<td>4.5 (4.5–4.5)</td>
</tr>
<tr>
<td>No</td>
<td>2.3</td>
<td>35,454</td>
<td>3,336</td>
<td>9.4 (9.1–9.7)</td>
</tr>
</tbody>
</table>

LTC, long-term care; CI, confidence interval.
*Fracture experience at each site, multiple cases.
†Combinations of fracture sites during the observation period.
cases per 100 person-years, while LTC initiation of lower extremity and spinal fractures were 18.2 and 8.8 cases per 100 person-years, respectively. The incidence rate of LTC initiation was 21.6% among older adults with dementia, 19.7% in those with nervous disease, and 11.1% in those with cerebral disease.

Fig. 1 shows the Kaplan-Meier curve of the incidence rate of LTC initiation depending on fracture experience and fracture sites according to sex. The incidence rate of LTC initiation was significantly higher among men and women who had previously experienced fractures than those without fractures. Half of all men and women required LTC around 87 years of age. In addition, half of the older adults with previous fractures entered LTC at age 84 compared to age 87 in people with no fracture history. Thus, older adults with fracture entered LTC around 3 years earlier than those without (Fig. 1A, 1B and Appendix 1). Moreover, men with fractures of all three sites (upper extremity, spine, and lower extremity) entered LTC 10 years earlier than those without any fractures, compared to 6 years earlier in women (Appendix 1).

Regarding the hazard ratio of LTC initiation by fracture experience, the hazard ratios increased 1.66-fold (95% CI, 1.61-1.71), 1.36-fold (95% CI, 1.32-1.40), and 2.25-fold (95% CI, 2.17-2.33) for the upper extremity, spinal, and lower extremity fracture groups, respectively, compared to those in the non-fracture group after adjusting for age, sex, and chronic diseases. Among participants in the all-fracture group with multiple recurrent fractures of the upper extremity, spine, and lower extremity, the hazard ratio increased 3.21-fold (95% CI, 2.71-3.81). Among those with chronic diseases, the hazard ratio of LTC initiation was highest for those with dementia (2.60; 95% CI, 2.55-2.65) compared with those without dementia (Table 3).
Table 3. Hazard ratios of long-term care initiation by age, sex, fracture site, and chronic disease

<table>
<thead>
<tr>
<th>Variable</th>
<th>aHR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>67–74</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>75–84</td>
<td>1.68 (1.65–1.71)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>85–94</td>
<td>6.33 (6.17–6.49)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>95+</td>
<td>6.28 (5.44–7.24)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1.03 (1.01–1.05)</td>
<td>0.0035</td>
</tr>
<tr>
<td>Multiple fracture sites</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No fracture</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Upper extremity</td>
<td>1.66 (1.61–1.71)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Spine extremity</td>
<td>1.36 (1.32–1.40)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Lower extremity</td>
<td>2.25 (2.17–2.33)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Upper extremity &amp; spine</td>
<td>2.03 (1.89–2.18)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Upper &amp; lower extremity</td>
<td>2.97 (2.70–3.26)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Spine &amp; lower extremity</td>
<td>2.12 (1.94–2.31)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>All fractures</td>
<td>3.21 (2.71–3.81)</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

aHR, adjusted hazard ratio; CI, confidence interval. The Cox proportional hazard model was adjusted for 22 chronic diseases as covariates.

DISCUSSION

The results of our analyses revealed three sets of patterns associated with fracture experience and LTC initiation in the Korean older population. First, fracture was associated with the probability of becoming an LTC recipient, increasing from 1.66- to 3.21-fold according to the fracture site within 10 years. In other words, those who experienced fractures entered LTC 3 years earlier. Secondly, the results varied according to the fracture site. The probability of becoming an LTC recipient was more than two times higher in those who had at least one lower extremity fracture. Thirdly, the variety of fracture sites was also important. Experiencing multiple recurrent fractures in both upper, lower extremity and spine increased the risk of entering LTC by more than 3-fold compared to the risk in the non-fracture group and was higher than the risk of entering LTC in patients with dementia. These results confirmed that the long-term outcome in patients with fractures differs by fracture site and multiple fracture sites. Given that the national LTC expenditure is about $4 billion in Korea, older individuals entering LTC 3 years earlier may significantly increase the LTC cost burden.

LTC initiation was significantly higher for lower extremity fractures. Hip fractures undermine disability-adjusted life years in older adults, thereby increasing disease burdens. This may be because lower extremity fractures lead to mobility limitation. Indeed, the likelihood of returning to the previous level of mobility is low in hip fracture patients. Only 34% of older adults who sustained a hip fracture returned to pre-fracture mobility function. Physical activity, balance, and mobility have been repeatedly demonstrated to be beneficial for improving physical function in older adults in terms of short-term and long-term effects. These results support the efficacy of preventing lower extremity fracture and restoring function and mobility to pre-fracture levels as to delay the need for LTC.

Multiple recurrent fractures in various body parts proved to be a stronger marker than dementia of a future need for LTC. This fracture-prone condition can be classified into high fall-risk, frail, and/or osteoporotic status in old ages. In this condition, a vicious cycle begins in which the slow recovery from fractures due to a fall and increased dependency lead to additional falls. To prevent multiple recurrent fractures among older adults, bone health promotion, fall prevention, and management after fall incidence must be performed simultaneously. In addition, comorbidity including osteoporosis, dementia, and other diseases must be considered. Fractures can also give rise to neurodegenerative diseases such as Parkinson disease and dementia (a major factor of LTC initiation), which may indirectly enhance care needs. A decrease in social activity due to fracture can also reduce cognitive stimulation and act as a risk factor for dementia. The study in Germany reported a higher rate of LTC initiation in people who experienced both dementia and extremity injuries compared to that in those who experienced each disease independently. Dementia may affect fractures and is a major factor associated with an increased rate of hospitalization due to fracture.

The difference in LTC initiation by fracture site was shared between men and women. However, the Kaplan-Meir curves showed a sex difference in the age of LTC onset. Men with extremity fractures entered LTC about 3 years earlier than those with spine fracture, while women entered LTC only 1 year earlier. In addition, participants with diverse fracture sites also became LTC recipients much earlier. Men with fractures of the upper and lower extremities and spine, regardless of whether they occurred simultaneously, became LTC recipients 10 years earlier than men without any fractures, compared to 6 years earlier in women. This result suggests that the fracture severity might be higher in men than in women. Several studies also reported higher mortality and institutionalization rates after hip fracture in men than in women. Our results add to this evidence by showing sex differences and the exact degrees of risk for initiating LTC in men and women.

The enormous individual and social burdens due to LTC in older adults may be reduced through interventions addressing the risk factors for lower extremity and multiple recurrent fractures.
ventions targeting fracture prevention and rehabilitation such as exercise therapy and environmental management are effective in terms of disability and physical function. These interventions should also consider sex differences in the impact of fractures.

Several limitations warrant consideration in generalizing our observations. First, since the National Health Insurance Service provides only limited datasets retrieved from insurance claim databases, analyses were performed for LTC initiation in a limited time. The data lacked information on socio-economic status, health behaviors, fall incidence, and other risk factors for fractures and LTC needs. Second, LTC initiation was only considered if it occurred within the years after the fracture. If the fracture was the reason for obtaining benefits from LTC insurance and occurred within the first 6 months, the information on the time of LTC initiation might be not accurate. Fractures that occurred 2-3 years before the first onset of LTC may be more closely related to the cause of disability, especially for cases requiring hospitalization. Consideration should be given to when the fracture occurred, and it is also necessary to distinguish between hospitalization and outpatient use after fractures. Third, although the use of medications can increase the risk of falls and fractures through various mechanisms and also affect LTC initiation, we excluded drug data. The overreporting of geriatric-related fractures might be due to the inclusion of the accident-driven fractures. Moreover, there was a lack of reliable information on fragility fractures based on clinical data.

In conclusion, fractures led to a nearly 2.5-fold increase in the risk of LTC initiation among older adults even after adjusting for chronic diseases in the model. To our knowledge, this is the first longitudinal study to report the association between fracture sites and LTC initiation using a nationally representative cohort data from older adults in Korea. A strong emphasis is needed on the prevention of geriatric-related fractures as a top priority strategy in actions to delay the initiation of LTC; it is important to build on the resilience of the older population and a sustainable society. In order to delay the onset of disability and to maintain independent lives as long as possible, prevention of fracture and sufficient rehabilitation care after fracture must be considered key interventions in LTC policies.

CONFLICT OF INTEREST DISCLOSURES

The researchers claim no conflicts of interest.

ACKNOWLEDGEMENTS

This work was supported by the Chung-Ang University Research Scholarship Grants in 2017, and the Korea Health Technology R&D Project through the Korea Health Industry Development Institute funded by the Ministry of Health & Welfare, Republic of Korea (No. HC15C1189). This study used the administrative claims data from Korean National Health Insurance Service (No. NHIS-2017-2-362). Data access was legally approved by Korean National Health Insurance Service and individual patients cannot be identified. The sponsors and Korean National Health Insurance Service had no role in this study.

REFERENCES

11. Papadimitriou N, Tselidis KK, Orfanos P, Benetou V, Ntzani EE,


### Appendix 1. Age (y) of long-term care initiation from life tables of survival analysis

<table>
<thead>
<tr>
<th></th>
<th>25% initiation</th>
<th></th>
<th>50% initiation</th>
<th></th>
<th>75% initiation</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>No fracture</td>
<td>82</td>
<td>82</td>
<td>87</td>
<td>87</td>
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<td>91</td>
</tr>
<tr>
<td>Upper extremity fracture only</td>
<td>79</td>
<td>80</td>
<td>83</td>
<td>84</td>
<td>87</td>
<td>87</td>
</tr>
<tr>
<td>Spine fracture only</td>
<td>82</td>
<td>81</td>
<td>86</td>
<td>85</td>
<td>90</td>
<td>90</td>
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<tr>
<td>Lower extremity fracture only</td>
<td>78</td>
<td>80</td>
<td>83</td>
<td>84</td>
<td>88</td>
<td>88</td>
</tr>
<tr>
<td>Upper extremity &amp; spine fracture</td>
<td>76</td>
<td>79</td>
<td>83</td>
<td>83</td>
<td>84</td>
<td>86</td>
</tr>
<tr>
<td>Upper extremity &amp; lower extremity fracture</td>
<td>77</td>
<td>78</td>
<td>81</td>
<td>82</td>
<td>84</td>
<td>86</td>
</tr>
<tr>
<td>Spine &amp; lower extremity fracture</td>
<td>79</td>
<td>79</td>
<td>82</td>
<td>83</td>
<td>89</td>
<td>88</td>
</tr>
<tr>
<td>All fractures</td>
<td>73</td>
<td>78</td>
<td>77</td>
<td>81</td>
<td>84</td>
<td>85</td>
</tr>
</tbody>
</table>
Background: The older population (≥65 years) has rapidly increased in size in recent years. Among them, the middle-to-oldest-old (≥75 years) tend to have a poor health status. Therefore, subdivision and evaluation of older patients with traumatic injury are required. We focused on the risk of femoral intertrochanteric fractures occurring in older adults due to minor falls and compared young-old and middle-to-oldest-old populations.

Methods: The medical records of patients who visited the emergency center due to hip injuries between March 2017 and March 2019 were retrospectively analyzed. Patients were divided into older adult (≥65 years) and non-older (age 18–64 years) groups; the older adult group was subdivided into young-old (65–74 years), middle-old (75–84 years), and oldest-old (≥85 years) groups. This study investigated the occurrence rate of femoral intertrochanteric fractures and related factors.

Results: The older adult group had a higher incidence of femoral intertrochanteric fractures than that in the non-older adult group (95.3% vs. 4.7%, p<0.001). However, there was no significant difference between young-old and non-older groups (58.8% vs. 41.2%, p=0.145). Middle-old to oldest-old age and osteoporosis were associated with an increased incidence of femoral intertrochanteric fractures (p<0.001, p=0.004).

Conclusion: A higher incidence of femoral intertrochanteric fractures from minor falls was found among middle-old to oldest-old patients compared to that in young-old patients. Therefore, physicians should perform more thorough physical examinations and radiograph reading in middle-old to oldest-old patients even if the patients do not complain of pain.

