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Aims and Scope

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

General Information

The official journal title has been *Annals of Geriatric Medicine and Research* since September 2016 which followed the Journal of the Korean Geriatrics Society (1997-2016, pISSN: 1229-2397, eISSN: 2288-1239). It is the official journal of the Korean Geriatrics Society (http://www.geriatrics.or.kr/eng/) and the Korean Society for Gerontology (http://www.korea-biogerontology.co.kr). It is published in English quarterly on the last days of March, June, September, and December. The journal publishes original research articles, case reports, reviews, special contributions, and commentaries. Review board consists of members in 7 different countries. Articles are welcome for submission from all over the world. The contents of this Journal are indexed in Web of Science, Scopus, PubMed, PubMed Central (PMC), EBSCO, DOAJ, Embase, KoreaMed, KoMCI, KCI, DOAJ/Crossref, and Google Scholar. It is accessible without barrier from Korea Citation Index (https://www.kci.go.kr) or National Library of Korea (http://nl.go.kr) in the event a journal is no longer published.

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Ethical Guidelines for Publishing in the *Annals of Geriatric Medicine and Research*

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**INTRODUCTION**

*Annals of Geriatric Medicine and Research* (AGMR) is the official journal of the Korean Geriatrics Society and the Korean Society for Gerontology. This peer-reviewed journal aims to provide new information on clinical and biological science and issues on policymaking for older adults. AGMR is the leading journal of geriatrics and gerontology in Korea, one of the world’s fastest-aging countries. As population aging has become a dominant demographic trend in East Asian countries, AGMR has also been rapidly growing and establishing its presence in this region. AGMR has been publishing articles in English since 2016; since that time, the general volume of submissions has been increasing, and the journal currently has nearly 100% citation growth annually.

As the journal continues to grow and receive increasing numbers of submissions every year, the editors seek to continuously examine and revise publication guidelines for authors to maintain credibility, transparency of scientific publications, and minimize potential adverse issues from conflicts of interest. In addition, as with increasing emphasis on publication ethics, it is our duty to meet those standards for high-quality scientific publications. Therefore, to strengthen ethical publishing and encourage authors to adhere to ethical policies, we have established publication guidelines that authors should comply with when submitting their manuscripts to AGMR. These guidelines are based on the International Standards for Editors and Authors by the Committee on Publication Ethics (COPE), the International Committee of Medical Journal Editors (ICMJE) Recommendations, and the Principles of Transparency and Best Practice in Scholarly Publishing—a joint statement by the COPE, Directory of Open Access Journals (DOAJ), World Association of Medical Editors (WAME), and Open Access Scholarly Publishers Association (OASPA).

*Annals of Geriatric Medicine and Research* (AGMR) aims to provide new information on clinical and biological science and issues on policymaking for older adults. This article summarizes the ethical guidelines of AGMR based on relevant recommendations from the International Standards for Editors and Authors, the International Committee of Medical Journal Editors, and the Principles of Transparency and Best Practice in Scholarly Publishing. All authors whose articles are to be published in AGMR should refer to these guidelines, which will mention that authors need to comply with the guidelines. The editorial board will also continuously monitor our responsibilities regarding ethical publishing. The combined efforts of authors, reviewers, and editors will help maintain the scientific excellence of AGMR.

**Key Words:** Ethics, Publications, Guidelines

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All authors whose articles are to be published in AGMR should reference these guidelines, which will indicate the authors’ compliance with the following guidelines.

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Authorship
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All persons who have made considerable efforts but are not eligible to be authors should be named in the Acknowledgments section of the article.

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For animal subjects, research should be performed ethically and should be based on the National or Institutional Guide for the Care and Use of Laboratory Animals.

Statement of Informed Consent and Institutional Approval
Clinical studies should be approved by the Institutional Review Board (IRB) of the author’s affiliated institution. In addition, a statement regarding the informed consent of human subjects should be retained. For studies involving animal subjects, approval is required by the Institutional Animal Care and Use Committee (IACUC). These documents may be requested for IRB/IACUC approval and study conduct.

Conflicts of Interest and Funding Sources
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For suspected cases of research or publication misconduct (fabricated data, plagiarism, changes in authorship, undisclosed conflict of interest, misappropriation of the ideas of others, ethical problems with the submitted manuscript, and inappropriate behavior in relation to misconduct), the editorial board will base its decision by following the flowchart provided by the COPE (http://publicationethics.org/resources/flowcharts).

CONCLUSION

The guidelines mentioned above are specifically organized for authors who wish to publish manuscripts in AGMR. These guidelines aim to maintain the ethical standards of publications while the journal has been experiencing substantial quantitative growth. While reviewers safeguard the scientific soundness of manuscripts, the editorial board also continuously monitors our responsibilities regarding ethical publishing. The combined efforts of the authors, reviewers, and editors will help to maintain the scientific excellence of AGMR.

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CONFLICT OF INTEREST
The authors claim no conflicts of interest.

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AUTHOR CONTRIBUTION
Conceptualization, JHN, HWJ, HG, JYL; Supervision, JYL; Writing-original draft, JHN; Writing-review & editing, HWJ, HG, JYL.

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INTRODUCTION

Aging is accompanied by a series of adverse changes, typically including the loss of 30%–40% of skeletal muscle mass, particularly type II fibers.\(^1\) The muscle mass at 60–70 years of age is approximately 70%–80% that in younger people (< 60 years old) and is also accompanied by diminished muscle strength.\(^2\) Certain characteristics commonly observed in older adults reflect limitations due to diminished muscular strength and mobility functions.\(^3,4\) Therefore, it is essential to develop exercise interventions that maintain mobility by countering the decline of muscular and mobility functions and improving the quality of life of older adults.\(^5\) However, it is difficult to apply conventional resistance exercises, which largely comprise isometric and concentric contractions, at sufficient intensity and amount to increase strength and improve function in older individuals with limited physical function and mobility.\(^6,7\) Thus, mechanism-based specific modalities have received attention; among these are the eccentric-based model, which we will introduce.

Eccentric exercise has been introduced as a specific method to improve muscle strength and mobility in older adults.\(^8,9\) Eccentric muscle contractions occur when an active muscle force increases substantially during lengthening.\(^8,10\) Eccentric or lengthening contractions often occur during routine daily activities, such as descending stairs or transitioning from standing to sitting.\(^11\) Training programs primarily employing repetitive sub-maximal eccentric muscle contractions are a common form of exercise and an effective mode of conditioning for improving muscular strength and mobility in older adults. However, some have argued that resistance exercise can increase the risk of injury, reduce participation, and lead to boredom due to extended repetition.\(^12\) Thus, it is essential to create specific exercise interventions that...
are effective at preventing or delaying functional decline based on age-related changes in the muscle and mobility systems of older adults.

We reviewed the literature on the effectiveness, appropriate protocols, and relevant mechanisms of eccentric exercise for the improvement of muscle and mobility function in older adults, especially in comparison with other forms of traditional resistance exercise.

EFFECTS OF AGING ON MOBILITY AND SKELETAL MUSCLE FUNCTION

Age-related sarcopenia is a geriatric syndrome characterized by the loss of skeletal muscle mass and strength, which can severely limit muscle function.\(^1\,^{13}\,^{15}\) The main consequences of these age-related changes are functional limitation, disability, increased susceptibility to injuries, and increased morbidity and mortality.\(^6\,^{17}\) The overall decline in functional independence may seriously compromise the quality of life of older adults. The mobility function is closely correlated with changes in the muscle force-velocity relationship,\(^19\) and a slower walking speed is one of the representative changes linked to functional limitations.\(^5\) The major changes reported in aging skeletal muscles observed in older adults include decreased muscle fiber number and muscle cross-sectional area, as well as defective regeneration.\(^15\) Fiber-type changes constitute one reported mechanism by which muscle function is lost with aging, with type II fibers being more susceptible to atrophy than type I fibers.\(^20\) Furthermore, specific changes in the intrinsic ability of aging muscles to generate force have also been observed.\(^21\) The intrinsic contractile characteristics related to the cross-bridge mechanics of single fibers are altered with aging.\(^21\) Both decreased contractile tissues and reduced force-generating capacity per cross-bridge affect the contractile properties of aging muscles.\(^22\,^{23}\) A decrease in the specific force (normalized force per cross-sectional area) and unloaded shortening velocity of type I and IIA fibers in older adults compared to younger adults have also been reported.\(^24\,^{25}\) These findings provide evidence that both intrinsic changes in muscle quality and a loss of muscle mass contribute to age-associated changes in skeletal muscle function.

To prevent age-related decline in physical function, exercise interventions that maintain or increase muscle mass and muscle quality are primarily considered. Regular resistance exercises have been shown to counteract most aspects of physiological deterioration due to aging.\(^26\,^{27}\) However, older individuals with limited ability to perform exercises may have difficulty participating in conventional exercise interventions and, even if they do participate, are often unable to exercise sufficiently for the intervention to be effective.\(^28\) Therefore, exercise interventions or modalities specific to age-related changes and functional limitations are required for mobility-impaired older populations.

ECCENTRIC EXERCISE AND ITS APPLICATION IN OLDER ADULTS

Traditional resistance exercises, which emphasize concentric contraction, are effective in improving muscle function and restoring physical function. However, they are limited as an exercise method in the context of the physiological changes accompanying advancing age.\(^28\) For older adults, exercises must provide substantial changes in the intrinsic properties of skeletal muscles to improve the performance of functional movements in daily life.\(^29\) To overcome the limitations of conventional exercise interventions, a more specific intervention strategy targeting the changing physiological characteristics and muscular function associated with aging is warranted. Among various intervention strategies, eccentrically-biased exercise, especially chronic eccentric exercise, is reportedly superior to conventional training in terms of increasing muscle strength and function in aging populations.\(^30\) As the interest in specific modalities to counteract age-related muscle atrophy or functional decline has increased, various types of interventions focusing on eccentric contraction have been applied to older populations in clinical and community-based settings.\(^3\) Thus, it is necessary to review the current and relevant literature on the effectiveness of eccentric exercise modalities, especially in terms of their comparative effectiveness to other modalities, specific protocols, and intervention settings, including the equipment or tools used in the interventions.