Key Words: Older adults, Accidental falls, Intertrochanteric fractures, Emergency

INTRODUCTION

The proportion of the older population aged ≥65 years in Korea was about 14.1% in 2015 and is expected to increase to greater than 20% by 2025, becoming a so-called ‘super-aged society’. This is the fastest annual aging rate in the world. With a rapid increase in the older population, the lack of medical research focusing on the older population is a major concern. The increase in the older adult population leads to their increased participation in social and leisure activities, thus increasing the frequency of trauma in this population. Furthermore, aging is significantly associated with decreased physiological ability, which is a cause of trauma, requiring special medical needs and treatment compared to other age groups.

Injuries from falls are the most common and major cause of trauma in older adults. This age group has a higher frequency and risk of falls than those of younger age groups. Falls among older adults also cause severe spontaneous damages and complications. Generally, as the number of older individuals hospitalized has increased recently, minor falls have also increased. The injuries and damage sustained from minor falls are more severe in older adults than...
those in non-older age groups. 

Many people visit emergency centers due to hip injuries caused by minor falls. Hip fractures are more likely to occur in older than in younger patients. Femur intertrochanteric fractures, usually caused by minor falls in older adults with osteoporosis, are the most common type of fracture around the hip. The frequency of femur intertrochanteric fractures is climbing due to the increased average life expectancy of older adults. Furthermore, diagnosis of these fractures may not be possible by simple plain radiography, thus, careful interpretation of radiographs and physical examination may be needed.

In younger patients, fractures are rare and more likely to be diagnosed because of severe resting pain. However, older patients usually experience more fractures than expected and less often complain of pain than younger individuals. Hence, increased time and effort are needed for the diagnosis of older patients with hip injuries caused by minor falls.

As the overall health status of older adults has gradually increased, their health conditions vary depending on their age. Therefore, the older adult population may have to be subdivided. Although the criteria differ, several studies have proposed divisions of this group into early and late (75 years) old age or young-old, middle-old, and oldest-old age for 65–74, 75–84, and at least 85 years, respectively. In Korea, the proportion of older individuals aged > 85 years is increasing rapidly, from approximately 60,000 in 1980 to an estimated 530,000 by 2015 and 1.15 million by 2026, the highest increase rate among all age groups.

Among older adults, the young-old have remained healthier than their counterparts in the past due to their better economic and nutritional status and frequent medical checkups. Therefore, the degree of damage and aftereffects that they acquire may differ for various traumas. Additionally, we have observed a rapid increase in the frequency of older patients visiting the emergency centers and who are diagnosed with intertrochanteric fractures due to minor fall injury. However, to our knowledge, no studies have yet been conducted to determine the incidence of femur intertrochanteric fractures among the rapidly increasing hip injuries of older adults.

Therefore, we investigated the differences in the incidence of femoral intertrochanteric fracture with age. Additionally, we aimed to determine the ages of patients who should be actively diagnosed with intertrochanteric fractures through examinations such as computed tomography (CT) scans.

**Materials and Methods**

**Patients**
The present study retrospectively reviewed the medical records of patients > 18 years of age who visited the emergency center due to hip injuries between March 2017 and March 2019. This emergency center is a local emergency center located in Seoul that sees approximately 30,000 patients annually. During the study period, 893 patients with hip injuries visited our emergency center, approximately 851 of whom were > 18 years of age.

Among these, 598 patients were included in the study. The reasons for exclusion included a mechanism of injury that was not a fall or was unclear, the patient was transferred to another hospital, missing or incorrect medical records, or lack of examination due to patient refusal or death upon visit. The study was approved by the Institutional Review Board of Kyung Hee University Hospital (No. KHUH 2019-07-050). Written informed consents were obtained.

**Study Protocols**

The target patients were divided into those aged > 65 years (older patients) and those aged 18–64 years (non-older patients). The older patients were then classified as young-old (aged 65–74 years), middle-old (75–84 years), or oldest-old (> 85 years). Falls were defined as ‘unexpected falls to the floor or other low position, without loss of consciousness.’ Minor falls were defined as ‘falling from a sitting or standing position to the ground, from a height of less than 1 meter, and below three steps’ and other cases were excluded.

The medical records of patients were reviewed to determine the age, sex, time of accident, drinking alcohol at the time of accident, hip radiograph findings, underlying diseases, and prognosis. The time of accident was defined as the time of the accident described by the patient or caregiver. Drinking alcohol was determined based on the patient’s smell and caretaker and paramedic statements. All hip radiograph examinations were read by imaging specialists and were assessed for the possible presence of femur intertrochanteric fractures. The type of intertrochanteric fracture was classified using Tronzo classification. Underlying diseases included stroke, osteoporosis, Parkinson disease, dementia, and cancer, which are known to affect low-energy fall injury and eventually cause femur intertrochanteric fracture. The prognosis was for patients hospitalized with femoral intertrochanteric fractures and, as of the time of discharge, discharged without complications was classified as a favorable prognosis, while cases of transfer or death due to complications were classified as unfavorable prognosis.

**Statistical Analysis**

The analysis of collected data was performed using PASW Statistics version 18.0 for Windows (SPSS Inc., Chicago, IL, USA). Data on categorical and continuous variables were presented as percentages and mean ± standard deviation, respectively. In univariate analysis, categorical variables were analyzed using chi-squared or Fisher exact
tests; normally-distributed continuous variables were analyzed using independent t-tests (Student t-tests) and normal distributions were analyzed using Shapiro–Wilk tests. Binary logistic regression analysis was performed on variables with significant results in univariate analysis. Findings were considered statistically significant if \( p < 0.05 \).

RESULTS

A total of 893 patients visited the emergency medical center during the study, including patients with pelvic damage. Among these, 598 patients were included in the study, except for 42 patients who were < 18 years of age, 134 patients who were not aware of the causes of their minor falls, 83 patients who were from other hospitals, 34 patients who had missing or incorrect information in their medical records, and 2 patients who did not undergo any examination. Among the patients included in the study, 162 were aged 18–64 years, 117 were in the young-old group (65–74 years), 217 were in the middle-old group (75–84 years), and 102 were in the oldest-old group (> 85 years) (Fig. 1).

A total of 150 patients had femur intertrochanteric fractures; the proportion was significantly higher in older patients than in non-older patients (4.7% vs. 95.3%, \( p < 0.001 \)). Additionally, the incidence of femur intertrochanteric fractures in the middle-old to oldest-old patients was significantly higher than in the non-older adults (92% vs. 8%, \( p < 0.001 \); 88.3% vs. 11.7%, \( p < 0.001 \)), but no significant difference was observed between the young-old patients and the non-older adult patients (58.8% vs. 41.2%, \( p = 0.145 \)). There was no significant difference in the frequency of femoral neck fracture and femoral subtrochanteric fracture (Table 1).

Of the 117 young-old patients, 48 (14%) were men and 69 (59%) were women; of the 217 middle-old patients, 57 (26.3%) were men and 160 (73.7%) were women; of the 102 oldest-old patients, 21 (20.6%) were men and 81 (79.4%) were women. The differences in sex ratios between the three patient groups were statistically significant (\( p = 0.002 \)). The frequency of drinking alcohol was higher in the middle-old patients than in the young-old and oldest-old patients but it was not statistically significant (\( p = 0.392 \)). Among the underlying diseases surveyed, the frequencies of stroke (21.4% vs. 23.5% vs. 21.6%, \( p = 0.877 \)) was higher in the middle-old patients, while those of dementia (0.9% vs. 5.1% vs. 14.4%, \( p < 0.001 \)) and osteoporosis (29.9% vs. 43.8% vs. 70.6%, \( p < 0.001 \)) were higher in the oldest-old patients and the frequencies of Parkinson disease (6.8% vs. 4.6% vs. 4.9%, \( p = 0.673 \)) and cancer (7.7% vs. 3.7% vs. 2.9%, \( p = 0.164 \)) were higher in the young-old than the middle-old to oldest-old patients but only the frequencies of dementia and osteoporosis were statistically significant.

The time of accident was trended higher for each group between 12:00 and 17:59 but was not statistically significant (\( p = 0.114 \)). The frequencies of intertrochanteric fractures were significantly higher in middle-old and oldest-old patients than that in young-old patients (8.5% vs. 36.9% vs. 52.0%, \( p < 0.001 \)) and, while Tronzo type 3 was trend to be higher in middle and oldest-old patient groups, the difference was not statistically significant (\( p = 0.907 \)). The frequency of unfavorable outcomes was trended higher in the middle and oldest-old patients but was also not statistically significant (0% vs. 1.4% vs. 2.9%, \( p = 0.238 \)) (Table 2).

Investigation of the relationship between femoral intertrochanteric fractures in older patients revealed that age > 75 years, sex, and osteoporosis were statistically significant (\( p < 0.001 \), \( p = 0.020 \), \( p < 0.001 \)), while other underlying conditions such as time of accident, drinking alcohol at the time of accident, stroke, dementia, Parkinson disease, and cancer were not. No significant associations were observed between femoral neck and femoral subtrochanteric fractures (Table 3).

A binary logistic regression of the factors that showed statistically significant differences in the single-variable analysis of the relationship between femoral intertrochanteric fractures in the older patients is shown in Table 4.

Fig. 1. Diagram of patients categories.
Table 1. Comparisons of incidence frequencies of femoral intertrochanteric fractures according to age group

<table>
<thead>
<tr>
<th></th>
<th>Intertrochanteric fracture (n = 150)</th>
<th>Non-intertrochanteric fracture (n = 448)</th>
<th>Others* (n = 303)</th>
<th>p-value*</th>
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<tbody>
<tr>
<td></td>
<td>Total (n = 448)</td>
<td>FNF (n = 130)</td>
<td>STF (n = 15)</td>
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<tr>
<td>Comparison 1</td>
<td></td>
<td></td>
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<td>&lt; 0.001</td>
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<tr>
<td>Non-older adults (A)</td>
<td>7 (4.7)</td>
<td>155 (34.6)</td>
<td>13 (10.0)</td>
<td>5 (33.3)</td>
</tr>
<tr>
<td>Older adults (B)</td>
<td>143 (95.3)</td>
<td>293 (65.4)</td>
<td>117 (90.0)</td>
<td>10 (66.7)</td>
</tr>
<tr>
<td>Comparison 2</td>
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<td></td>
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<td>0.145</td>
</tr>
<tr>
<td>Non-older adults (A)</td>
<td>7 (41.2)</td>
<td>155 (59.2)</td>
<td>13 (26.5)</td>
<td>5 (55.6)</td>
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<tr>
<td>Young-old (B1)</td>
<td>10 (58.8)</td>
<td>107 (40.8)</td>
<td>36 (73.5)</td>
<td>4 (44.4)</td>
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<td>Comparison 3</td>
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<td>&lt; 0.001</td>
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<td>Non-older adults (A)</td>
<td>7 (8.0)</td>
<td>155 (53.1)</td>
<td>13 (19.4)</td>
<td>5 (45.5)</td>
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<td>Middle-old (B2)</td>
<td>80 (92.0)</td>
<td>137 (46.9)</td>
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<td>6 (54.5)</td>
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<td>Comparison 4</td>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
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<tr>
<td>Non-older adults (A)</td>
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<td>13 (32.5)</td>
<td>5 (100)</td>
</tr>
<tr>
<td>Oldest-old (B3)</td>
<td>53 (88.3)</td>
<td>49 (24.0)</td>
<td>27 (67.5)</td>
<td>0 (0.0)</td>
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<tr>
<td>Comparison 5</td>
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<td>&lt; 0.001</td>
</tr>
<tr>
<td>Young-old (B1)</td>
<td>10 (11.1)</td>
<td>107 (43.9)</td>
<td>36 (40.0)</td>
<td>4 (40.0)</td>
</tr>
<tr>
<td>Middle-old (B2)</td>
<td>80 (88.9)</td>
<td>137 (56.1)</td>
<td>54 (60.0)</td>
<td>6 (60.0)</td>
</tr>
<tr>
<td>Comparison 6</td>
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<tr>
<td>Young-old (B1)</td>
<td>10 (15.9)</td>
<td>107 (68.6)</td>
<td>36 (57.1)</td>
<td>4 (100)</td>
</tr>
<tr>
<td>Oldest-old (B3)</td>
<td>53 (84.1)</td>
<td>49 (31.4)</td>
<td>27 (42.9)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Comparison 7</td>
<td></td>
<td></td>
<td></td>
<td>0.008</td>
</tr>
<tr>
<td>Middle-old (B2)</td>
<td>80 (60.2)</td>
<td>137 (73.7)</td>
<td>54 (66.7)</td>
<td>6 (100)</td>
</tr>
<tr>
<td>Oldest-old (B3)</td>
<td>53 (39.8)</td>
<td>49 (48.0)</td>
<td>27 (33.3)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

Values are presented as number (%).