This review searched the PubMed, Medline, Embase, and Cochrane Library databases in January 2021, using the following keywords: older adults, aging, eccentric exercise, eccentric contraction, muscle strength, and physical function. Based on the titles and some parts of the articles when needed, we screened the literature to select articles that met the following inclusion criteria: (1) participants aged 60 years or older, (2) randomized controlled trial, and (3) at least one group that performed eccentric exercise. We restricted our review to studies in English, owing to the translation of non-English language studies and lack of resources for review. The primary database search yielded 111 articles. After removing duplicates, 92 articles were considered potentially relevant and screened for content. Among them, 67 articles were excluded based on the training characteristics and study objectives. Of the 25 studies reviewed, 10 met our predetermined criteria (Fig. 1). Detailed information from each article, including author, year of
Eccentric contraction also tends to produce relatively high intensity with low volume, making it an attractive exercise option in strength programs to improve physical performance in older adults. \(^{40}\)

**THE BENEFITS OF ECCENTRIC CONTRACTION IN OLDER ADULTS**

Eccentric exercise consists mainly of eccentric isotonic contractions, wherein the muscle is forcefully lengthened. Eccentric exercise has various benefits in older adults. Eccentric contraction facilitates higher force production compared to other types of resistance exercises. \(^{31}\) The relative preservation of eccentric strength in older adults compared to isometric and concentric strength is well-established (Fig. 2). This reserve of eccentric strength could be beneficial in resistance training programs for people with reduced levels of muscle force. \(^{45}\) Eccentric contraction also tends to entail higher contraction velocities and reduced dependent con-

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**Table 1**

<table>
<thead>
<tr>
<th>Objective</th>
<th>To investigate the use of eccentric exercise to improve muscle and mobility function in older adults</th>
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| Date Source | - PubMed (n=65)  
- Google Scholar (n=14)  
- EMBASE (n=17)  
- Cochrane (n=15) |
| Study selection |  
- Inclusion criteria  
  - Randomized controlled trial  
  - At least one group involving eccentric exercise  
  - Participants who are over the 60 years old  
  - At least one functional outcome measure |
| Articles excluded |  
- 15 studies (Protocols=4; Not eccentric exercise=11) |
| Articles selected for literature review |  
- 10 studies met inclusion criteria |

**Fig. 1.** Flowchart of the methodology used in this review.

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publication, study design, and exercise characteristics (type, intensity, frequency, and duration) is shown in Table 1. As these studies employed different eccentric exercise programs and protocol treatments, it is difficult to determine whether the effects observed were solely due to eccentric exercise.

Some studies \(^{31,32}\) used specialized equipment, such as eccentric ergometers, isokinetic dynamometers, and flywheel ergometers. Kim et al., \(^{31}\) Mueller et al., \(^{33}\) and LaStayo et al. \(^{32}\) used eccentric ergometers for eccentric training. Mueller et al. \(^{33}\) reported a significant increase in isometric strength. Isokinetic strength and power were also significantly increased following training using an eccentric ergometer. \(^{32}\) However, LaStayo et al. \(^{32}\) reported no significant differences between traditional resistance and eccentric groups in the fall risk variables of mobility and leg extensor muscle power. However, as this study did not employ power training in the eccentric or conventional resistance exercise, it would be hard to expect significant changes in variables related to power output. Squat-based exercise interventions using a flywheel in the study by Sanudo et al. resulted in significant increases in balance and power in older participants. \(^{33}\) Raj et al. \(^{34}\) employed eccentric exercises using an isokinetic dynamometer, which resulted in significant improvement in maximum one-repetition maximum (1RM) exercises and isometric and isokinetic torque. Collectively, these results indicated that the use of specialized equipment for eccentric contraction provided significant benefits in muscle and mobility function in older adults.

Other than interventions with specialized equipment, other studies have applied various types of eccentric contraction protocols. \(^{36-40}\) Eccentric exercise interventions, such as regular body squats without a device and the use of a leg extension machine, have been performed in older adults. \(^{40,42}\) These studies showed significant improvements in isometric, eccentric, and concentric peak torque, demonstrating that basic manual resistance exercise training emphasizing eccentric muscle contractions could improve muscle strength and physical function. Dias et al. \(^{46}\) reported on the application of eccentric (concentric and eccentric phases set at 1.5 and 4.5 seconds, respectively) and conventional resistance (concentric and eccentric phases set at 1.5 seconds training) in older women. Both eccentric and concentric training improved knee extension at 1RM, the Timed Up-and-Go test, and the 6-meter walk test. \(^{46}\) Other studies reported that the effect of eccentric exercise was not superior to that of conventional resistance exercise, and some outcomes indicated no effects. Eccentrically-biased training using a leg press resulted in no significant improvements in leg extension strength, leg curl strength, or 1RM maximal strength. \(^{37,38}\) This finding probably indicated insufficient training to induce adaptation or that the adaptation failed to affect muscle strength or functional ability.

These results indicated that pure eccentric exercise using specialized equipment might improve overall muscle strength to a greater extent than eccentrically-biased or combined eccentric and concentric contraction \(^{31,43}\) and that this treatment modality can overload the muscular system at a low energy cost. \(^{39}\) Therefore, eccentric exercise can produce relatively high intensity with low volume, making it an attractive exercise option in strength programs to improve physical performance in older adults. \(^{40}\)
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Participant characteristics</th>
<th>Device &amp; modality</th>
<th>Intervention</th>
<th>Outcomes (p-value)</th>
</tr>
</thead>
</table>
| Kim et al.    | 2019  | ET (n = 8), CT (n = 8)       | Eccentric ergometer, leg press | - ET: 50% of estimated 1RM tested via eccentric device, two times (30 min) per week.  
- CT: 50% of estimated 1RM tested via the EN dynamic seated leg press, two times (30 min) per week. Duration: 8 weeks | Significant improvements in muscle strength, isokinetic and isometric power, and physical function (stair climb and gait speed, \( p < 0.05 \)). |
| Mueller et al.| 2009  | ET (n = 23), RT (n = 23), CT (n = 16) | Eccentric ergometer, leg press, leg curl | - ET: initial load on the eccentric ergometer (females 30 W, males 50 W)  
- RT: 20-min training (leg press, knee extension, leg curl, hip extension)  
- CT: no exercise Duration: 12 weeks | Significant increase with ET in isometric leg extension (8.4%) and eccentric muscle coordination (-43%) \( (p < 0.05) \). |
| LaStayo et al.| 2017  | ET (n = 68), CT (n = 66)    | Eccentric ergometer, leg press | - ET: 60 min per session, three times per week  
- CT: 3 sets of 15 repetitions of a seated bilateral leg press, 60%–65% of 1RM Duration: 16 weeks | No group differences in the numbers surviving without a fall \( (p = 0.565) \) or near-fall \( (p = 0.678) \). |
| Raj et al.    | 2012  | ET (n = 13), CT (n = 12)    | Isokinetic dynamometer       | Both ET and CT improved 1RM (Δ23%–35%, \( p < 0.01 \)), 6-m fast walk (Δ5%–7%, \( p < 0.01 \)), and concentric torque at 60 and 120°/sec (Δ6%–8%, \( p < 0.05 \)) | Significant improvements in TUG and COPAP in ET compared with CT  
Mean power also increased in ET  
No group differences in the numbers surviving without a fall \( (p = 0.565) \) or near-fall \( (p = 0.678) \). |
| Sanudo et al. | 2019  | ET (n = 18), CT (n = 18)    | YoYo leg extensor flywheel ergometer, leg press | Volume: - ET: 4 sets of 9 repetitions (2 repetitions at the beginning of each set to initiate the flywheel movement, 7 maximal bilateral repetitions accelerating the wheel in concentric action).  
- CT: 3 sets of 10 repetitions at 50% of 1RM Duration: 16 weeks | |
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Participant characteristics</th>
<th>Device &amp; modality</th>
<th>Intervention</th>
<th>Outcomes (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen et al.</td>
<td>2017</td>
<td>ET (n = 13), CT (n = 13)</td>
<td>Leg extension machine</td>
<td>Volume: 30–60 min per session (3 and 6 sets) - ET: 10%–100% or 1RM - CT: 50%–100% of 1RM Duration: 12 weeks</td>
<td>Functional physical fitness (30-second chair stand) and maximal concentric contraction strength of the knee extensors (eccentric &gt; concentric).</td>
</tr>
<tr>
<td>Gluchowski et al.</td>
<td>2017</td>
<td>ET (n = 11), EBT (eccentric-biased, n = 11), CT (n = 11)</td>
<td>Leg press</td>
<td>Volume: 4 sets of 10 repetitions, 70% of 1RM - ET: only performed eccentric phase (2–1) - EBT: performed the concentric phase bilaterally (2–1–2 tempo) - CT: 2 sec to lift the load (concentric), 1-sec pause, then 2-sec lowering (eccentric) phase Duration: 8 weeks</td>
<td>No significant differences between groups in eccentric maximal strength, functional capacity assessments, body composition, and blood biomarkers.</td>
</tr>
<tr>
<td>Dias et al.</td>
<td>2015</td>
<td>26 healthy elderly women: ET (n = 13), CT (n = 13)</td>
<td>Leg press, knee extension machines</td>
<td>Volume: ET, concentric and eccentric phases performed using 1.5 and 4.5 sec, respectively. CT, 1.5 sec for the concentric phase and 1.5 sec for the eccentric phase Duration: 12 weeks</td>
<td>Both ET and CT improved knee extension 1RM (24%–26%), TUG test (11–16%), 6-m walk test (9%–12%) (p &lt; 0.05)</td>
</tr>
<tr>
<td>Katsura et al.</td>
<td>2019</td>
<td>ET (n = 9), CT (n = 8)</td>
<td>Chair and push squats</td>
<td>Volume: - ET: sitting down in a chair - CT: standing up from a chair (2–5 sets of 10–15 repetitions) Home-based training included; 2–3 sets of 10–15 repetitions each day at least 2 days a week Duration: 8 weeks</td>
<td>Significant difference in muscle thickness (21.6% increase), MVC (38.3% increase); TUG (16.7% decrease) and balance (35.1% less movement) (p &lt; 0.05)</td>
</tr>
</tbody>
</table>

ET, eccentric training; CT, concentric training; 1RM, one-repetition maximum; LST, low-intensity resistance training with slow movement and tonic force generation; LN, low-intensity normal speed; TUG, Times Up and Go; MVC, maximal voluntary contraction; COPAP, anterior-posterior center of pressure.
traction velocities.46

Another advantage of eccentric exercise compared to concentric exercise for older adults is the lower metabolic cost and cardiorespiratory burden for the same amount of exercise, which enables efficient muscle strengthening with low energy consumption.47,48 The low metabolic cost and minimal cardiorespiratory burden imposed by eccentric exercise could be a therapeutic advantage for older adults, who are often vulnerable to metabolic demands. Thus, chronic eccentric exercise may be effectively used by older people who are functionally limited because high energy consumption is not required.

Delayed onset of muscle soreness (DOMS) is a known risk factor that interferes with exercise continuation (Fig. 2). DOMS includes pain, swelling, tenderness, and stiffness due to extracellular matrix damage, impaired sarcolemma permeability, and ultrastructural damage induced by eccentric contraction. However, this phenomenon occurs less frequently in older adults, mainly due to the characteristics of their muscles, in which type II fibers are predominately reduced.49 Additionally, high-intensity or high-volume eccentric exercise results in increased cross-sectional area of type II muscle fibers,50,51 as well as a shift toward fast type II muscle phenotypes.52 Therefore, eccentric exercise is considered an exercise intervention strategy that reflects the physiological characteristics of older individuals and is expected to be safe and effective.

Fig. 2. Advantages of eccentric contraction in older adults. DOMS, delayed onset of muscle soreness.

**MECHANISMS OF MUSCLE FUNCTION IMPROVEMENT BY ECCENTRIC EXERCISE**

Previous experimental studies have proposed mechanisms to explain muscle quality change following eccentric muscle contractions.53-60 Detailed information, including subject characteristics, exercise device and modality, and type of intervention in these studies, are shown in Table 2. Downhill treadmill exercise,53,54,56 single or repeated bouts of lengthening contraction,61,62 and electrical stimulation55,57 have been utilized as experimental models for eccentric exercise interventions.

Da Rocha et al.63 reported that overtraining (OT) protocols—downhill running-based overtraining (OTR/down), uphill running-based overtraining (OTR/up), and overtraining without inclination (OTR)—tended to induce a proinflammatory state and lead to skeletal muscle tissue injury. Indeed, proinflammatory cytokines were more sensitive to the OTR/down than to the OTR/up or OTR. Hyldahl et al.63 reported significant changes in the levels of two cytokines (monocyte chemoattractant protein-1 [MCP-1] and interferon γ-induced protein 10 kDa [IP-10]) following eccentric contraction, indicating a potential role for IP-10 as a mediator of satellite cell activity and muscle regeneration. Overall, proinflammatory responses suggesting muscle damage or remodeling were upregulated following eccentric but not concentric contraction. Furthermore, muscle damage induced by eccentric exercise acutely upregulated proinflammatory cytokines (e.g.,
Table 2. Experimental studies of mechanical and biochemical effects of eccentric contraction

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Subject characteristics</th>
<th>Device &amp; Modality</th>
<th>Intervention</th>
<th>Mechanisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lomonosova et al.</td>
<td>2014</td>
<td>56 male Wistar rats (3 months old)</td>
<td>Downhill treadmill</td>
<td>Downhill treadmill running: speed of 20 m/min on a -10° incline for 40 min One day before eccentric exercise testing by running at 5 m/min with a 2° uphill grade for 15 min</td>
<td>Exercise induced an up-regulation of nNOS mRNA expression level in soleus muscles when compared with muscles of control non-exercised rats.</td>
</tr>
<tr>
<td>Da Rocha et al.</td>
<td>2017</td>
<td>8 week old male C57BL/6 mice OTR (n = 16), OTR/up (n = 16), OTR/down (n = 16), CT (n = 16)</td>
<td>Uphill &amp; downhill treadmill</td>
<td>Treadmill running: 5 days, 10 min/day at 3 m/min; rodents performed the incremental load test</td>
<td>In the soleus, the OTR/down group increased all analyzed proinflammatory cytokines, the OTR/up group only increased IL-6.</td>
</tr>
<tr>
<td>Chavanelle et al.</td>
<td>2014</td>
<td>Male Wistar rats (n = 18, age 3 months)</td>
<td>Uphill &amp; downhill treadmill</td>
<td>Motor driven treadmill at various speed and inclines (+15%; 0%; -15%; -30%) Rest for 3 min, run at 15 cm/sec with increase of 5 cm/sec every 3 minutes</td>
<td>At the same mechanical intensity, the eccentric muscle contraction generated muscle force with lower oxygen cost compared to concentric contractions.</td>
</tr>
<tr>
<td>Lavagnino et al.</td>
<td>2014</td>
<td>Sprague-Dawley rats (n = 5, 1 month; n = 5, 3 month; n = 5, 12 month)</td>
<td>Cyclic exercise and tendon contraction</td>
<td>Individual rat tail tendon fascicles (RTTfs) from 5 rats from each age group were cyclically loaded to 2% strain at 0.17 Hz for 2 hours</td>
<td>The amount of initial tendon elongation after cyclic exercise was age-dependent, with older tendons having significantly less elongation than younger tendons.</td>
</tr>
<tr>
<td>Kim et al.</td>
<td>2016</td>
<td>Sprague-Dawley rats (young, 4 months; late middle-aged, 20 months) YC (n = 7), LMC (n = 7), LMD (n = 8), LMU (n = 7)</td>
<td>Uphill &amp; downhill treadmill</td>
<td>21 m/min at +10° slope for uphill training; 16 m/min with a -16° slope for downhill training: 60 min/day, 5 days/week for 8 weeks</td>
<td>BMD levels more increased in the downhill training group relative to the uphill training group in late-middle-aged bone.</td>
</tr>
<tr>
<td>West et al.</td>
<td>2018</td>
<td>Fischer 344 Brown Norway rats, male adult (10 months) and old (30 months)</td>
<td>Electrical stimulation</td>
<td>The muscles in the anterior compartment (tibialis anterior; extensor digitorum longus) undergo high-force lengthening contraction as a result of the stronger antagonist muscles in the posterior compartment</td>
<td>Protein synthesis response in old rats was associated with decreased IRS1 protein levels.</td>
</tr>
<tr>
<td>Hill et al.</td>
<td>2017</td>
<td>10-week-old (n = 40, young) and 78-week-old (n = 40, aged) female CD-1 mice</td>
<td>Electrical stimulation</td>
<td>The muscle was activated by electrical stimulation. Each preparation was allowed to stabilize for 10 min before performing isometric contractions</td>
<td>The ability of older EDL to withstand better the damaging effects of a sustained bout of eccentric muscle activity compared with younger EDL.</td>
</tr>
<tr>
<td>McBride et al.</td>
<td>1995</td>
<td>Female, 6- and 32-month-old Fisher 344/Brown Norway rats</td>
<td>Electrical stimulation</td>
<td>Stimulation: 100 Hz Trains provided for 2.5-sec maximum contractile force 4 sets of six repetitions with a 20-sec rest between repetitions and a 5-min rest between sets</td>
<td>The aged muscles generated a greater percentage of their maximum tension at lower stimulus frequencies.</td>
</tr>
</tbody>
</table>

nNOS, neuronal nitric oxide synthase; IL, interleukin; OTR: overtrained by running without inclination; OTR/up or down: overtrained by uphill or downhill running; CT: sedentary mice; YC: young control; LMC: late middle-aged; LMD: late middle-aged downhill; LMU: late middle-aged uphill; BMD, bone mineral density; EDL, extensor digitorum longus muscle.
increased interleukin-6 (IL-6) and, over a longer term, down-regulated proinflammatory cytokines and upregulated anti-inflammatory cytokines (e.g., increased IL-10). 66

Satellite cell activity is important for skeletal muscle health throughout the human lifespan. Eccentric but not concentric contractions are associated with a transient damage response, the repair of which appears to be a function of satellite cells. Moreover, eccentric contractions promoted a greater satellite cell response than concentric contractions. 67 Eccentric exercise also reportedly upregulated muscle-specific genes associated with muscle cell hypertrophy. 68-69 Thus, eccentric muscle contraction is useful when a high degree of muscle strength is required, as it can stimulate satellite cell activity and boost anabolic signaling. 28,66

Kim et al. 67 reported that the rectus femoris (RF) but not vastus lateralis (VL) muscle mass was significantly increased in the downhill training group and that mTOR and MyoD expression in the RF muscle was likely significantly increased by downhill running exercise. Therefore, eccentric exercise may be suitable for improving muscle growth, repair, and remodeling. In this context, West et al. 70 observed that protein synthesis in old muscle was directed toward repairing muscle damage rather than synthesizing myofibrillar proteins that would increase muscle size and strength under electrical stimulation. In addition, one in-vitro study assessing muscle activity under electrical stimulation reported better responses to the damaging effects of a sustained bout of eccentric muscle activity in older extensor digitorum longus muscle (EDL) compared to younger EDLs. 69 Collectively, the results of these studies demonstrated the beneficial effects of eccentric exercise in inducing skeletal muscle growth and enhancing skeletal muscle function in aged groups.