Patients were divided into two main group: 18–64 years (group A; non-older adults, n=7) and ≥65 years (group B; older adults, n=143). Group B was again subdivided into three subgroups: 65–74 years (group B1; young-old, n=10), 75–84 years (group B2; middle-old, n=80), and ≥85 years (group B3; oldest-old, n=53).

FNF, femoral neck fracture; STF, subtrochanteric fracture.

*Others included femoral greater trochanteric fractures, femoral shaft fractures, and distal femoral fractures.

By chi-square and Fisher exact tests, respectively.

The prevalence and mortality rates of trauma are higher among older adults than those among younger adults due to the decreased ability of older adults to cope with aging processes such as reduced visual acuity, hearing loss, physical disability, drug use, baseline disease, and cognitive impairment. These characteristics differ in their clinical patterns from trauma between older and younger adults. Therefore, the actual severity of the trauma tends to be underestimated at an earlier stage. Moreover, older patients more often require long-term and complicated in-patient treatment processes, which has led to increased interest and study of older adults in trauma fields.

In the United States, about 340,000 femoral fractures are reported annually. Femoral fractures, the most common major fracture among older adults, are also the most common causes of hospitalization in older trauma patients. The mechanism of fracture is falling from a standing height. In particular, the reason for the high frequency in older adults is related to reduced femoral bone strength with increasing age.

With the increase in the average life expectancy, the older population has increased and their quality of life has improved due to social and economic development in this population. The older adult population consists of different age groups, from relatively healthy 65-year-olds to older adults > 85 years of age who have difficulty moving; therefore, it is difficult to classify them as a single group. Therefore, viewing all older persons aged > 65 years using the same standards may be inappropriate and establishing a finer-scale classification is necessary. Young-old persons are rela-
tively healthy and active. They often enjoy continuous self-development and active leisure as they did when they were younger. In contrast, older adults > 75 years of age are more likely to experience fatal diseases and often have a combination of geriatric diseases such as heart disease, hypertension, diabetes, cancer, and osteoporosis. These geriatric diseases are chronic degenerative diseases that require long-term treatment and increased medical resource utilization and medical costs.34,35) The middle-old to oldest-old individual experiences fewer activities of daily living compared to those in young-old individuals.36) Moreover, chronic disease morbidity significantly increases, which results in a variety of dysfunction, loss of function, and pathological changes.37) Several studies have reported a significant increase in complications and mortality from various trauma in middle-old patients aged 75 years.38-40) Additionally, the common risk factors for minor falls, such as weakness of balance or strength,41) increase in the middle-old and oldest-old individuals.37) Hence, these populations are more vulnerable to minor falls compared to the other age groups. Hip injuries due to minor falls in older adults are the most common injuries.42) In particular, femur intertrochanteric fractures have the highest mortality rate among all femoral fractures43) and have emerged as an important study in the area of trauma for in older adults. However, few studies have subdivided older adults with minor fall injury according to age. Specifically, no study has assessed the incidence of femoral intertrochanteric fractures due to minor falls among middle and oldest-old patients.

In our study, the incidence of femur intertrochanteric fractures did not vary significantly between young-old and non-old individuals; however, the incidence of femur intertrochanteric fractures was approximately 13 times higher in the middle-old and oldest-old individuals than that in young-old individuals. This result is significant because it differs from those of previous studies that showed an increased frequency of femoral intertrochanteric fractures in individuals aged 65 years.12,25,44) Additionally, as age and underlying disease increase, bone mineral density decreases significantly, making patients more vulnerv

| Table 2. Comparisons of characteristics between the young-old, middle-old, and oldest-old age groups |
|-----------------------------------------------|----------------|----------------|----------------|----------------|----------------|
| Number of patients                            | Young-old (65–74 y) | Middle-old (75–84 y) | Oldest-old (≥ 85 y) | p-value |
| Sex                                           | 117 | 217 | 102 |                    |
| Male                                          | 48 (41.0) | 57 (26.3) | 21 (20.6) | 0.002 |
| Female                                        | 69 (59.0) | 160 (73.7) | 81 (79.4) |                    |
| Drunken state                                 | 2 (1.7) | 4 (1.9) | 0 (0.0) | 0.392 |
| Underlying disease                            |                     |                     |                     |                     |
| Cerebrovascular accident                      | 25 (21.4) | 51 (23.5) | 22 (21.6) | 0.877 |
| Dementia                                      | 1 (0.9) | 11 (5.1) | 15 (14.4) | < 0.001 |
| Osteoporosis                                  | 35 (29.9) | 95 (43.8) | 72 (70.6) | < 0.001 |
| Parkinson’s disease                           | 8 (6.8) | 10 (4.6) | 5 (4.9) | 0.673 |
| Malignancy                                    | 9 (7.7) | 8 (3.7) | 3 (2.9) | 0.164 |
| Accident time                                 |                     |                     |                     | 0.114 |
| 0:00–5:59                                     | 6 (5.1) | 25 (11.5) | 15 (14.7) |                    |
| 6:00–11:59                                    | 29 (24.8) | 69 (31.8) | 31 (30.4) |                    |
| 12:00–17:59                                   | 51 (43.6) | 78 (35.9) | 32 (31.4) |                    |
| 18:00–23:59                                   | 31 (26.5) | 45 (20.7) | 24 (23.5) |                    |
| Intertrochanteric fracture                    | 10 (8.5) | 80 (36.9) | 53 (52.0) | < 0.001 |
| Subtype (Tronzo classification)               |                     |                     |                     | 0.907 |
| Type 1                                        | 2 (20.0) | 7 (8.8) | 8 (15.1) |                    |
| Type 2                                        | 1 (10.0) | 12 (15.0) | 9 (17.0) |                    |
| Type 3                                        | 3 (30.0) | 36 (45.0) | 20 (37.7) |                    |
| Type 4                                        | 4 (40.0) | 23 (28.7) | 15 (28.3) |                    |
| Type 5                                        | 0 (0) | 2 (2.5) | 1 (1.9) |                    |
| Unfavorable outcome†                          | 0 (0) | 3 (1.4) | 3 (2.9) | 0.238 |

Values are presented as number (%).

*By chi-square and Fisher exact tests, respectively.

†Unfavorable outcome indicates cases of transfer or death due to complications.

Compared to young-old individuals, middle and oldest-old individuals are expected to have more severe hip impact and damage from fall injuries. In our study, the incidence of femur intertrochanteric fractures did not vary significantly between young-old and non-old individuals; however, the incidence of femur intertrochanteric fractures was approximately 13 times higher in the middle-old and oldest-old individuals than that in young-old individuals. This result is significant because it differs from those of previous studies that showed an increased frequency of femoral intertrochanteric fractures in individuals aged 65 years.12,25,44)


Femoral Intertrochanteric Fractures associated with Minor Falls in the Middle-old to Oldest-old Patients 129
Table 3. Clinical variables related to the development of femoral intertrochanteric fractures from minor falls in older patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intertrochanteric fracture (n = 143)</th>
<th>Non-intertrochanteric fracture</th>
<th>p-value&lt;sup&gt;†&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Total (n = 293)</td>
<td>FNF (n = 117)</td>
<td>STF (n = 10)</td>
</tr>
<tr>
<td>Young-old (65–74 y)</td>
<td>10 (7.0)</td>
<td>107 (36.5)</td>
<td>36 (30.8)</td>
</tr>
<tr>
<td>Middle-old (75–84 y)</td>
<td>80 (55.9)</td>
<td>137 (46.8)</td>
<td>54 (46.2)</td>
</tr>
<tr>
<td>Oldest-old (≥ 85 y)</td>
<td>53 (37.1)</td>
<td>49 (16.7)</td>
<td>27 (23.1)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>31 (21.7)</td>
<td>95 (32.4)</td>
<td>32 (27.4)</td>
</tr>
<tr>
<td>Female</td>
<td>112 (78.3)</td>
<td>198 (67.6)</td>
<td>85 (72.6)</td>
</tr>
<tr>
<td>Drunken state</td>
<td>0 (0)</td>
<td>6 (2.0)</td>
<td>2 (1.7)</td>
</tr>
<tr>
<td>Accident time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0:00–5:59</td>
<td>17 (11.9)</td>
<td>29 (9.9)</td>
<td>10 (8.5)</td>
</tr>
<tr>
<td>6:00–11:59</td>
<td>42 (29.4)</td>
<td>88 (30.0)</td>
<td>40 (34.2)</td>
</tr>
<tr>
<td>12:00–17:59</td>
<td>55 (38.5)</td>
<td>105 (35.8)</td>
<td>45 (38.5)</td>
</tr>
<tr>
<td>18:00–23:59</td>
<td>29 (20.3)</td>
<td>71 (24.2)</td>
<td>22 (18.8)</td>
</tr>
<tr>
<td>Underlying disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>31 (21.7)</td>
<td>67 (22.9)</td>
<td>31 (26.5)</td>
</tr>
<tr>
<td>Dementia</td>
<td>8 (5.6)</td>
<td>19 (6.5)</td>
<td>10 (8.5)</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>87 (60.8)</td>
<td>115 (39.2)</td>
<td>63 (53.8)</td>
</tr>
<tr>
<td>Parkinson disease</td>
<td>7 (4.9)</td>
<td>16 (5.5)</td>
<td>6 (5.1)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>6 (4.2)</td>
<td>14 (4.8)</td>
<td>2 (1.7)</td>
</tr>
</tbody>
</table>

Values are presented as number (%).

FNF, femoral neck fracture; STF, subtrochanteric fracture.

*Others included femoral greater trochanteric fractures, femoral shaft fractures, and distal femoral fractures.

†By chi-square and Fisher exact tests, respectively.

Table 4. Risk factors related to the development of femoral intertrochanteric fractures from minor falls in older patients by multivariate logistic regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p-value&lt;sup&gt;*&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>1.233</td>
<td>0.743</td>
<td>2.047</td>
</tr>
<tr>
<td>Middle and oldest-old</td>
<td>6.620</td>
<td>3.309</td>
<td>13.245</td>
</tr>
<tr>
<td>Middle-old (75–84 y)</td>
<td>6.248</td>
<td>3.089</td>
<td>12.657</td>
</tr>
<tr>
<td>Oldest-old (≥ 85 y)</td>
<td>11.573</td>
<td>5.436</td>
<td>24.639</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>1.906</td>
<td>1.231</td>
<td>2.949</td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval.

*<p<0.05 in multivariate analysis were entered into the binary logistic regression analysis.
Femoral Intertrochanteric Fractures associated with Minor Falls in the Middle-old to Oldest-old Patients

The researchers claim no conflicts of interest.

In our study, the incidence of femoral intertrochanteric fractures caused by minor fall injuries in the middle-old and oldest-old patients was higher than that in young-old patients. Therefore, the imaging results of middle-old and oldest-old patients should be carefully read even if the patients do not complain of pain. If necessary, hip CT should also be performed. Moreover, increased attention should be paid to middle-old and oldest-old patients with stroke or dementia than to young-old patients.

The limitation of this study was that it was conducted in a single emergency center located in a metropolitan urban area where people with relatively good nutrition or high socioeconomic status were more likely to reside; thus, there may be bias in the patient distribution or propensity. Additional multicenter studies including local emergency centers will provide more accurate results on the incidence of femoral intertrochanteric fractures according to age groups of older patients.

CONFLICT OF INTEREST DISCLOSURES

The researchers claim no conflicts of interest.

REFERENCES

The purpose of this study was to identify the risk factors and causes of short-term mortality after emergency department (ED) discharge in older patients.

Methods: This population-based cohort study used nationwide health insurance claims data in Korea from 2008 to 2014. The causes of death and diagnoses of patients who died within 1 week after discharge from EDs (1-week ED death) were obtained. The risk factors for 1-week ED death were calculated using Cox proportional hazard regression analyses.