Eccentric muscle contraction generates muscle force with a lower metabolic demand (e.g., lower oxygen cost) for the same mechanical intensity as concentric contraction. 59 At the muscle cell level, the reduced energy cost of eccentric muscle contraction compared to isometric and concentric contractions has been explained based on the cross-bridge theory. Huxley 71 found that cross-bridges were not necessarily tied to the hydrolysis of one adenosine triphosphate (ATP) per cross-bridge cycle (as is typically assumed for isometric and concentric contractions); rather, one ATP molecule was hydrolyzed per multiple cross-bridge cycles in eccentric contractions. However, some have argued that the higher force and lower energy cost of eccentric contractions are difficult to fit into the cross-bridge theory. Unmeasurable assumptions regarding cross-bridge properties, such as stiffness, duty ratio, and energy states, are required to estimate the energy storage capabilities of cross-bridges during muscle contraction. Therefore, other theories have been proposed to account for muscle properties during eccentric contraction, such as residual force enhancement, the long-lasting increase in force that persists after stretching the active muscle; nonuniform sarcomere length; and titin-actin interactions. 60

Eccentric exercise can cause substantial changes in intramuscular structures, such as muscle fascicle length. 69 Lengthening eccentric contractions can increase muscle fascicle length, which decline with immobilization and can be increased through regular eccentric exercises. 18 Furthermore, eccentric loading can increase the number of sarcomeres in muscle fibers. 47-48 Butterfield et al. 48 reported significantly increased sarcomere number in the vastus intermedius of rats after 10 days of downhill walking training. The existence of the sarcomeric protein myotilin was suggested to play a role in the development of new sarcomere structures after stretching stimulation. 70

SAFETY AND ADVERSE EFFECTS

As eccentric contractions have traditionally been associated with muscle damage, eccentric exercise has routinely been discouraged. However, some evidence indicates that eccentric exercise can be safely and effectively performed in older adults. Mueller et al. 33 and Sanudo et al. 31 suggested that muscle damage can be avoided by carefully increasing the muscle load over repeated exercise sessions beginning with a very low eccentric load—30 W and 50 W for women and men, respectively; 33 first 3 weeks using one flywheel with a moment inertia of 0.025 kg·m² and after week 4, a flywheel with a moment inertia of 0.05 kg·m². 33 LaStayo et al. 71,72 reported that damage is inevitable when high eccentric forces are generated in muscles naive to eccentric contractions. However, no symptoms of damage, inflammation, or soreness occurred if the magnitude and duration of the force production were increased gradually.

In older adults with disease or those recovering from surgery, a phased progression of non-painful, non-injurious eccentric exercises is universally feasible owing to the relatively low exertion required. 73 In addition, 1:1 supervision and familiarization using progressively increased effort and load are recommended to ensure good form, comfort, and consistent performance and to reduce injury risk. Additionally, fall risk in older adults during stair descent, peak heart rate, systolic blood pressure, cardiac index, and expired ventilation were lower during eccentric exercise of equivalent volume to those of concentric exercise. 73-74 Eccentric exercise is currently performed to progressively increase the duration, frequency, and intensity of the exercise sessions and minimize the symptoms of damage. 75 Thus, eccentric exercise interventions are considered safe and suitable alternatives to traditional
resistance exercises.

However, the level of intensity, the method of load progression, and the mode of delivery of eccentric exercise have been less studied compared to those in traditional resistance exercises, such as isometric or concentric contraction. In particular, little is known about the specific protocols for eccentric exercise in aging muscles that are more susceptible to injury. Therefore, further studies are needed to develop a program that optimizes the intensity, duration, and modes of eccentric training while minimizing adverse effects in older adults.

CONCLUSION

Studies have been conducted in the last decade to elucidate the effects of eccentric contraction on aging muscles in older adults. We reviewed relevant literature on the use of the eccentric mode and its application, in which eccentric exercise has gained a great deal of interest across many fields. In addition, experimental studies can be used to reveal its mechanisms and benefits. The main finding of this review was that eccentric exercise is more effective than other traditional resistance exercises in improving muscle strength and mobility function in older adults. In particular, eccentric exercises using a specific device may more practically enable pure eccentric contractions. Eccentric exercise produces relatively greater force and eccentric contractions. Eccentric exercise produces relatively greater force and lengthen: properties and consequences of eccentric contractions. News Physiol Sci 2001;16:256-61.


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Therapeutic Effects of Functional Electrical Stimulation on Physical Performance and Muscle Strength in Post-stroke Older Adults: A Review

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INTRODUCTION

Stroke, a neurological disorder attributed to focal injury of vascular origin to the central nervous system, is the third-leading cause of death worldwide and an important cause of disability in older adults. Approximately one-third of patients die owing to stroke, one-third experience secondary recurrent strokes, and most of the remaining patients live with mobility limitations. More than 80% of stroke survivors have gait impairment and often cannot walk independently to perform daily activities. Stroke-related disabilities are largely responsible for low physical performance, especially among older adults, and can also lead to sarcopenia because physical performance is a key aspect in sarcopenia development. Indeed, hemiparetic stroke can result in muscle abnormalities with denervation, disuse, inflammation, and remodeling of muscle tissues. This may be related to the disrupted synaptic transmission of motor neurons that innervate muscle fibers after stroke, which can lead to decreased number of motor units and changes in muscle structure. Hence, appropriate interventions are needed to prevent these changes. Identifying effective treatment strategies to improve gait disorders and the consequent loss of muscle mass after stroke is warranted. New modalities such as functional electrical stimulation (FES) are the most commonly used techniques to recover from foot drop. FES dates back to the 1700s when Luigi Galvani conducted experiments on the leg muscles of frogs. In the 1800s, Guillaume-Benjamin Duchenne, who described the muscle disease “Duchenne muscular dystrophy,” developed a non-invasive technique to stimulate muscles using electric stimulus applied to the surface of the skin. Although FES has been utilized for several years, its therapeutic effects on physical performance and skeletal muscle function remain to be fully elucidated.
decades, it was not until the 1960s that its therapeutic uses and effects on skeletal muscles were more commonly reported. In 1961, Liberson et al. introduced a novel idea for the correction of gait disorder using electrical stimulation. Subsequent studies have reported that FES is an effective method to correct gait disorders in individuals post-stroke. Two meta-analyses also assessed the therapeutic effects of FES on muscle strength and physical performance in post-stroke patients; however, they did not consider muscle mass. Given recent findings on stroke-related sarcopenia, studies on the effect of FES on muscle mass, muscle strength, and physical performance should be systematically examined, especially in older adults. Therefore, this study reviewed the therapeutic effects of FES on physical performance and proposed hypotheses for its subsequent effects on muscle mass and muscle strength in post-stroke older adults.

FUNCTIONAL ELECTRICAL STIMULATION

Principles of FES
FES is the clinical application of electric current to a decentralized muscle. Neuromuscular electrical stimulation involves placing electrodes on a motor point and sending an electric current to produce muscle contraction. The technique can generate functional movements in individuals with paralysis caused by damage to the central nervous system. It entails the use of a low-energy electrical pulse and generates muscle contractions in a sequence to promote tasks such as walking or grasping. Specifically, FES electrically stimulates the dorsiflexor muscles (i.e., the tibialis anterior [TA]) of the foot, which facilitates ankle dorsiflexion during the swing phase of gait and allows for a more natural gait pattern.

FES has several advantages for gait training in patients with stroke. It can be used to enhance muscle strength and physical performance by increasing the range of motion and decreasing muscle weakness and spasticity. FES can also be used to relearn recruitment and timing of muscle activation in the paretic lower limb, which further helps in producing a normal gait. Individuals who experience stroke may have foot drop or weakness in the muscles lifting the foot during walking, which can further lead to falls or secondary health problems. If muscle contraction is appropriately timed and coordinated, gait performance can be facilitated in individuals with paralyzed lower extremities, such as patients who experience stroke. Thus, FES activation of muscles in the paralyzed limb is important to improve gait performance.

Types of Stimulation in FES
Electrical stimulation can be classified into invasive and non-invasive stimulation electrodes. Invasive stimulation electrodes are further separated into implanted and percutaneous electrodes, which differ in their placement duration and depth. Implanted electrodes are more suitable for longer-term use than percutaneous electrodes and are placed near the target nerve. Percutaneous electrodes are more suitable for short-term use than implanted electrodes and typically penetrate the skin by partially stimulating the targeted motor neurons. The typical current amplitude for both implanted and percutaneous electrodes is 25 mA. Invasive stimulation electrodes commonly require surgery; therefore, their placement and electrical intensity cannot be changed. In contrast, non-invasive stimulation electrodes self-adhere to the body surface. Unlike the fixed current amplitude of invasive stimulation electrodes, the typical current amplitude for non-invasive stimulation varies from 2 mA to 120 mA. Their placement on the skin also facilitates early intervention, which results in better recovery. Moreover, the electric intensity can be modified without surgery. However, targeting deep muscles is not feasible because stimulation of these muscles often requires greater intensity, which may result in stimulating untargeted muscles.

No studies have directly compared invasive and non-invasive electrical stimulation in post-stroke patients. However, previous studies have demonstrated the effectiveness of both methods in patients with spinal cord injury (SCI). Demchak et al. reported a greater cross-sectional area of the vastus lateralis muscle in the leg undergoing non-invasive electrical stimulation than that of the non-stimulated leg. Gad et al. also reported a higher increase in handgrip strength in the presence of non-invasive stimulation. The invasive approach also showed a restoring effect on walking and independent standing in individuals with SCI. Thus, both invasive and non-invasive electrical stimulation can help increase muscle cross-sectional area and muscle strength in patients with SCI. Furthermore, selecting an appropriate electrical stimulation method according to the patient’s condition is recommended.

Mechanisms of FES
Although the clinical effects of FES on gait patterns have been reported, the mechanism is not yet clearly understood. “Central” and “peripheral” mechanisms have been proposed to describe the therapeutic effects of FES. The peripheral mechanism of FES involves improving the muscle strength, flexibility, range of motion, and muscle spasticity of the paralyzed limb. While these improvements in muscle fitness may appear to have lasting effects, none of the peripheral mechanisms can explain these lasting effects. Instead, the central mechanism has attracted increasing attention to account for these effects. The central mechanism of FES is as follows (Fig. 1). First, FES can stimulate both afferent sensory and motor nerve fibers. A previous preclinical showed that a change in
Prolonged peripheral stimulation can induce excitability of the human motor cortex and reorganize the motor networks of the corresponding muscles. The results of studies suggest that FES-triggered afferent feedback may facilitate persistent brain plasticity. Second, electrical stimulation can antidromically activate motor nerve fibers, which are then polarized when the antidromic impulses of the fibers reach the anterior horn cell. The combination of FES-induced antidromic impulse and voluntary movement promotes pre- and postsynaptic coupling and synaptic remodeling, which are necessary for changes in neural plasticity. Thus, these two hypotheses have been proposed as plausible mechanisms by which FES corrects and improves gait patterns.

**Therapeutic Effects of FES on Gait in Post-stroke Patients**

The benefits of FES on gait performance of patients with chronic stroke are summarized in Table 1. In their single-subject study, Daly et al. reported that gait training with functional neuromuscular stimulation improved the gait patterns in older adults with chronic stroke. Specifically, the use of a combined treatment resulted in significant improvements in volitional knee flexion function compared to conventional treatment alone. Israel et al. reported a case series of stroke patients, in which two participants showed improved functional ambulation and decreased ankle plantarflexion, demonstrating that overground gait training with FES can improve foot clearance during gait. In addition, a pilot study reported that patients who had experienced a stroke produced greater propulsive force via the combination of treadmill and overground walking at a maximal speed with FES, which was accompanied by improvements in functional balance and walking ability. As balance ability is an important goal of stroke rehabilitation, a recent study reported that the combination of balance training with FES was is acceptable and effective in improving static and dynamic balance. In a long-term follow-up randomized controlled trial over 12 months, FES showed similar effects to ankle-foot orthosis in all primary outcomes related to gait quality and function, suggesting that FES may be an appropriate alternative to orthosis for individuals with chronic stroke.

FES treatment of the dorsiflexors is effective in correcting foot drop to balance gait patterns after stroke but not in correcting asymmetric weight-shifting during gait. One reason for the asymmetric gait pattern is the lack of activation of the hip abductors, which work as pelvic stabilizers. A previous study reported that FES-triggered gait training of the gluteus medius (GM) and TA improved gait velocity, dynamic balance, and gait symmetry during walking, among patients aged < 60 years. In that study, FES applied to the GM stabilized the pelvic muscles in the stance phase, while FES applied to the TA strengthened the ankle dorsiflexors in the swing phase, which improved functional gait performance in individuals with chronic hemiparetic stroke. These findings were consistent with those reported by Kim et al., who demonstrated that FES applied to the GM in the stance phase and TA in the swing phase of gait improved gait performance in patients who had experienced a stroke. Specifically, the combined effect of GM activation with TA generates a more normal gait pattern than that generated by TA activation alone. Consequently, FES treatment of the hip abductors and dorsiflexors has the potential to improve gait symmetry and gait speed during walking. The recovery of stroke-induced gait disorders through FES treatment in middle-aged patients aged < 60 years may have a positive effect on sarcopenia prevention in those aged > 60 years.

As in chronic stroke, FES also affects physical performance in patients with subacute stroke, as summarized in Table 2. Several studies have reported that FES can increase dorsiflexor strength in the swing phase of gait to prevent foot drop after stroke, which can further improve gait performance. Tong et al. reported that the therapeutic combined effect of FES and gait training was superior to gait training alone in individuals after acute stroke. They reported significant improvements in Barthel Index, Berg Balance Scale, Functional Ambulation Categories scale, 5-m timed walking test, and Motricity Index in the combination group compared to those in the training alone group after 4 weeks of treatment. Moreover, these improvements persisted even after 6 months. In one pilot study, the “gait training with FES” group had a larger effect size of gait speed than the “gait training only” group, indicating a superior
<table>
<thead>
<tr>
<th>Study</th>
<th>Participants (mean age)</th>
<th>Muscle strength / Function</th>
<th>Post-stroke duration</th>
<th>Device</th>
<th>FES intervention (type)</th>
<th>Activity / Task</th>
<th>Main findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daly et al. (2000)</td>
<td>2 participants with chronic stroke (68.5 y)</td>
<td>Muscle function deficits for LE</td>
<td>&gt; 1 y after the stroke</td>
<td>Electrical stimulation device (Staodyn EMS+2; Staodyn, Longmont, CO, USA)</td>
<td>FES applied for 30 min, once daily, 5 days per week for 7 mo. Frequency of 30 Hz, pulse duration of 300 μs, intensity of 1–6 mV.</td>
<td>Home exercise and gait training</td>
<td>Improved volitional gait pattern with surface-stim electrical stimulation.</td>
</tr>
<tr>
<td>Bethoux et al. (2015)</td>
<td>495 individuals with foot drop post-stroke (64.09 y)</td>
<td>Foot drop can ambulate &gt; 10 m at &gt; 0.0 m/s and &lt; 0.8 m/s.</td>
<td>FES group: 6.90 ± 6.43 y Control group: 6.86 ± 6.64 y</td>
<td>WalkAide (WA; Innovative Neurotronics, Austin, TX, USA)</td>
<td>Not applicable</td>
<td>Participants wear FES device for 6 mo</td>
<td>Increased 10-m walk test, 6-minute walk test, and modified Emory Functional Ambulation Profile scores in the FES group.</td>
</tr>
<tr>
<td>Lee (2020)</td>
<td>49 participants (63.49 y)</td>
<td>Brunnstrom stage ≥ 4</td>
<td>Control group: 15.25 ± 6.89 mo Experimental group: 16.00 ± 6.49 mo</td>
<td>EMG-triggered stimulation device (Stiwell med4; MED-EL, Innsbruck, Austria)</td>
<td>EMG-triggered FES with balance training for 40 min a day, 5 days a week, for 6 weeks. Frequency of 30–35 Hz, pulse width of 300 μs pulse intensity of 5–60 mA.</td>
<td>Balance training: 1. Static posture 2. Standing posture with both foot 3. Forward/backward standing posture 4. Moving from left to right in a standing posture 5. Static posture with plantarflexion/dorsiflexion</td>
<td>Greater improvements in static and dynamic balance abilities in the experimental group than in the control group. Increased ankle muscle activation in the experimental group.</td>
</tr>
<tr>
<td>Israel et al. (2011)</td>
<td>2 participants with foot drop post-stroke (62.5 y)</td>
<td>MMT: Participant 1: 3 or 4/5 (LE muscle groups). Participant 2: 4/5 (LE muscle groups)</td>
<td>Participant 1: 10 y post-stroke Participant 2: 9 y post-stroke</td>
<td>pFES device (Bioness L300 neuroprosthesis; Bioness Inc., Valencia, CA, USA)</td>
<td>pFES applied for 60 min per session, 3 sessions per week for 6 weeks. A pulse of 200 μs, intensity of 21–66 mA.</td>
<td>Overground gait training: walking at self-selected or fast speed, up and down stairs, and outdoors</td>
<td>Decreased ankle plantarflexion during gait. Decreased time to complete the modified Emory Functional Ambulation Profile. Increased gait speed in only 1 participant.</td>
</tr>
<tr>
<td>Awad et al. (2014)</td>
<td>13 individuals with locomotor deficits after stroke (61.0 y)</td>
<td>Fugl-Meyer: 13–24</td>
<td>3.22± 3.05 y</td>
<td>A customized, real-time FES system</td>
<td>FES applied for 30 min per session, 3 sessions per week for 12 weeks. Frequency of 30 Hz, pulse width of 300 μs.</td>
<td>Treadmill (27 min) and overground walking (3 min)</td>
<td>Increase in paretic propulsive force. Increase in functional balance and walking function.</td>
</tr>
</tbody>
</table>

FES, functional electrical stimulation; LE, lower extremity; MMT, manual muscle test.
<table>
<thead>
<tr>
<th>Study</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Yan et al. (2005)</td>
<td>46 participants (70.9 y)</td>
<td>MMT grade ≤ 3 (hip flexors)</td>
<td>9.2 ± 4.1 days after stroke</td>
<td>Two dual-channel stimulators (Respond Select; Empi Inc.)</td>
<td>FES applied for 30 min, 5 days per week for 3 weeks.</td>
<td>Applied while lying down</td>
<td>Decreased composite spasticity score. Increased ankle dorsiflexion torque.</td>
</tr>
<tr>
<td>Ng et al. (2008)</td>
<td>54 participants (67.9 y)</td>
<td>FAC &lt; 3</td>
<td>2.5 ± 1.2 weeks</td>
<td>Two single-channel FES stimulators (model R01–0093; Jockey Club Rehabilitation Engineering Centre, The Hong Kong Polytechnic University, Hong Kong, China)</td>
<td>FES was applied for 20 min, 5 days per week for 4 weeks, with a total of 20 training sessions.</td>
<td>Frequency of 40 Hz, pulse of 400 μs, rising and falling edge ramps of 0.3 seconds.</td>
<td>Effect size difference between the “training” group and “training with FES” group on gait speed was not small. Although not significant, the training with FES group showed a more superior treatment effect.</td>
</tr>
<tr>
<td>Tong et al. (2006)</td>
<td>2 participants (67.0 y)</td>
<td>BI score: Patient A, 10; Patient B, 35; BBS score: Patient A, 4; Patient B, 16; FAC score: Patient A, 1; Patient B, 1</td>
<td>4 weeks after-stroke</td>
<td>Two single-channel FES stimulators (model R01–0093; Jockey Club Rehabilitation Engineering Centre)</td>
<td>FES applied for 20 min, 5 days per week for 4 weeks (12 total sessions).</td>
<td>Frequency of 40 Hz, pulse of 400 μs, rising and falling edge ramps of 0.3 seconds.</td>
<td>Improvements in Barthel Index, Berg Balance Scale, Functional Ambulation Categories Scale, 5-m timed walking test score, and Motricity Index.</td>
</tr>
<tr>
<td>Peri et al. (2016)</td>
<td>46 participants (74.1 y)</td>
<td>MI: Experimental group: 76.13 ± 9.52 MI; Control group: 64.14 ± 19.00 MI</td>
<td>14.1 ± 2.7 days</td>
<td>8-channel current-controlled stimulator (RehaMove2; Hasomed GmbH, Magdeburg, Germany)</td>
<td>FES applied for 25 min, 15 days for 3 weeks, with active cycling at the maximum intensity tolerated by the patient.</td>
<td>Frequency of 25 Hz, pulse duration of 250 μs, current amplitude of 35–36 mA.</td>
<td>Improved cycling and walking ability post-acute stroke after FES-augmented active cycling training.</td>
</tr>
<tr>
<td>Bauer et al. (2015)</td>
<td>37 participants (61.43 y)</td>
<td>FAC ≤ 2; Brunnstrom stage 4</td>
<td>42.0 ± 4.50 days</td>
<td>8-channel current-controlled stimulator (Ref: 649200; Parameter: 111; Empi, Inc.; Munich, Germany)</td>
<td>FES applied for 20 min, 5 days per week for 4 weeks</td>
<td>Frequency of 25 Hz, pulse duration of 250 μs, current amplitude of 35–36 mA.</td>
<td>Improved Functional Ambulation Classification and Performance Oriented Mobility Assessment in the FES training group compared to the control group.</td>
</tr>
</tbody>
</table>