Results: The rate of 1-week ED death was 0.5% among 133,251 individuals aged ≥65 years discharged from EDs. In multivariate analysis, the top five ED discharge diagnoses associated with an increased risk of 1-week ED death were hypotension and vascular disease (adjusted hazard ratio [aHR]=5.11; 95% confidence interval [CI], 3.03–8.63), neoplasm (aHR=4.89; 95% CI, 3.77–6.35), coronary artery disease (aHR=3.83; 95% CI, 2.73–5.39), dyspnea (aHR=3.41; 95% CI, 2.48–4.68), and respiratory disease (aHR=2.25; 95% CI, 1.73–2.92). The most common causes of 1-week ED death were neoplasm (14.8%), senility (13.8%), and cerebrovascular disease (11.7%).

Conclusion: Neoplasm, coronary artery disease, and respiratory disease were the discharge diagnoses associated with an increased risk of short-term mortality after ED discharge. Neoplasm was the leading cause of short-term mortality after ED discharge in older patients.

Key Words: Aged, Mortality, Emergency departments, Risk factors
causes and risk factors of early death after ED discharge in older populations are not well known.

The purpose of this study was to identify the causes of death in older patients who died after ED discharge and to determine the risk of early death according to the ED discharge diagnoses.

**MATERIALS AND METHODS**

**Data and Setting**

The present study used data from the National Health Insurance Service (NHIS) senior cohort database. The senior cohort database includes approximately 550,000 randomly sampled comprising 10% of the 5.5 million older adults aged ≥ 60 years nationwide. This database includes information on age, sex, income-based health insurance premiums, disease classification codes, treatment, prescription history, and date and cause of death. The causes of death in Statistics Korea, based on death medical certificates issued by physicians, are linked to the NHIS cohort. This study was approved by the Institutional Review Board of Hanyang University Hospital, which waived the requirement for informed consent (No. HYUH 2019-01-029).

**Study Population**

We included cases in which older patients aged 65 years or older were discharged from the ED between January 2008 and December 2014. We defined patients who visited EDs using codes from the NHIS in Korea for the management of emergency care; namely, AC101 (regional emergency medical center), AC103 (local emergency medical center), and AC105 (local emergency medical facility). If a patient visited the ED several times, each visit was considered a unique visit. Patients who visited the ED or were hospitalized during the prior 30 days were excluded. We also excluded patients who were admitted or who died on the same day as the ED visit. Finally, patients with duplicate claims were excluded.

**Definitions of Variables**

The outcome variable of this study was death within 1 week of the ED visit (1-week ED death). The causes of death were classified according to the International Classification of Disease, 10th Revision (ICD-10) codes (Supplementary Table S1). We investigated characteristics such as age, sex, quintile of the health insurance premiums, and comorbidities. In Korea, health insurance premiums reflect household income levels, in which individuals with higher incomes also have higher health insurance premiums. The comorbidities were defined as cases with one or more diagnostic codes in the inpatient setting or with two or more codes in the outpatient setting in the 3 years before the ED visit (Supplementary Table S2). ED discharge diagnoses were categorized using ICD-10 codes (Supplementary Table S3). We used only the main diagnostic codes as the ED discharge diagnoses.

**Data Analysis**

Among the baseline patient characteristics, continuous variables were presented as median (interquartile range [IQR]) categorical variables as frequencies (%). These baseline characteristics were compared by Wilcoxon rank-sum or Fisher exact tests, as appropriate. The primary outcome was the risk factors for 1-week ED death. Fisher exact tests were performed to determine the difference in the rate of ED discharge diagnosis between the 1-week ED death and survival groups. All significant variables with p-value less than 0.05 in the univariate analysis were included in the multivariate analysis to identify the risk factors for 1-week ED death. Multivariate analysis was performed using Cox proportional hazard regression. Adjusted hazard ratios (aHRs) and confidence intervals (CIs) were

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**Fig. 1.** Study flow diagram.

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calculated by adjusting for age, sex, and income quantiles. Subgroup analysis was performed after dividing the patients into three groups according to the ED level (regional emergency medical center, local emergency medical center, or local emergency medical facility). We identified the discharge diagnoses associated with significantly increased risks of 1-week ED death in the same way as the main analysis. The secondary outcome was the causes of 1-week ED death. Statistical analyses were performed using SAS Enterprise Guide version 7.13 (SAS Institute Inc., Cary, NC, USA) and R software (https://www.r-project.org/).

RESULTS

Characteristics of the Study Population

A total of 217,291 cases of older patients aged 65 years or more were discharged from EDs between 2008 and 2014. After excluding 84,040 ED visits, 133,251 ED visits were finally included in the analyses (Fig. 1). Of the included patients, 725 (0.54%) died within 1 week. The basic characteristics of the study population are shown in Table 1. The median age of the patients was 75 years (IQR, 72–80 years). The median age of the patients in the 1-week ED death group was 81 years (IQR, 75–87 years). The ratio of men was higher in the 1-week ED death group (47%) than that in the survival group (42.3%). The 1-week ED death group had higher ratios of comorbidities such as acute myocardial infarction, cancers, arrhythmia, congestive heart failure, renal failure, stroke, and cirrhosis than those in the survival group.

Risk Factors and Causes of 1-week ED death

Table 2 shows the frequencies and percentages of discharge diagnoses of the ED. Injury and poisoning (14.3%) was the most common ED discharge diagnosis in the 1-week ED death group, followed by neoplasm (10.6%) and respiratory disease (10.5%). In the multivariate analysis, the risk of 1-week ED death increased by 11% (aHR = 1.11; 95% CI, 1.10–1.12) with age (Table 3). Women had a lower risk of 1-week ED death compared to that in

<table>
<thead>
<tr>
<th>Table 1. Baseline characteristics of the study population</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total (n = 133,251)</strong></td>
</tr>
<tr>
<td>Age (y)</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Insurance premiums (quintile)</td>
</tr>
<tr>
<td>1 (lowest income)</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5 (highest income)</td>
</tr>
<tr>
<td>Comorbidities (prior 3 years)</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>Asthma</td>
</tr>
<tr>
<td>All cancers</td>
</tr>
<tr>
<td>Arrhythmia</td>
</tr>
<tr>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>Coronary artery disease (excluding AMI)</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Osteoporosis</td>
</tr>
<tr>
<td>Renal failure</td>
</tr>
<tr>
<td>Stroke</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
</tr>
</tbody>
</table>

Values are presented as median (range) or number (%).
AMI, acute myocardial infarction.
*Wilcoxon rank-sum test or the Fisher exact test, as appropriate.
men (aHR = 0.77; 95% CI, 0.66–0.89). Patients with the fifth quintile of insurance premiums (the highest income group) had a 27% (aHR = 0.73; 95% CI, 0.60–0.88) lower risk of 1-week ED death than that in patients with incomes in the first quintile. The ED discharge diagnosis with the highest risk of 1-week ED death was hypotension and vascular disease (aHR = 5.11; 95% CI, 3.03–8.63). The most common disease in this group was hypotension (n = 6, 40%). The diagnoses at ED discharge with the second-highest risk of 1-week ED death were neoplasm (aHR = 4.89; 95% CI, 3.14–7.96), CAD (aHR = 3.83; 95% CI, 2.73–5.39), symptom of dyspnea (aHR = 3.41; 95% CI, 2.48–4.68), and respiratory disease (aHR = 2.25; 95% CI, 1.73–2.92). In addition, patients discharged with cerebrovascular disease and endocrine metabolic disease had an increased risk of 1-week ED death.

The diagnosis with the lowest risk of mortality was ear and mastoid disease (aHR = 0.05; 95% CI, 0.01–0.36). In addition, the risks of 1-week ED death were lower in patients with discharge diagnoses of dizziness, non-traumatic musculoskeletal disease, abdominal pain, injury and poisoning, and gastrointestinal disease.

Subgroup Analysis
In subgroup analysis, neoplasm, CAD, and symptom of dyspnea had increased risks, the same as observed in the main analysis of total included patients (Table 5). Local emergency medical facilities had the highest aHR of hypotension and vascular disease (aHR = 9.17; 95% CI, 4.03–20.91), followed by neoplasm (aHR = 6.49; 95% CI, 3.91–10.76), CAD (aHR = 5.59; 95% CI, 3.14–9.96), and symptom of dyspnea.

Table 2. Univariate analysis of discharge diagnosis for 1-week death after emergency department discharge (n=133,251)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Survival (n = 132,526)</th>
<th>Death within 1 week (n = 725)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious disease</td>
<td>7,361 (5.6)</td>
<td>28 (3.9)</td>
<td>0.050</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>2,943 (2.2)</td>
<td>77 (10.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hematologic disease</td>
<td>212 (0.2)</td>
<td>2 (0.3)</td>
<td>0.325</td>
</tr>
<tr>
<td>Endocrine and metabolic disease</td>
<td>4,460 (3.4)</td>
<td>39 (5.4)</td>
<td>0.005</td>
</tr>
<tr>
<td>Mental and behavioral disease</td>
<td>1,543 (1.1)</td>
<td>6 (0.8)</td>
<td>0.718</td>
</tr>
<tr>
<td>Nervous system disease</td>
<td>3,326 (2.5)</td>
<td>15 (2.1)</td>
<td>0.550</td>
</tr>
<tr>
<td>Eye disease</td>
<td>525 (0.4)</td>
<td>0 (0.0)</td>
<td>0.126</td>
</tr>
<tr>
<td>Ear and mastoid disease</td>
<td>4,474 (3.4)</td>
<td>1 (0.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1,166 (0.9)</td>
<td>3 (0.4)</td>
<td>0.230</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>2,064 (1.6)</td>
<td>39 (5.4)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Non-atherosclerotic heart disease</td>
<td>1,055 (0.8)</td>
<td>7 (1.0)</td>
<td>0.528</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>3,815 (2.9)</td>
<td>44 (6.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>359 (0.3)</td>
<td>6 (0.8)</td>
<td>0.016</td>
</tr>
<tr>
<td>Hypertension and vascular disease</td>
<td>516 (0.4)</td>
<td>15 (2.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>5,701 (4.3)</td>
<td>76 (10.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hepatobiliary and pancreatic disease</td>
<td>1,042 (0.8)</td>
<td>9 (1.2)</td>
<td>0.198</td>
</tr>
<tr>
<td>Gastrointestinal disease</td>
<td>8,874 (6.7)</td>
<td>27 (3.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Skin disease</td>
<td>2,300 (1.7)</td>
<td>5 (0.7)</td>
<td>0.030</td>
</tr>
<tr>
<td>Non-traumatic musculoskeletal disease</td>
<td>3,208 (2.4)</td>
<td>5 (0.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Genitourinary disease</td>
<td>5,887 (4.4)</td>
<td>33 (4.6)</td>
<td>0.856</td>
</tr>
<tr>
<td>Symptom: dizziness</td>
<td>6,394 (4.8)</td>
<td>5 (0.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Symptom: chest pain</td>
<td>2627 (2.0)</td>
<td>9 (1.2)</td>
<td>0.180</td>
</tr>
<tr>
<td>Symptom: abdominal pain</td>
<td>6,163 (4.7)</td>
<td>15 (2.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Symptom: fever</td>
<td>1,383 (1.0)</td>
<td>9 (1.2)</td>
<td>0.579</td>
</tr>
<tr>
<td>Symptom: dyspnea</td>
<td>2,201 (1.7)</td>
<td>46 (6.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Symptom: other symptom</td>
<td>12,089 (9.1)</td>
<td>70 (9.7)</td>
<td>0.605</td>
</tr>
<tr>
<td>Injury and poisoning</td>
<td>37,568 (28.3)</td>
<td>104 (14.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Other disease</td>
<td>329 (0.2)</td>
<td>4 (0.6)</td>
<td>0.110</td>
</tr>
</tbody>
</table>

Values are presented as number (%).

*Fisher exact tests.

The causes of death for 1-week ED death are shown in Table 4. Neoplasm (14.8%) was the most frequent cause of death, followed by senility (13.8%), cerebrovascular disease (11.7%), injury and poisoning (11.4%), and CAD (9.8%).
DISCUSSION

In this study, the rate of 1-week ED death was 0.5%. The top five discharge diagnoses associated with an increased risk of short-term mortality were hypotension and vascular disease, neoplasm, CAD, symptom of dyspnea, and respiratory disease. The most common causes of death were neoplasm (14.8%), senility (13.8%), cerebrovascular disease (11.7%), injury and poisoning (11.4%), and CAD (9.8%).

Gabayan et al reported a rate of 1-week ED death of 0.05% among 475,829 patients from 12 hospitals in California discharged from the ED. Obermeyer et al. studied 10,093,678 patients included in a 20% sample of the US Medicare population, reporting a 1-week mortality rate of 0.12%. The mean ages of the subjects included in these two studies were 47 and 62 years, respectively. Our study of older patients with a median age of 75 showed a 1-week ED mortality rate of 0.5%.

Multivariate analysis of the association between ED discharge diagnosis and 1-week ED death showed the highest risk for hypotension and vascular disease (aHR = 5.11). These results were not reported in previous studies and indicate that older patients with hypotension or vascular disease should be more seriously considered for hospitalization. In addition, as hypotension itself may be a secondary change rather than a primary diagnosis, additional evaluation should be considered. Neoplasm had an increased risk (aHR = 4.89), consistent with previous studies. Gabayan et al. reported an odds ratio (OR) of 3.7 for 1-week ED death due to neoplasm in patients with a mean age of 47 years. The median age of the patients in our study was 75 years and the aHR for short-term ED death in patients with neoplasm was 4.89. Rivera et al. analyzed cancer patients who visited the ED, reporting that complications such as pneumonia, septicemia, heart failure, and ileus were associated with hospitalization. Therefore, hospitalization should be considered for patients with neoplasms even if they have the same disease. The risk of 1-week ED death in CAD patients increased by 3.83-fold, similar to previous studies. Gabayan et al. reported an OR of CAD of 3.8. More careful observation is needed for patients discharged from the ED with CAD diagnosis or related symptom such as chest pain. In the present study, increased risks were observed for patients with dyspnea.

Table 3. Multivariate analysis investigating risk factors for 1-week death after emergency department discharge (n=133,251)

<table>
<thead>
<tr>
<th>Discharge diagnosis in the emergency department</th>
<th>Adjusted HR*</th>
<th>95% CI*</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension and vascular disease</td>
<td>5.11</td>
<td>3.03–8.63</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>4.89</td>
<td>3.77–6.35</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>3.83</td>
<td>2.73–5.39</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Symptom: dyspnea</td>
<td>3.41</td>
<td>2.48–4.68</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>2.25</td>
<td>1.73–2.92</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>2.07</td>
<td>0.92–4.68</td>
<td>0.079</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>2.02</td>
<td>1.46–2.79</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Endocrine and metabolic disease</td>
<td>1.59</td>
<td>1.13–2.24</td>
<td>0.007</td>
</tr>
<tr>
<td>Gastrointestinal disease</td>
<td>0.58</td>
<td>0.39–0.86</td>
<td>0.007</td>
</tr>
<tr>
<td>Injury and poisoning</td>
<td>0.51</td>
<td>0.41–0.65</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Skin disease</td>
<td>0.47</td>
<td>0.19–1.13</td>
<td>0.093</td>
</tr>
<tr>
<td>Symptom: abdominal pain</td>
<td>0.46</td>
<td>0.27–0.78</td>
<td>0.004</td>
</tr>
<tr>
<td>Non-traumatic musculoskeletal disease</td>
<td>0.29</td>
<td>0.12–0.71</td>
<td>0.007</td>
</tr>
<tr>
<td>Symptom: dizziness</td>
<td>0.16</td>
<td>0.07–0.39</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Ear and mastoid disease</td>
<td>0.05</td>
<td>0.01–0.36</td>
<td>0.003</td>
</tr>
</tbody>
</table>

HR, hazard ratio; CI, confidence interval.
*Cox proportional hazard regression analyses.

(aHR = 4.79; 95% CI, 2.97–7.74).
Table 4. Causes of death in patients who died within 1 week of discharge from the emergency department (n=725)

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoplasm</td>
<td>107 (14.8)</td>
</tr>
<tr>
<td>Senility</td>
<td>100 (13.8)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>85 (11.7)</td>
</tr>
<tr>
<td>Injury and poisoning</td>
<td>83 (11.4)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>71 (9.8)</td>
</tr>
<tr>
<td>Pneumonia and pneumonitis</td>
<td>54 (7.4)</td>
</tr>
<tr>
<td>Endocrine and metabolic disease</td>
<td>34 (4.7)</td>
</tr>
<tr>
<td>Other death</td>
<td>31 (4.3)</td>
</tr>
<tr>
<td>Asthma and COPD</td>
<td>28 (3.9)</td>
</tr>
<tr>
<td>Infectious disease</td>
<td>19 (2.6)</td>
</tr>
<tr>
<td>Genitourinary disease</td>
<td>17 (2.3)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>15 (2.1)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>12 (1.7)</td>
</tr>
<tr>
<td>Nervous system disease</td>
<td>11 (1.5)</td>
</tr>
<tr>
<td>Non-atherosclerotic heart disease</td>
<td>10 (1.4)</td>
</tr>
<tr>
<td>Hypotension and vascular disease</td>
<td>10 (1.4)</td>
</tr>
<tr>
<td>Gastrointestinal disease</td>
<td>10 (1.4)</td>
</tr>
<tr>
<td>Mental and behavioral disease</td>
<td>8 (1.1)</td>
</tr>
<tr>
<td>Hepatobiliary and pancreatic disease</td>
<td>5 (0.7)</td>
</tr>
<tr>
<td>Non-traumatic musculoskeletal disease</td>
<td>4 (0.6)</td>
</tr>
<tr>
<td>Shock</td>
<td>2 (0.3)</td>
</tr>
<tr>
<td>Hematologic disease</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Missing data</td>
<td>8 (1.1)</td>
</tr>
</tbody>
</table>

COPD, chronic obstructive pulmonary disease.

Table 5. Subgroup analyses investigating risk factors for 1-week death after emergency department discharge according to emergency department levels

<table>
<thead>
<tr>
<th></th>
<th>Adjusted HR*</th>
<th>95% CI*</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regional emergency medical center</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptom: dyspnea</td>
<td>4.91</td>
<td>2.37–10.17</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>4.63</td>
<td>2.82–7.61</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>3.43</td>
<td>1.66–7.11</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Local emergency medical center</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neoplasm</td>
<td>4.53</td>
<td>3.18–6.44</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hypotension and vascular disease</td>
<td>4.27</td>
<td>2.00–9.10</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>3.37</td>
<td>2.06–5.49</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Symptom: dyspnea</td>
<td>2.48</td>
<td>1.52–4.04</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hepatobiliary and pancreatic disease</td>
<td>2.29</td>
<td>1.07–4.88</td>
<td>0.032</td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>1.98</td>
<td>1.35–2.92</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Local emergency medical facility</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotension and vascular disease</td>
<td>9.17</td>
<td>4.03–20.91</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>6.49</td>
<td>3.91–10.76</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>5.59</td>
<td>3.14–9.96</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Symptom: dyspnea</td>
<td>4.79</td>
<td>2.97–7.74</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>3.71</td>
<td>2.36–5.83</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>2.91</td>
<td>1.98–4.27</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Discharge diagnoses with significantly increased risks are shown.

HR, hazard ratio; CI, confidence interval.

*Cox proportional hazard regression analyses.
heart disease (11.3%). These results are similar to our findings that neoplasm, cerebrovascular disease, and CAD were the main causes of short-term death. Of note is the increasing rate of cerebrovascular disease and CAD-related mortality in Korea. In our study, senility was the second leading cause of death, likely because many physicians may indicate unclear diagnoses as the cause of death.

Subgroup analysis showed increased aHR for hypotension and vascular disease as the ED level increased. Similar to of total included patients, symptoms of dyspnea, as well as neoplasm and CAD accounted for the highest risks of 1-week ED death in all three groups. The aHRs for these risk factors were highest in local emergency medical facilities compared to those in the other two subgroups. In particular, hypotension and vascular disease had the highest aHR of 9.17.

This study has several strengths. This nationwide population-based study focused on older patients had a large sample size including both men and women. Understanding these patients will be helpful because the number of older patients visiting EDs is increasing. However, this study has some limitations that should be considered when interpreting the results. First, we could not distinguish between patients with hopeless discharge and patients who died unexpectedly. For example, our data did not contain information on do-not-resuscitate orders. Second, the cause of death and discharge diagnoses were recorded by clinicians and could have been inaccurate. However, considering the large number of the study population, the overall pattern of outcomes could be confirmed. Lastly, the database used in this study was sample data, which might have different characteristics from those of the entire older population. However, as the study included 550,000 individuals, the standard error would be minimal.

In conclusion, the rate of death within 1 week among older patients discharged from the ED was 0.5%. Clinicians should consider the increased risk for short-term mortality among older patients with ED discharge diagnoses of neoplasm, CAD, and respiratory disease. Neoplasm was the leading cause of short-term death in this population.

CONFLICT OF INTEREST DISCLOSURES

The researchers claim no conflicts of interest.

ACKNOWLEDGEMENTS

This study utilized the National Health Insurance Service database (No. NHIS-2019-2-095). The interpretations and conclusions reported here do not represent those of the National Health Insurance Service.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via http://doi.org/10.4235/agmr.19.0029.

REFERENCES


Background: Spinal sarcopenia is receiving renewed attention as a cause of spinal sagittal imbalance. However, the relationships between spinal sarcopenia and spinal sagittal balance (SSB) have not been thoroughly investigated. We evaluated the relationships between SSB parameters and sarcopenic indices with lumbar paraspinal muscle (LPM) quantity and strength in healthy older adults.

Methods: Twenty-four healthy community-dwelling older women were enrolled. Demographic variables, conventional sarcopenic indices, isometric back muscle strength, and SSB parameters, as well as results of functional examinations and lumbar spine computed tomography scan with LPM cross-sectional area (CSA) and density assessments, were examined. The independent effect on the sum of the total LPM CSA was determined using multivariable regression analysis adjusted for age, appendicular skeletal muscle mass, gait speed, handgrip strength, back extensor strength, and pelvic tilt (PT) angle.

Results: PT angle was significantly correlated with the sum of the total LPM CSA and mean LPM density (r=-0.502, p=0.015 and r=0.504, p=0.014, respectively). Furthermore, PT angle was an independent factor for the sum of the total LPM CSA (β=-0.610, p=0.021) in the multivariate regression models (R²=0.320).

Conclusion: Our data suggest that PT angle was significantly correlated with LPM CSA in healthy older women. To our knowledge, this is the first report to investigate the relationships of sarcopenic indices and spinal muscle degeneration with SSB.

Key Words: Sarcopenia, Spine, Paraspinal muscles, Lumbosacral region, Kyphosis

INTRODUCTION

The spine is an inevitable site of sarcopenia owing to the large muscles surrounding it. Sarcopenia of the lumbar paraspinal muscles (LPMs) has been receiving renewed attention as a cause of spinal degeneration. Both atrophy and fatty changes in paraspinal muscles originating from sarcopenia are associated with functional disorders and chronic back pain.1)

Conventional indices to define sarcopenia—appendicular skeletal muscle mass (ASM), handgrip strength (HGS), and gait speed—cannot reflect regional sarcopenia and its clinical outcomes. A cross-sectional study of 821 subjects with knee osteoarthritis and 4,103 controls showed that low skeletal muscle mass in the lower limbs was correlated with the presence of knee osteoarthritis, whereas whole-body skeletal muscle mass was not.10 The authors suggested the need for limb-specific muscle mass examinations to assess the effects of skeletal muscles on a specific joint. Therefore, regional measurements should be performed to evaluate the outcome of sarcopenia in focal areas.

However, there are few simple and clinically valid measuring tools to assess sarcopenia in the spine. Whole-body dual-energy X-ray absorptiometry and bioimpedance analysis (BIA) to measure ASM cannot be applied to spinal sarcopenia; thus, tomographic imaging such as computed tomography (CT) and magnetic resonance imaging (MRI) are required to measure paraspinal muscle quantity. Moreover, tools to verify the function and perfor-
mance of paraspinal muscle are more difficult to evaluate. To assess paraspinal muscle strength, expensive special equipment such as isokinetic dynamometry is required. Furthermore, there is no standardized test for spinal muscle performance.