FES, functional electrical stimulation; AMT, abbreviated mental test; BBS, Berg Balance Scale; BI, Barthel Index; FAC, Functional Ambulatory Category; MI, Motricity Index; MMT, manual muscle test.
treatment effect; however, no significant differences were observed. Anther pilot study showed that active cycling training with FES may be effective in improving gait velocity in the subacute recovery period after stroke, although no group effect was found. The results of these pilot studies may have been more robust if the sample sizes were larger. A study comparing the effect of active interventions involving leg cycling with and without FES performed three times weekly for 20 minutes each session for 4 weeks showed improved walking and balance abilities in the FES group. Thus, the application of FES in the subacute phase of stroke may have a positive effect on physical performance. Several studies have demonstrated that FES helps patients with subacute and chronic stroke recover from low physical performance.

**Therapeutic Effects of FES on Muscle Mass and Strength in Post-stroke Patients**

However, few studies have demonstrated the effectiveness of FES in increasing muscle mass and strength in patients after stroke, especially in older adults. Several studies showed that FES significantly improved muscle strength in middle-aged patients with subacute and chronic stroke. Dorsiflexor muscle strength significantly increased by 56.6% in the “combination of FES and conventional rehabilitation” group and by 27.7% in the “conventional rehabilitation alone” group. These findings can be explained by the fact that FES reduces muscle spasticity through motor recovery, which further improves muscle strength. In addition, 18 patients with subacute and chronic stroke who participated in a 12-week conventional rehabilitation program combined with FES showed significantly improved dorsiflexor strength, measured by surface EMG signal. The combined effects of FES and rehabilitation also increased the maximal voluntary contractions of the dorsiflexors in middle-aged patients with stroke. The previous studies showing that FES increased muscle strength in middle-aged patients with stroke suggest the positive effects of FES on muscle mass, which is positively correlated with muscle strength. Muscle mass and strength may also be correlated in stroke survivors. Most studies were conducted among participants with a median age of 50 years, an age range that also encompasses older adults. Therefore, the same results may be observed in older adults, although studies with larger samples of older adults are required. Moreover, FES significantly restored muscle mass in denervated muscles of patients after SCI, although the patient age was relatively low. As stroke and SCI share common features, FES may also restore muscle mass in post-stroke patients.

In addition, FES may improve muscle mass by altering muscle-specific transcriptional mechanisms. During muscle contraction, muscle fibers produce and release myokines, which have local

and systemic effects on the body. FES in older adults changes this myokine secretion, especially that of insulin-like growth factor-1 (IGF-1). A previous study showed that neuromuscular electrical stimulation induced increased expression of IGF-1 and its downstream pathways, a well-known major anabolic signal for skeletal muscle development, and decreased expression of MuRF-1 and Atrogin-1, which are muscle atrophy-related ubiquitin ligase genes. Considering these changes at the molecular level, FES may also be effective in counteracting muscle atrophy in older adults.

**CONCLUSION**

The findings of the current review suggest some benefits of FES in improving physical performance and muscle strength and increase the possibility of its subsequent positive effects on muscle mass in older adults with stroke. FES can also facilitate static and dynamic balance activities by strengthening weakened dorsiflexors in the swing phase and hip abductors in the stance phase to support weight-bearing and upright posture. Thus, FES, especially when combined with rehabilitation, can be used to optimize physical performance, including gait performance, and ameliorate the consequent loss of muscle mass and strength in older adults after stroke.

**ACKNOWLEDGMENTS**

**CONFLICT OF INTEREST**

The researchers claim no conflicts of interest.

**FUNDING**

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**AUTHOR CONTRIBUTION**

Conceptualization, CWW, MK; Data curation, CWW, HES; Funding acquisition, CWW, HL; Investigation, CWW, MK, YS, HES, JYJ, DL; Project administration, CWW; Supervision, CWW, MK; Writing–original draft, HES; Writing–review & editing, MK, DL, JYJ, YS, DHY, SK, JY, MKK, HL, CWW.

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INTRODUCTION

Population aging is the most important medical, demographic, and social change of the 21st century and a public health phenomenon. Based on the Global Population Vision 2019, 703 million people are aged 65 years and over globally, accounting for 9% of the world’s population. The number of older people globally is estimated to reach 1.5 billion people by 2050. The aging trend continues rapidly in Turkey. According to the Turkish Statistical Institute (TUIK), in 2020, the older population has increased by 22.5% in the last 5 years, and older adults account for 9.5% of the total population. It has been observed that this increase is especially greater in people in the age range of 85 years and above. Aging is a multidimensional phenomenon that includes physiological, psychosocial, and biological changes. Aging is defined as a continuous process under cumulative, progressive, intrinsic, and deleterious factors. Frailty is an important concept in the science of aging and a very common aging syndrome. Frailty is defined as a state of increased vulnerability due to reduced physiological reserves and function in different organ systems when exposed to stress in individuals of the same chronological age. Frailty is strongly associated with negative outcomes such as disability, hospitalization, admission to the nursing home, and falls and death. Empowerment has become a common term in the health literature. Several definitions and approaches have been proposed for empowerment. According to the World Health Organization,
empowerment is defined as individuals who and social process in which individuals have more control over decisions and actions that affect their health. Empowerment affects people’s participation in health behaviors, promotes autonomy and self-care behaviors, takes responsibility for their health, reduces healthcare costs, and improves general health. Purposeful empowerment in older people enhances well-being, a healthy lifestyle, and social bonds, minimizing the effects of age-related complications and enabling older people to live independently. The Otago exercise program is based on each person’s tolerance. It has been developed by health professionals and includes empowerment, balance, and aerobic exercise. It was first developed and tested at the University of Otago in New Zealand. Several studies have indicated that exercise and individual multifactorial interventions are involved in delaying or reversing frailty and increasing empowerment, quality of life, and well-being. The present study aimed to assess the impact of Otago exercises on frailty and empowerment in older people living in a nursing home. We hypothesizes that older people who participate in the intervention groups will show significant improvements in these outcomes compared to their peers in the control group.

MATERIALS AND METHODS

Study Design and Study Population

This experimental and randomized controlled trial (Fig. 1) was conducted at Izmir Narlidere Nursing Home from September 2016 to June 2017. The study population consisted of people aged 65 years and older residing in Narlidere Nursing Home. The study participants continued receiving the optimal medical treatment recommended by their physicians throughout the study. Inclusion criteria were being 65 years of age or older and having the ability to read and write in the Turkish language. Exclusion criteria were needing palliative care; having loss of sight, hearing, and other senses that prevented communication; having a previous diagnosis of dementia, hypotension (systolic blood pressure < 90 mmHg, diastolic blood pressure < 60 mmHg), anemia (hemoglobin level < 9 g/dL), any acute metabolic disorder, uncontrolled hypertension (systolic blood pressure > 160 mmHg, diastolic blood pressure > 100 mmHg), uncontrolled arrhythmia, stable/unstable angina pectoris, uncontrolled metabolic and chronic disease, and advanced cerebrovascular and peripheral vascular insufficiency; having undergone surgery during the last 6 weeks; and having any physical disability that prevents exercising. Fig. 1 showed a flowchart of the study participants.

The Ethics Committee of Ege University Faculty of Medicine approved this study (No. 70198063-050.06.04). All procedures performed followed the principles of the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The patients were informed of the study protocols in detail and provided their written consent.

Fig. 1. Flowchart of the study procedure.
Randomization
This study used a convenience and stratified random sampling method. To balance the different individual effects of the exercise program, we classified them according to age and sex. The participants were assigned to each research group using a simple random method (coin flipping). The groups were as follows: the Otago exercise group (OEG/intervention group) or control group (CG).

The sample size for the present study was calculated to detect a significant clinical difference on the EFS test. Using G*Power version 3.1 a test power (1–β error probability), of 0.80, and α = 0.05 reliability (type 1 error probability), the research sample size was calculated to be 29 older people for each group to detect a mean difference ≥ 1 in the EFS (SD = 0.5). The sample size was increased by 25% to consider the probability of dropout during follow-up. The final sample size was 72 older people, equally distributed between the two groups (36 participants in each group). However, one participant in the OEG was excluded owing to the need to undergo acute cholecystitis surgery after the start of the study. Hence, this study included 71 older people.

Interventions
Participants in the OEG performed exercises for 45 minutes each on 3 days a week for 12 weeks, plus 30 minutes of walking the other 3 days of the week. The OEG also received 10 30-minute sessions of empowerment-based training. In both OEG and CG, we performed measurements before and after the 3-month intervention and compared them statistically.