Spinal sagittal balance (SSB) is an important indicator of outcomes of lumbar spine surgery and non-operative treatment of spinal stenosis. While SSB can be affected by sex and ethnicity, aging itself is the most important cause of spinal sagittal imbalance. LPM degeneration is one of the causes of spinal sagittal imbalance. An MRI-based study reported the relationship between the estimated LPM volume and sagittal curvature magnitude. One cross-sectional study suggested that the muscle thickness of the erector spinae and echo intensity of the lumbar multifidus were independent variables of SSB.

However, the relationships between spinal sarcopenia and SSB have not been thoroughly investigated. Thus, we evaluated the relationships of SSB parameters and sarcopenic indices with LPM quantity and strength in healthy older adults. We hypothesized that SSB parameters could reflect LPM mass and back extensor strength.

MATERIALS AND METHODS

Study Population
Healthy community-dwelling older (≥65 years) women who could independently walk more than 100 m were consecutively enrolled in a single center from July 2018 to December 2018. Participants who had experienced the following were excluded: (1) low back pain with moderate severity (numeric rating scale 5 and over); (2) history of any type of lumbar spine surgery; (3) history of hip fracture surgery and arthroplasty of the hip or knee; (4) disorders of the central nervous system such as stroke, parkinsonism, or spinal cord injury; (5) communication disorder such as severe hearing loss; (6) musculoskeletal conditions affecting physical function such as limb amputation; (7) long-term use of corticosteroids due to inflammatory disease; (8) malignancy requiring treatment within 5 years; and (9) other medical conditions requiring active treatment; additionally, individuals who refused to participate in the study were also excluded.

Conventional Sarcopenia Work-Up
BIA (InBody 720; InBody, Seoul, Korea) was used to analyze body composition including lean body and fat masses. ASM was calculated as the sum of the lean mass in the bilateral upper and lower extremities and standardized by dividing by the squared height (ASM/HT², kg/m²). HGS was measured using a hand-grip dynamometer (T.K.K.5401; Takei Scientific Instruments, Tokyo, Japan), as described previously. Briefly, participants were asked to perform the following while sitting in a straight-backed chair with their feet flat on the floor: adduct and neutralally rotate the shoulder, flex the elbow to 90°, and place the forearm in a neutral position with the wrist between 0° and 30° extension and between 0° and 15° ulnar deviation. Participants were instructed to squeeze the handle as hard as possible for 3 seconds, and the maximum contraction force (kg) was recorded. Gait speed was measured using a 6-meter usual gait speed (m/s) as recommended by the Asian Working Group for Sarcopenia. The definition and cutoffs for sarcopenia were also adopted from these guidelines.

Functional Examinations and Questionnaires
Functional examination using a short physical performance battery (SPPB) was derived from three objective physical function tests (i.e., time taken to cover 4 m at a comfortable walking speed, time taken to stand from sitting in a chair five times without stopping, and ability to maintain balance for 10 seconds in three different foot positions at progressively more challenging levels). A score from 0 to 4 was assigned to the performance of each task, with higher scores indicating better body function. The Timed Up and Go test (TUG) has shown excellent test-retest reliability in older adults. The participants were provided with verbal instructions to stand up from an armchair, walk 3 m as fast as possible, turn back at a cone set out by the researchers, walk back, and sit down in the chair. They were allowed to wear their regular footwear and use a walking aid if needed. A stopwatch was started on the word ‘go’ and stopped when the participant was completely seated with their back against the backrest. The time to complete the test was recorded in three consecutive trials using the first trial to familiarize the participants with the test. The best time from the three trials was analyzed. The Oswestry Disability Index (ODI) is one of the most commonly used instruments for measuring disability in spinal disorders. It consists of 10 items that assess the level of pain and interference with several physical activities. We used the Korean version of the ODI. The Back Performance Scale (BPS) consists of five tests: sock test, pick-up test, roll-up test, fingertip-to-floor test, and lift test. The five tests comprising the BPS demonstrate associations with each other and each test contributes to the high internal consistency, implying that the tests share a common characteristic in measuring physical performance. The BPS sum score (0–15) is calculated by adding the individual scores for the five tests.

Isometric Back Muscle Strength
We measured the isometric back extensor strength using a handheld dynamometer (PowerTrack II; JTECH Medical, Salt Lake City, UT, USA). Briefly, the participants stood in full extension
with their backs to a wall and feet flat on the floor with heels touching the wall. An inelastic belt was looped through the anchor rails and secured firmly 1 cm below the anterior superior iliac spine to restrain movement and maintain participant contact with the wall during the test. The participants were instructed to flex forward approximately 15° at the hips so that the dynamometer could be positioned posterior to the spinous process of the 7th thoracic vertebrae. In this way, counter pressure was provided by the fixed wall behind the participants’ back to avoid tester-induced variations in resistance. Although this method is novel, it showed a strong positive relationship with back extensor strength measured using the gold-standard isokinetic dynamometry and high inter-instrument validity and reliability.19)

**Spinal Sagittal Balance**

For each patient, one lateral radiograph of the whole spine was obtained and digitized. All measurements were performed using imaging software (INFINITT PACS M6; INFINITT Healthcare, Seoul, Korea), as previously described.20,21) The following spinopelvic radiographic parameters were analyzed: sacral slope (SS), pelvic incidence (PI), pelvic tilt (PT), lumbar lordosis (LL), thoracic kyphosis (TK), and sagittal vertical axis (SVA).

**LPM Measurement by Spine CT Scan**

Lumbar spine CT scans (Ingenuity CT; Philips Healthcare, Cleveland, OH, USA) were performed to measure the cross-sectional area (CSA) and mean density (in Hounsfield unit [HU]) of the LPM (multifidus [MF] and erector spinae [ES]).22) The mean density reflected the degree of intramuscular fat content because the values decreased as the fat content increased. Before each CT scan, a calibration was performed using air as the standard. CT scanning was performed with the participant in the supine position with a 120-kV and 140-mA protocol. Using 1-mm thin-section axial CT scan images, the axial images were reformatted with each lumbar intervertebral disc level (T12/L1-L5/S1) parallel to the adjacent vertebral endplates. These axial images at each intervertebral disc level were reconstructed at 2.5-mm intervals, which included cross-sectional images of LPM. The measurement of ES and MF was performed from the level of L1/L2 to L5/S1 using a specially designed radiological workstation (MEDIP; MEDICALIP, Seoul, Korea) (Fig. 1). The CSA was measured by manually constructing points around the outer margins of the individual muscles using a touchscreen LCD monitor (XPS 15 9570; Dell Inc., Round Rock, TX, USA) and digital touchscreen pen (PN556W Dell Active Pen; Dell Inc.). After the CSA and mean density of paraspinal muscles were separately measured on the bilateral sides, the mean and sum values at all levels were calculated.23)

All demographic and clinical data, including CT scan images, were obtained with the approval of the Institutional Review Board of SMG-SNU Boramae Medical Center (No. 16-2017-45). Written informed consent was obtained from all participants.

**Statistical Analysis**

The relationships between sarcopenic indices and functional outcomes with SSB parameters were measured by Pearson correlation coefficients. The independent effects on the sum of the total LPM

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Fig. 1. Measurements of cross-sectional area and density of lumbar paraspinal muscle. (A) Computed tomography axial image at the L3/4 disc level and (B) three-dimensional reconstructed bird’s-eye view from the top-left of the participant.
CSA were determined using multivariate regression models adjusted for six key factors: age, \(^7\) ASM/Ht\(^2\), HGS, gait speed, \(^8\) back extensor strength, \(^9\) and PT angle. ASM/Ht\(^2\) and HGS were included because they are the basic variables for diagnosing sarcopenia and PT was included in the regression analysis as the most relevant variable of SSB. An adjusted model was developed through backward elimination with a significance level of 0.2 to enter and 0.05 to retain. We also evaluated possible multiple collinearities between covariates by correlation analysis and collinearity statistical tests (tolerance and variance inflation factor tests) during regression analysis. IBM SPSS Statistics version 21.0 for Windows (IBM Corp., Armonk, NY, USA) was used for all analyses. p-values of less than 0.05 were considered statistically significant.

RESULTS

The baseline characteristics of 24 older women are shown in Table 1. Their mean age was 76.8 \(\pm\) 4.2 years. Among conventional sarcopenic indices, the ALM/Ht\(^2\), HGS, and gait speed were 6.30 \(\pm\) 0.79 kg/m\(^2\), 20.0 \(\pm\) 3.4 kg, and 0.87 \(\pm\) 0.16 m/s, respectively. No participant met the diagnostic criteria for sarcopenia.

Among the conventional sarcopenic indices, only HGS was positively correlated with SPPB (\(r = 0.521, p = 0.011\)). While both HGS and ASM/Ht\(^2\) tended to have positive correlations with LPM mean density and back extensor strength, they were not significant (Table 2). Among SSB parameters, PT angle was significantly correlated with the sum of the total LPM CSA and mean LPM density (\(r = -0.502, p = 0.015\) and \(r = 0.504, p = 0.014\), respectively) (Fig. 2). The LL angle was also correlated with the ODI and the sum of the total LPM CSA (\(r = -0.423, p = 0.045\) and \(r = 0.439, p = 0.036\), respectively). Only PI angle was significantly correlated with back extensor strength (\(r = -0.490, p = 0.018\)) (Table 3).

Finally, among the six key variables, multivariate regression models adjusted by the other variables revealed PT angle to be an independent factor for the sum of the total LPM CSA (\(\beta = -0.610, p = 0.021\), \(R^2 = 0.320\)) (Table 4).

DISCUSSION

The most important finding of this study was that only PT angle was significantly correlated with the sum of the total LPM CSA in healthy older women. Because we used multivariate regression models adjusted for potential factors, including age and ASM, SSB parameters might be independent factors affecting spinal sarcopenia.

In the current study, conventional sarcopenic indices (ASM, HGS, and gait speed) were not correlated with LPM mass, back extensor strength, and spine specific functional outcomes. Even ASM was not correlated with LPM CSA (\(r = 0.181, p = 0.535\)). Therefore, conventional muscle mass measurements that sum limb muscle masses to define sarcopenia do not reflect the clinical features of spinal sarcopenia. Jeon et al. \(^{25}\) reported that low limb muscle mass was correlated with only knee joint radiological degeneration and not hip or spine. Therefore, site-specific muscle mass investigation is necessary to evaluate the effect of skeletal muscle on specific regions.

Among the several SSB parameters, only PT angle was significantly correlated with both LPM quantity (CSA) and quality (density), while LL angle was only correlated with LPM quantity. PT is the angle between a vertical line originating at the center of the femoral head and a line starting from the center of the femoral head to the midpoint of the endplate of S1. In simple terms, this angle describes the rotation of the pelvis around the femoral heads. PT increases with age, and high PT is needed to maintain an up-
Table 2. Correlations between sarcopenic indices and functional outcomes

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Age</th>
<th>BMI</th>
<th>ASM/Ht²</th>
<th>Gait speed</th>
<th>Handgrip strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPPB</td>
<td>0.063</td>
<td>-0.243</td>
<td>-0.241</td>
<td>0.599*</td>
<td>0.521*</td>
</tr>
<tr>
<td>TUG</td>
<td>-0.014</td>
<td>0.415*</td>
<td>0.458</td>
<td>-0.369</td>
<td>-0.296</td>
</tr>
<tr>
<td>ODI</td>
<td>-0.064</td>
<td>0.047</td>
<td>0.341</td>
<td>-0.170</td>
<td>-0.099</td>
</tr>
<tr>
<td>BPS</td>
<td>0.171</td>
<td>0.502*</td>
<td>0.288</td>
<td>-0.250</td>
<td>-0.307</td>
</tr>
<tr>
<td>Sum of total LPM CSA</td>
<td>-0.220</td>
<td>0.158</td>
<td>0.181</td>
<td>-0.272</td>
<td>-0.017</td>
</tr>
<tr>
<td>Mean of total LPM density</td>
<td>-0.099</td>
<td>-0.005</td>
<td>0.159</td>
<td>0.078</td>
<td>0.076</td>
</tr>
<tr>
<td>Back extensor strength</td>
<td>-0.321</td>
<td>0.310</td>
<td>0.207</td>
<td>-0.058</td>
<td>0.366</td>
</tr>
</tbody>
</table>

BMI, body mass index; ASM, appendicular skeletal muscle mass; Ht², height squared; CSA, cross-sectional area; SPPB, short physical performance battery; TUG, Timed Up and Go test; ODI, Oswestry Disability Index; BPS, Back Performance Scale; LPM, lumbar paraspinal muscle.

*p<0.05 by Pearson correlation coefficient.

Table 3. Correlations between spinal sagittal balance indices and functional outcomes

<table>
<thead>
<tr>
<th>Predictor</th>
<th>LL</th>
<th>TK</th>
<th>PT</th>
<th>SS</th>
<th>PI</th>
<th>SVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPPB</td>
<td>-0.028</td>
<td>-0.021</td>
<td>0.015</td>
<td>-0.158</td>
<td>-0.121</td>
<td>-0.084</td>
</tr>
<tr>
<td>TUG</td>
<td>-0.010</td>
<td>0.030</td>
<td>0.170</td>
<td>0.046</td>
<td>0.097</td>
<td>0.042</td>
</tr>
<tr>
<td>ODI</td>
<td>-0.423*</td>
<td>-0.414*</td>
<td>0.169</td>
<td>-0.109</td>
<td>-0.010</td>
<td>0.165</td>
</tr>
<tr>
<td>BPS</td>
<td>0.128</td>
<td>-0.046</td>
<td>0.026</td>
<td>0.100</td>
<td>0.013</td>
<td>0.299</td>
</tr>
<tr>
<td>Sum of total LPM CSA</td>
<td>0.439*</td>
<td>0.399</td>
<td>-0.502*</td>
<td>-0.080</td>
<td>-0.251</td>
<td>-0.394</td>
</tr>
<tr>
<td>Mean of total LPM density</td>
<td>0.319</td>
<td>0.388</td>
<td>-0.504*</td>
<td>0.335</td>
<td>0.036</td>
<td>-0.221</td>
</tr>
<tr>
<td>Back extensor strength</td>
<td>-0.161</td>
<td>0.285</td>
<td>-0.087</td>
<td>-0.385</td>
<td>-0.490*</td>
<td>-0.110</td>
</tr>
</tbody>
</table>

LL, lumbar lordosis; TK, thoracic kyphosis; PT, pelvic tilt; SS, sacral slope; PI, pelvic incidence; SVA, sagittal vertical axis; SPPB, short physical performance battery; TUG, Timed Up and Go test; ODI, Oswestry Disability Index; BPS, Back Performance Scale; LPM, lumbar paraspinal muscle; CSA, cross-sectional area.

*p<0.05 by Pearson correlation coefficient.

Table 4. Multivariate regression analysis

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Standard error</th>
<th>Standardized coefficients</th>
<th>t</th>
<th>p-value</th>
<th>R</th>
<th>Adjusted R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>1070.403</td>
<td>-</td>
<td>13.857</td>
<td>0.000</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pelvic tilt</td>
<td>51.061</td>
<td>-0.610</td>
<td>-0.266</td>
<td>0.021</td>
<td>0.610</td>
<td>0.320</td>
</tr>
</tbody>
</table>

Fig. 2. Scatter grams showing the relationships between pelvic tilt angle and LPM CSA (A) and mean density (B). LPM, lumbar paraspinal muscle; CSA, cross-sectional area.
right posture to compensate for kyphosis.\textsuperscript{26} While other SSB parameters such as LL and SVA can be easily affected by posture and position, the PT is a reproducible and reliable measure of global sagittal alignment regardless of the level of training.\textsuperscript{27,28} PT is also correlated with health-related quality of life in adult spinal deformity.\textsuperscript{29}\textsuperscript{29} Therefore, among the SSB parameters, the association of PT with spinal sarcopenia warrants further investigation.

Isokinetic back muscle strength positively affects SSB.\textsuperscript{30} A cohort study in older adults also reported the negative correlation between spinal inclination and back muscle strength (r = -0.294).\textsuperscript{30} However, in our study, back extensor strength was not independently associated with SSB, contrary to the hypothesis, although there was a simple correlation between back extensor and PI (r = -0.490). There are two potential explanations for this conflict. If the values of back extensor strengths measured in this study were normal because participants were healthy community-dwelling older women without sarcopenia, they might not affect SSB due to the ceiling effect. Another assumption was that the muscle strength measured in this study was the isometric back extensor strength, which might not be valid in older adults. Therefore, back extensor strength might be better to be evaluated using the gold-standard isokinetic dynamometer.

Our study had several limitations. First, this was a cross-sectional study and not a prospective investigation. In addition, the sample size (n = 24) was not sufficient for a good prediction level in the regression model.\textsuperscript{31} Thus, the longitudinal SSB effects on spinal sarcopenia and causal relationship between SSB and spinal sarcopenia could not be verified. However, we will prospectively follow-up and evaluate the participants to answer these questions in a future study. Second, bias was possible in the participant selection. Because we enrolled only healthy and community-dwelling older women, there were no women with sarcopenia. Therefore, even though we compared sarcopenic indices to functional outcomes and SSB parameters, these outcome variables might be skewed to a healthy population and might not reflect sarcopenia and paraspinal muscle degeneration. Recently, Ohyama et al.\textsuperscript{32} reported the relationship between sarcopenia and spinopelvic parameters in 126 participants, 21.4% of whom were patients with sarcopenia. The authors reported larger SVA and TK in the sarcopenia group than those in the group without sarcopenia among patients with a spinopelvic mismatch. Thus, participants diagnosed with sarcopenia should be sufficiently included in the target population. Finally, we did not investigate the global alignment and proportion (GAP) score, which can denote ‘normal’ and ‘pathologic’ standing sagittal alignment and shape as a single score for every magnitude of pelvic incidence.\textsuperscript{33} In the GAP, the optimal sagittal alignment is based on four factors deviating from their ideal curves and these factors are proportionally related to the PI.\textsuperscript{34} Therefore, future studies should describe the SSB by measuring a single variable, such as the GAP score, rather than listing several different variables.

In conclusion, our data suggest PT angle was significantly correlated with LPM CSA in healthy older women. To our knowledge, this is the first report to investigate the relationships between sarcopenic indices and spinal muscle degeneration with SSB.

\section*{Conflict of Interest Disclosures}

The researchers claim no conflicts of interest.

\section*{Acknowledgements}

This research was funded by the Korean Geriatrics Society.

\section*{References}

8. Meakin JR, Fulford J, Seymour R, Welsman JR, Knapp KM. The relationship between sagittal curvature and extensor mus-

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Spinal sarcopenia and spinal sagittal balance


Efficacy and Safety of X-incision with Inversed Morcellation in Holmium Laser Enucleation of the Prostate: Comparison to Conventional Morcellation

Dae Hyoung Park, Jong Bouk Lee, Chun Ha Hwang, Jong Hyun Yoon, Jung Hyun Jo, Tae Wook Jeong, Woong Na
Department of Urology, National Medical Center, Seoul, Korea

Background: Three-quarters of aged men experience lower urinary tract symptoms with benign prostate hypertrophy (BPH). Transurethral resection of the prostate (TURP) and holmium laser enucleation of the prostate (HoLEP) are standard endosurgical procedures in patients with BPH. Previous studies reported better results in patients undergoing HoLEP than in those undergoing TURP. Methods: This study compared the efficiency and safety of conventional morcellation and morcellation performed after X-incision during enucleation, a newly added technique in HoLEP. Overall, 174 patients were selected as the final study population. The populations were stratified with respect to resected volumes. A t-test were used to compare the conventional morcellation and X-incision procedure groups. Results: In morcellation times and rates, there were significant differences in stratified resected mass (g) between the groups. The results also showed a decreased incidence of bladder injury as a surgical complication. Conclusion: We believe morcellation performed after X-incision procedure during enucleation is efficient and safe for older adults with BPH.

Key Words: HoLEP, Morcellation, BPH, Enucleation

INTRODUCTION

Three-quarters of aged men experience low urinary tract symptoms (LUTS) with benign prostate hypertrophy (BPH). These symptoms can be alleviated by medications; however, some patients with dysuria eventually undergo surgical treatment to prevent relative symptoms and diseases such as urinary retention, urinary tract infection (UTI), and urinary stones. In these cases, transurethral resection of the prostate (TURP) and holmium laser enucleation of the prostate (HoLEP) are considered standard endosurgical operations for patients with BPH.

After Gilling et al. first described HoLEP in 1995, its use has steadily increased. In the early days of laser prostatectomy, it was not useful due to serious complications such as long-term urinary obstruction and dysuria. However, with the development of sophisticated technologies, HoLEP is now used broadly and is recognized as an effective procedure on par with TURP while providing outstanding results in dissection, coagulation, and vaporization. Moon et al. reported less hemorrhage in HoLEP than in TURP in prior BPH patients. In addition, compared to those who underwent TURP, patients who underwent HoLEP had outstanding results of the International Prostate Symptom Score (IPSS) at 12 months and maximum flow rates. Accordingly, there has been a paradigm shift to HoLEP as the primary surgery in modern BPH, which alleviates LUTS and improves urodynamic study (UDS).

HoLEP with mechanical morcellation can be divided into two processes: gross tissue resection or enucleation and morcellation to extract enucleated prostatic tissue from the body. The early practice of leaving prostate tissue in the bladder after HoLRP caused problems. Techniques using transurethral grasper were considered but the enucleated prostatic tissue was sometimes too large to extract from the bladder.
Since the development of Holmium: yttrium-aluminum-garnet (YAG) lasers, HoLEP was more practical by making enucleation of prostatic tissue easier. However, handling of the resected tissue remained a difficult task. Thanks to transurethral morcellators, large tissue masses are no longer a significant problem; however, major drawbacks like the potential for bladder injury and low suction efficacy remain.\(^8\)\(^\text{10}\)

To overcome these challenges, in 2012, Chen et al.\(^11\) described an improved morcellation procedure during enucleation. This procedure included three stages: (1) roughening of the tissue surface during enucleation, (2) adoption of different methods according to volume sizes during morcellation, and (3) removal of prostatic tissue by laser or suction of the prostatic fossa. Evolution of this method roughens the surface during enucleation for better and easier morcellation. Enucleation partially resects the tissue into an X-shape to form parts per site before the tissue is shredded. In addition, the resected tissue is massed together to be suctioned out simultaneously during morcellation (Fig. 1).

In the conventional method, morcellation of large and solid tissue requires significant time and additional resection of tissue in the bladder, which can lead to increased risks of bladder injury. Therefore, the present study compared the efficacy and safety of conventional morcellation and morcellation carried out after X-incision during enucleation, which is a newly-added technique in HoLEP.

**MATERIALS AND METHODS**

**Participants**
Patients with a medical history of prostate surgery, or repeated surgery, or surgery involving surgery for a kidney stone were excluded from this analysis.

Data were collected from 465 patients who visited a general hospital in Seoul, Korea between January 2012 and December 2018. Among them, 291 patients with missing data (more than one variable) on prostate-specific antigen (PSA) level, operation time, morcellation time, transrectal ultrasound (TRUS), and resected weight were excluded. Therefore, a total of 174 patients (93 patients who underwent conventional morcellation and 81 who underwent X-incision during enucleation) were included as the final study population (Fig. 2).

This study was approved by the Institutional Review Board of the National Medical Center (No. H-1901-098-002), which waived the requirement for written informed consent.

**Equipment and Procedure**
Morcellation was performed using a 26-Fr nephroscope and morcellator (VersaCut Morcellator; Lumenis Inc., Yokneam, Israel)
from 80 to 100 W. A VersaPulse power holmium laser was used for prostate adenoma enucleation with a 26-Fr resectoscope (Karl Storz, El Segundo, CA, USA). The operator performed an X-incision before enucleation to make the prostate adenoma rougher and more resistant. If bleeding occurred, the operator performed dissection and coagulation. The enucleated prostatic tissue was cut into four pieces with one X-shaped incision per site range. The scope of the prostate within each site range was defined as the middle-sized lobe, and the operator performed X-incisions while sizing the prostatic tissue by 1 × 1 cm roughly at a good distance of resecting the tissue with laser. For example, if one site of the lobe area measured 2 × 2 cm, X-incisions were performed for four parts. Each incision required 3-4 seconds to perform; thus, in total, an average of 60 seconds was required per lobe site.