Otago Exercise Group
The Otago Exercise Program includes strengthening, balancing, and walking exercises. The Otago exercises were performed in four levels (summarized in Supplementary Table S1). All exercises were performed in 9-member groups under the supervision of a researcher with Otago Exercise Program certification and a nursing home physiotherapist at the Narlidere Nursing Home gym using a practical display method on the pre-programmed days and hours. In all trainings, the characteristics of the older people were considered. We used visual tools (projectors, etc.) to facilitate learning and enhance the knowledge of the older people about training and also provided them a booklet describing the Otago exercises and containing photos of the exercises, some examples of which are included in Supplementary Figs. S1 and S2. Ankle cuff weights, weighing about 0.5 kg, were used in lower extremity resistance exercises under the supervision of a physiotherapist. We also observed the warm-up and cool-down movements before and after exercise. More detail is available from the Otago Medical School University of Otago (https://www.livestronger.org.nz/assets/Uploads/acc1162-otago-exercise-manual.pdf).

The OEG also received 10 30-minute empowerment-based training sessions on topics such as self-care behaviors, problem-solving, decision-making, self-motivation, psychosocial coping, resource utilization, and self-efficacy.

Control Group
The CG received routine health care at Narlidere Nursing Home, including monthly physician visits, tests, prescription medications, and continued daily activities. The CG participants were asked not to participate in any intervention training program during the 3-month study period. To observe the ethical principles in the present study, after completing the research data, knowledge on the concepts of empowerment training and the Otago training program and its applications was also provided to the CG.

Assessments
After providing the necessary information about the study, we obtained written informed consent form from the participants. The participants then completed the research data forms enabling data collection on sociodemographic characteristics, and Edmonton Frail Scale (EFS) and Elderly Empowerment Scale (EES) scores in person. The sociodemographic characteristics form consisted of two parts. The first part included age, sex, educational status, occupation, income level, marital status, number of children, and the place where participants spent much of their time. The second part assessed the participants’ health status, including questions on chronic disease, history of hospitalization, medication use, exercise pattern, sleep pattern, smoking, and alcohol consumption.

We applied the EFS to assess frailty status. The scale was developed by Rolfson et al. at the University of Alberta in Canada to describe frailty in older people. The EFS consists of nine dimensions and includes a total of 11 items for the comprehensive assessment of aging as a determinant of frailty. Its dimensions include cognition, general health status, functional independence, social support, medication usage, nutrition, mood, continence, and functional performance. The scores range from 0 to 17. The maximum score, 17, indicates the highest level of frailty. Robust and frail participants were defined based on EFS scores as follows: robust (≤ 5 points), pre-frail (6–7 points), and frail (≥ 8 points). The validity and reliability of the Turkish version of this scale were examined by Aygor et al. with a reported Cronbach’s alpha coefficient of 0.75.

We also used the EES to assess empowerment status. This scale for older people was developed from the Diabetes Empowerment Scale-Short Form (DES-SF) by Anderson et al. and was later translated into Turkish. The EES includes eight items (one item
for each subscale). The eight subscales include satisfaction and dissatisfaction related to old age, identification and achievement of personally meaningful goals, application of a systematic problem-solving process, coping with aspects of living with old age, stress management, appropriate social support, self-motivation, and making cost/benefit decisions about behavior changes. Each item is scored on a 5-point Likert scale, ranging from 5 (strongly agree) to 1 (strongly disagree). The minimum and maximum scale scores are eight and 40 points, respectively, with higher scores indicating stronger empowerment.  

The validity and reliability of the scale in Turkish were examined by Jahanpeyma et al., with a reported Cronbach’s alpha of 0.883.

**Statistical Analyses**

We used IBM SPSS Statistics for Windows (version 22.0; IBM, Armonk, NY, USA) to analyze the data. The categorical variables are expressed as number and percentage, while continuous variables are expressed as mean and SD. Between-group differences were determined using chi-squared and independent t-tests. In statistical evaluations of the variables, we assessed the normality of the variables using Kolmogorov–Smirnov tests. Independent-samples t-test and paired-samples t-test were used in pairwise comparisons and within-group and between-group evaluations because they were consistent with the normal distribution. p < 0.05 was considered statistically significant.

**RESULTS**

The mean ages of the OEG and CG (74.6 ± 5.9 and 75.8 ± 4.5 years, respectively) were similar, and most participants in both groups were female (74.3% and 75%, respectively). The other demographic characteristics of the two groups were similar, except for marital status (Table 1). We also did not observe significant differences in mean and SD of baseline EES and EFS scores between the OEG and CG (Table 1). We also performed within-group and between-group assessments after calculating the median and mean values for each of the scales before and 3 months after the intervention. The mean EFS before and 3 months after the intervention differed significantly in the OEG (p = 0.0001). The mean and SD of EFS before the intervention, 4.60 ± 2.13, decreased to 3.46 ± 1.17 after the intervention, indicating the effectiveness of the Otago exercise program on preventing or delaying frailty. However, we observed no significant changes in the CG (p = 0.999).

We also observed a significant difference between the two groups in the mean EFS values 3 months after the intervention (p = 0.018) (Table 2).

Examination of frailty status in the OEG before the intervention showed that 25.7% of the participants were pre-frail, and this decreased to 2.9% 3 months after the intervention. Eight pre-frail and three participants got the robust status 3 months after the intervention, and no participants experienced frailty (Table 3).

In the OEG, the mean EFS differed significantly between before and 3 months after the intervention (p = 0.0001). The mean and standard deviation of EES before the intervention, 18.23 ± 2.22, increased to 20.77 ± 1.93 after the intervention. However, we observed no significant changes in the CG (p = 0.831). The two groups also showed a significant difference in the mean values of EES 3 months after the intervention (p = 0.0001) (Table 4).

**DISCUSSION**

The present study assessed the impact of the Otago Exercise Program on frailty and empowerment in older people aged 65 and over who were residing in nursing homes. Frailty is a biological syndrome in older adults. The factors affecting frailty include a combination of deficiencies in strength, balance, motor processing, cognition, nutrition, endurance, and physical activity. Our comparisons of the mean EFS scores before and 3 months after the intervention showed a significant difference between the OEG and CG (p = 0.0001). Sadjapong et al. also reported a significant change (< 0.01) in the frailty score of the intervention group compared to the control group. Hsieh et al. also observed a significant change (p < 0.01) in frailty score in the intervention group than the control group. Finally, Ferreira et al. observed that older people in the exercise program showed a 34% reduction in the prevalence of frailty criteria compared to a reduction of approximately 6% in the control group. In our study, most of the older people in the exercise group had a pre-fraility status. We observed an approximately 73% reduction in the number of older people classified as frail in the OEG. In contrast, we observed no significant change between the pre-exercise and post-exercise periods in the CG. Yu et al. also observed a significant decrease in frailty score in the intervention group (1.3, p < 0.001) but had increased in frailty score in the control group. In general, our results are comparable with those of previous studies. However, contrary to other studies, Takano et al. showed that the implementation of 4-month exercise interventions did not significantly affect frailty status.

Empowerment is a multidimensional topic in health and includes the areas of self-care behaviors; self-efficacy; self-control; problem-solving, obtaining support; motivation; psychosocial coping; decision-making; resource utilization; and the relationships of individuals with healthcare providers, healthcare systems, and healthcare services. Empowerment affects the participation of people in self-care behaviors, sense of responsibility, taking pre-
Table 1. Baseline demographics characteristics of the participant groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Otago group (n = 35)</th>
<th>Control group (n = 36)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>74.60 ± 5.94</td>
<td>75.8 ± 4.54</td>
<td>0.350</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>26 (74.3)</td>
<td>27 (75.0)</td>
<td>0.580</td>
</tr>
<tr>
<td>Male</td>
<td>9 (25.7)</td>
<td>9 (25.0)</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>8 (22.2)</td>
<td>21 (58.3)</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>0 (0)</td>
<td>1 (2.7)</td>
<td>0.004</td>
</tr>
<tr>
<td>Divorced/separated/widowed</td>
<td>27 (77.8)</td>
<td>14 (39.0)</td>
<td></td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elementary school or lower</td>
<td>1 (2.9)</td>
<td>3 (8.3)</td>
<td></td>
</tr>
<tr>
<td>Middle school</td>
<td>5 (14.3)</td>
<td>6 (16.7)</td>
<td>0.739</td>
</tr>
<tr>
<td>High school</td>
<td>12 (34.3)</td>
<td>10 (27.8)</td>
<td></td>
</tr>
<tr>
<td>University</td>
<td>17 (48.5)</td>
<td>17 (47.2)</td>
<td></td>
</tr>
<tr>
<td>Income</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Income &gt; expenses</td>
<td>1 (2.9)</td>
<td>2 (5.6)</td>
<td>0.572</td>
</tr>
<tr>
<td>Income = expenses</td>
<td>34 (97.1)</td>
<td>34 (94.4)</td>
<td></td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homemaker</td>
<td>8 (22.9)</td>
<td>9 (25.0)</td>
<td>0.832</td>
</tr>
<tr>
<td>Retired</td>
<td>27 (77.1)</td>
<td>27 (75.0)</td>
<td></td>
</tr>
<tr>
<td>Smoking habit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>13 (37.1)</td>
<td>13 (38.9)</td>
<td>0.562</td>
</tr>
<tr>
<td>No</td>
<td>22 (62.9)</td>
<td>23 (61.1)</td>
<td></td>
</tr>
<tr>
<td>Alcohol use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>11 (31.4)</td>
<td>13 (36.1)</td>
<td>0.434</td>
</tr>
<tr>
<td>No</td>
<td>24 (68.6)</td>
<td>23 (63.9)</td>
<td></td>
</tr>
<tr>
<td>Chronic disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>24 (68.6)</td>
<td>31 (86.1)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>11 (31.4)</td>
<td>5 (13.9)</td>
<td>0.068</td>
</tr>
<tr>
<td>Edmonton Frail Scale score</td>
<td>4.60 ± 2.13</td>
<td>4.36 ± 1.93</td>
<td></td>
</tr>
<tr>
<td>Elderly Empowerment Scale score</td>
<td>18.23 ± 2.22</td>
<td>17.69 ± 1.89</td>
<td></td>
</tr>
</tbody>
</table>

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

Table 2. Within-group and between-group comparisons of EFS scores before and 3 months after the intervention

<table>
<thead>
<tr>
<th>EFS</th>
<th>Otago group</th>
<th>p-value (within-group)</th>
<th>Control group</th>
<th>p-value (within-group)</th>
<th>p-value (between-group)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-intervention</td>
<td>Median (min–max)</td>
<td>5 (1–8)</td>
<td>4.60 ± 2.13</td>
<td>4 (1–8)</td>
<td>4.36 ± 1.93</td>
</tr>
<tr>
<td>Post-intervention</td>
<td>Median (min–max)</td>
<td>4 (1–6)</td>
<td>3.46 ± 1.17</td>
<td>0.0001</td>
<td></td>
</tr>
</tbody>
</table>

EFS, Edmonton Frail Scale.
Significance defined as p<0.05.