 Normally, four X-incisions were required to roughen the surface. While the incisions were not intended to completely separate the resected tissues, this did occasionally occur. The tissue was then completely dissected until it remained attached to the bladder neck in a mushroom shape. Tissue removal was performed by retrograde morcellation. Every operation was performed by one operator with experience with more than 500 procedures.

Statistical Analysis
IBM SPSS Statistics version 19.0 for Windows (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Descriptive statistics were determined for baseline characteristics such as age and prostate volume during TRUS. The conventional morcellation and X-incision procedure group were also compared, with patients who did not undergo X-incision designated as group 1 and those who underwent X-incisions designated as group 2. Statistical analysis included t-tests, with p-values less than 0.05 considered significant. To remove bias in the t-tests, the populations were stratified by resected mass (< 20, 21–40, 41–60, and > 61 g).

RESULTS
This study included 174 patients with a mean age of 71.5 ± 7.3 years. Two patients had missing PSA data. Except for these two patients, the mean PSA level was 6.7 ± 12.7 ng/mL. The mean TRUS volume (mL) was 56.4 ± 27.9 mL. The mean morcellation time and resected mass were 271.7 ± 176.8 seconds and 24.9 ± 23.3 g, respectively (Table 1). Group 1 included 93 patients with a mean age of 71.9 ± 7.7 years and mean PSA of 5.8 ± 12.2 ng/mL except for one participant with missing PSA values. The mean TRUS volume was 53.0 ± 26.3 mL and the mean morcellation time and resected mass were 286.1 ± 196.2 seconds and 19.9 ± 19.4 g, respectively. Group 2 included 81 patients with a mean age of 71.0 ± 6.8 years and mean PSA of 7.8 ± 13.2 ng/mL except for one participant without PSA data. The mean TRUS volume was 60.3 ± 29.4 mL and the mean morcellation time and resected mass were 255.2 ± 151.1 seconds and 30.6 ± 26.2 g, respectively. There were statistically significant differences in resected mass and morcellation rate. The two groups were stratified according to resected mass for descriptive and t-test analyses.

In group 1, the mean age was 70.9 ± 6.9 years for patients with resected masses less than 21 g, 71.7 ± 8.1 years for 21–40 g, 75.1 ± 5.9 years for 41–60 g, and 80.0 ± 14.0 years for > 61 g. The mean morcellation time for patients with resected masses under 20, 21–40, 41–60, and over 61 g were 187.4 ± 83.0, 379.6 ± 63.6, 551.6 ± 126.0, and 830.0 ± 116.5 seconds, respectively. The mean morcellation rate calculated as the resected mass per minute in each resected mass group were 3.7 ± 1.6, 4.3 ± 0.5, 5.2 ± 1.1, and 5.7 ± 1.1 g/min, respectively. In group 2, the mean age of patients with resected masses under 20, 21–40, 41–60, and over 61 g were 71.3 ± 7.3, 71.0 ± 6.0, 71.2 ± 7.1 and 70.0 ± 6.8 years, respectively. The mean morcellation times for these groups were 146.4 ± 76.6, 276.2 ± 109.3, 388.5 ± 115.8, and 470.4 ± 93.0 seconds, respectively. The mean morcellation rates were 5.9 ± 4.3, 7.1 ± 3.5, 8.5 ± 3.3, and 10.9 ± 3.1 g/min, respectively. There were no significant differences in age and PSA values between the two groups for each resected amount. The difference in TRUS volume between the two groups was significant only for resected mass of 41–60 mL. The differences in morcellation time and rate were statistically significant for all stratified resected mass groups (Table 2).

DISCUSSION
This study evaluated the efficiency and safety of morcellation by merging the resected tissues as much as possible while making a rough surface during enucleation in HoLEP.

Group 2 underwent X-incision during enucleation and showed reduced morcellation time and higher morcellation rate compared with the group that underwent conventional morcellation.

Lee et al.12) reported that an inverse morcellation technique was
Table 2. Descriptive statistics of baseline characteristics and t-tests stratified by resected mass

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>&lt; 20 g</th>
<th>21-40 g</th>
<th>41-60 g</th>
<th>&gt; 61 g</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1 (n = 93)</td>
<td>Group 2 (n = 81)</td>
<td>t p-value</td>
<td>Group 1 (n = 65)</td>
<td>Group 2 (n = 38)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>71.9± 7.7</td>
<td>71.0± 6.8</td>
<td>0.807 0.421</td>
<td>70.9± 6.9</td>
<td>71.3± 7.3</td>
</tr>
<tr>
<td>PSA (ng/mL)</td>
<td>5.8± 12.2 (n = 92)</td>
<td>7.8± 13.2</td>
<td>-0.994 0.322</td>
<td>5.6± 13.8</td>
<td>4.9± 10.8</td>
</tr>
<tr>
<td>TRUS (mL)</td>
<td>53.0± 26.3</td>
<td>60.3± 29.4</td>
<td>-1.746 0.083</td>
<td>45.8± 24.2</td>
<td>44.8± 12.2</td>
</tr>
<tr>
<td>Morcellation time (s)</td>
<td>286.1± 196.2</td>
<td>255.2± 151.1</td>
<td>1.153 0.251</td>
<td>187.4± 83.0</td>
<td>146.4± 76.6</td>
</tr>
<tr>
<td>Resected mass (g)</td>
<td>19.9± 19.4</td>
<td>30.6± 26.2</td>
<td>-2.827 0.005</td>
<td>10.2± 4.0</td>
<td>1.1± 4.7</td>
</tr>
<tr>
<td>Morcellation rate</td>
<td>4.0± 1.5</td>
<td>7.2± 4.1</td>
<td>-6.572 0.001</td>
<td>3.7± 1.6</td>
<td>5.9± 4.3</td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation.
PSA, prostate-specific antigen; TRUS, transrectal ultrasonography; Morcellation rate, resected amount (g) per minute.
*p<0.05.
safer and more efficient than the existing upward technique. This technique removes the glade between the blade and bladder wall with suction by placing the blade in the inverse position. Benefits such as improved morcellation efficiency and reducing bladder injury have been reported. Therefore, the present study applied the inverse technique based on the preceding research (Table 3). Rijo et al.13) proved that morcellation using a mechanical morcellator is a safe and appropriate procedure to remove adenoma after enucleation, while Chen et al.11) proposed three stages for more effective morcellation; namely roughening the gland surface, restriction of gland activity by contact with the morcellator blade, and loosening of hard and dense tissue.

The potential risks of morcellation include bladder injury and perforation.14) Nonetheless, complications such as prostate capsule perforation during enucleation and bladder injury during morcellation have been dismissed as trivial. Rather, they have been considered the outcome of the learning curve.2) This could be prevented to some extent by enlarging the bladder capacity before morcellation; however, it is restrictive and, to be certain, adenoma pretreatment and morcellation technique should be included. Hurle et al.14) proposed that bladder injury could be alleviated only by improving the surgical technique while reporting a high rate of bladder injury of approximately 9% (bladder mucosal injury, 8.3%; bladder perforation, 0.6%) after morcellation.

Our study results showed increased morcellation rates and reduced incidences of complications such as bladder injury following X-incisions to roughen resected prostatic tissue during enucleation. The results suggest that HoLEP combined with mechanical morcellation could replace TURP. This procedure could be considered as the primary operation for modern prostate surgery and X-incisions during enucleation could be adopted for easier and safer morcellation. There are currently insufficient studies on easier, faster, and safer morcellation. Although techniques to roughen the gland surface have been proposed, large-scale studies are scarce.

The present study could not exclude the possibility of author bias as the procedures were executed by a single operator. The study did not include patients who underwent HoLEP from 2009 to 2011 and included only patients who underwent surgery after 2012, thus reducing the possibility of a learning curve. However, as this study was not performed under the same circumstances, operator bias cannot be excluded.

In conclusion, morcellation performed after the X-incision procedure during enucleation as a newly adopted technique during HoLEP operation was efficient and safe; however, more case studies and research on this procedure are required.

### CONFLICT OF INTEREST DISCLOSURES

The researchers claim no conflicts of interest.

### REFERENCES


### Table 3. Morcellation efficiency rates

<table>
<thead>
<tr>
<th>Study</th>
<th>Morcellation efficiency rate (g/min)</th>
<th>Bladder injury cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ishikawa et al.15)</td>
<td>6.7 (inverse technique)</td>
<td>NA</td>
</tr>
<tr>
<td>Lee et al.12)</td>
<td>1.93 ± 1.14 (upward technique)</td>
<td>11 (13)</td>
</tr>
<tr>
<td></td>
<td>4.06 ± 0.95 (inverse technique)</td>
<td>2 (2.5)</td>
</tr>
<tr>
<td>Hurle et al.14)</td>
<td>2.3 ± 1.5</td>
<td>19 (5.7)</td>
</tr>
<tr>
<td>Kim et al.16)</td>
<td>4.3</td>
<td>NA</td>
</tr>
<tr>
<td>Rijo et al.13)</td>
<td>11.0 (7.70–16.0)</td>
<td>2 (NA)</td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation or median (min-max). NA, not applicable.


What is the Optimal Tool to Measure Gait Speed in a Clinical Setting?

Dae Young Kim1,2, Seung-Lyul Oh1

1Aging & Mobility Biophysics Laboratory, Department of Rehabilitation Medicine, Seoul National University Bundang Hospital, Seongnam, Korea
2Health and Exercise Science Laboratory, Department of Kinesiology, Seoul National University, Seoul, Korea

Physical changes due to age, cognitive decline, reduced agility to cope with the risk of falling, and environmental factors are becoming a significant threat to healthy aging.1) In older adults, reduced gait speed is strongly associated with the risk of falls and limited physical functional capacity.2,3) Gait speed measurement is the most important and simple test to assess changes in the physical function of older adults.4-6) Gait speed is used not only to evaluate physical function but also to assess the general health status and diagnose sarcopenia in older adults.7) Generally, manual stopwatch measurement is the most frequently used method to evaluate gait speed because it is easy, simple, fast, convenient, and economical and can be performed without the need for experts.8,9) However, with the emerging importance of gait speed measurement, automatic sensors are increasingly used for more accurate measurement.10)

We read the article by Jung et al.11) with great interest. Our laboratory measures gait speed using automatic sensors and manual stopwatch. We agree with the results of the study performed by Jung et al.11) in their cross-comparisons of gait speed measured using four different versions of automatic sensors and a conventional stopwatch. Until now, gait speed has mainly been measured manually using a stopwatch in clinical settings; however, gait speed assessment requires more accurate and consistent measurement for assessing the physical function in older adults. Therefore, cross-comparison of gait speed assessed by various automatic walking measurement equipment and stopwatch is an exciting and meaningful topic. In particular, we thank Jung et al.11) for their impressive research on a more advanced version of the automatic sensor.

We previously compared the results of gait speed measured using automatic sensors by beam-breaking to those measured by manual stopwatch according to the starting protocols (standing start or moving start).12) We suggested the need for careful attention to avoid miscalculation when gait speed was measured manually using a stopwatch with a moving start. The use of automatic measuring equipment is recommended when a moving start is used as the starting protocol. Therefore, not only the timing method (manual stopwatch vs. automatic timer) but also the starting protocol (standing vs. moving start) require consideration in the study of gait speed measurement.

One disadvantage of measurement by the beam-breaking system described by the authors is an enlarged fanning effect in participants with wide-based gait or veering tendency.11) To compensate for this problem, assessment of trunk movement with the sensor facing the participant’s trunk rather than the side of the ankle has been proposed. However, this method requires some consideration. First, in the moving start method, the automatic measurement equipment is located in front of the end of walking, which may interfere with regular straight walking. Moreover, measurement of gait speed using longitudinal one-dimensional light detection and ranging technology requires a linear distance of about 10 m within the measurable range, imposing a space limitation in the clinical setting. The clinical utility of this equipment will be enhanced with troubleshooting of these issues in further studies.

CONFLICT OF INTEREST DISCLOSURES

The authors claim no conflicts of interest.

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Corresponding Author: Seung-Lyul Oh, PhD
Aging & Mobility Biophysics Laboratory, Department of Rehabilitation Medicine, Seoul National University Bundang Hospital, 82 Gumi-ro 173beon-gil, Bundang-gu, Seongnam 13620, Korea
E-mail: oh3328@snu.ac.kr
ORCID: https://orcid.org/0000-0002-4730-6686

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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 research 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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