Table 3. Frailty status before and 3 months after the interventions

<table>
<thead>
<tr>
<th>Frailty status</th>
<th>Otago group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Robust</td>
<td>Frail</td>
</tr>
<tr>
<td>Pre-intervention</td>
<td>23 (65.7)</td>
<td>9 (25.7)</td>
</tr>
<tr>
<td>Post-intervention</td>
<td>34 (97.1)</td>
<td>1 (2.9)</td>
</tr>
</tbody>
</table>

Values are presented as number (%).
ventive measures, and decision-making among older adults regarding their health issues to promote health in this population. We applied the EES to assess the empowerment status of older people in the present study. The mean EES before and 3 months after the intervention differed significantly among the OEG and CG (p = 0.001), with higher mean values among participants in the OEG group compared to those in the CG. However, few published studies have assessed the impact of empowerment at the individual or community level. Most studies have been conducted on people with diabetes and different disease groups. Castillo et al. reported a significant reduction in glycated hemoglobin (HbA1C) levels and systolic blood pressure after providing empowerment training for people with type 2 diabetes; however, they observed no significant change in body mass index (BMI). Furthermore, Tang et al. observed significant reductions in HbA1C and BMI among participants with diabetes in empowerment-based self-management support programs. Yeh et al. demonstrated effective results for empowerment and perceived control after 12 weeks of an empowerment training and exercise program in people with heart failure, while Aliakbari et al. observed a significant change (p < 0.001) in the mean of behavioral ability, self-efficacy, and empowerment score only in the intervention group after providing empowerment training for patients with chronic obstructive pulmonary disease. Karaman et al. reported a significant increase in the mean score of the empowerment scale in older people with heart failure who received the intervention. Finally, in their systematic review of 13 studies, Kuipers et al. reported that four studies did not show significant changes in the empowerment of the intervention group.

The limitations of the present study include the short follow-up period, small sample size, and single study area. Thus, the evaluation of the long-term effects with larger sample sizes and in different geographical areas is recommended. Another limitation was that we did not examine the relationship between demographic variables and frailty. Moreover, most of the participants were women; thus, the results may not fully reflect the older population.

In conclusion, the Otago Exercise Program showed positive effects on preventing or delaying frailty and enhancing empowerment in older adults; thus, it may be an effective intervention for preventing and reducing frailty in old-aged nursing home residents.

The study results showed that the implementation of the Otago Exercise Program may be effective in improving physical function and increasing independence in older adults, reducing hospitalization, and reducing costs imposed on the medical system. Therefore, the Otago Exercise Program is recommended as an effective intervention to prevent/delay frailty and increase empowerment in older adults living in nursing homes.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4235/agmr.21.0095.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

None.

AUTHOR CONTRIBUTION

Conceptualization: SS, FŞA, YY, PJ; Data curation and Formal analysis: SS, PJ; Investigation and Methodology: SS, FŞA, YY, PJ; Project administration: SS, PJ; Supervision: SS, FŞA, YY; Writing-original draft: SS, FŞA, YY, PJ; Writing-review and editing: FŞA, YY, PJ.

REFERENCES


INTRODUCTION

Gastric cancer (GC) is the fifth most common cancer and third most common cause of cancer-related deaths worldwide. The incidence and prevalence of GC are high, particularly in East Asia, including in South Korea. While a large-scale nation-led endoscopy surveillance program to reduce GC-related deaths in South Korea has shown considerable effect, GC-related death still ranked 4th among carcinomas in 2020. In addition, its peak incidence occurs in the seventh decade of life; thus, the incidence of GC is expected to increase owing to the extended lifespan of the general population. Furthermore, there are no specific surveillance and treatment guidelines for older age groups, making it difficult to determine the upper limit of the age of surveillance, diagnostic examinations, and invasive treatments. Another potential factor increasing the risk of GC-related death is the reluctance of both older adult patients and medical experts to receive or perform standard examinations or treatments due to the risk of complications. The present study compared the characteristics of GC in older patients to those of younger patients with GC and to those of previous studies to help guide treatment for GC in older adults.
MATERIALS AND METHODS

Study Population
Initially, we selected 3,074 patients aged ≥ 18 years from a prospective surgical cohort of patients who were diagnosed with gastric adenocarcinoma and underwent surgical treatment at Seoul National University Bundang Hospital (SNUBH) between 2003 and 2017. We previously reported the effects of Helicobacter pylori eradication treatment, p53 overexpression, and incidence of metachronous GC in this cohort.5,7 The following patients were excluded from the present study: those with incomplete medical records or unclassified histology, those who were lost to follow-up, those with a prior history of other cancers at the time of diagnosis, and those with other inoperable diseases. Finally, we included 2,983 patients in the analysis and classified them into three groups based on age: I (young, age < 65 years, n = 1,680), II (early old, age 60–74 years, n = 919), and III (old, age ≥ 75 years, n = 384) (Fig. 1). We defined old age as 65 years and older based on previously published studies. We also conducted additional analysis of patients ≥ 75 years of age. Since the average life expectancy is increasing, so we tried to assess the difference between the relatively young and super-aged older adults. Data such as sex, age, death (including causes of death), histologic type of cancer, and social history such as alcohol consumption, smoking, and family history of GC were collected from surgical and medical records and reviewed using the Clinical Data Warehouse. Family history was defined as at least one patient with GC among first-degree relatives. Otherwise, the patient was categorized as having no relevant family history. The presence of atrophic gastritis or intestinal metaplasia was confirmed by histological examination based on the modified Sydney Classification for endoscopic biopsy in the antrum and body, which was performed at the time of cancer diagnosis. If one or more of the three preoperative tests for H. pylori (urease breath test, rapid urease test, or histology) showed a positive result, the patient was considered H. pylori-positive; otherwise, they were categorized as H. pylori-negative. We verified the dates and causes of death of the enrolled patients through cross-review of data from the National Statistical Office.

Statistical Analysis
The outcomes were overall and gastric cancer-specific survival. Student t-test and chi-square test were used for comparisons between groups. Univariate and multivariate Cox proportional hazards analyses were used to identify risk factors, and variables with p < 0.2 in the univariate analyses were used as covariates in the multivariate analysis. The Kaplan-Meier estimator method and log-rank tests were used to compare survival. Analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Statistical significance was set at p < 0.05. All data are available upon reasonable request from the corresponding author.

Ethical Considerations
The study was reviewed and approved by the Institutional Review Board of Seoul National University Bundang Hospital (No. B-1902-523-107) and registered at clinicaltrials.gov (NCT 03978481). As this study was performed retrospectively, the IRB permitted a waiver of informed consent. All authors had access to the study data and approved the final manuscript.

RESULTS

Baseline Clinicopathological Characteristics
The baseline clinicopathological features of the patients are shown in Tables 1 and 2. Of the 2,983 patients, 1,680 were aged < 65 years (group I), 919 were aged 65–74 years (group II), and 384 were aged ≥ 75 years (group III). A higher proportion of younger patients reported alcohol consumption and smoking (p < 0.001 for both drinking history and smoking history), as well as H. pylori infection (p < 0.001). Intestinal metaplasia was more common in group II than in the other groups (p = 0.006). Sex and atrophic gastritis did not differ significantly between the groups (sex, p = 0.333; atrophic gastritis, p = 0.074) (Table 1). Cancer of the gastric body and diffuse-type histology were more common in younger patients, and cancer of the gastric antrum and intestinal-type histology increased with age (tumor location p < 0.001 and histologic type p < 0.001, respectively). Lymph node metastasis, cancer stage, and surgical methods did not differ significantly.

![Fig. 1. Study flow chart. GC, gastric cancer.](www.e-agmr.org)
according to age (node metastasis, $p < 0.779$; TNM stage, $p = 0.471$; surgical method, $p = 0.504$). p53 overexpression was more common in groups II and III than in group I ($p = 0.004$) (Table 2). The results of additional analysis according to age and sex are provided in Supplementary Table S1. While females in groups II and III had more advanced cancer and lymph node metastasis than in males in groups II and III, the differences were not statistically significant. Comparisons according to tumor location showed that the incidences of cardia cancers increased with age, and associated risk factors included the presence of intestinal metaplasia and p53 overexpression. The detailed features of cardia and non-cardia cancers are described in Supplementary Table S2.

### Risk Factors for GC-Related Death

Cox univariate and multivariate analyses were performed to determine the risk factors for GC-related death (Table 3). In univariate analyses, older age, female sex, lack of a family history of GC, $H.\ pylori$ negativity, advanced-stage cancer, diffuse or mixed type histology, middle- or lower-third tumor location, and lymph node metastasis were identified as potential risk factors. In multivariate analyses, the risk factors for GC-related death were old age, $H.\ pylori$ negativity, advanced-stage cancer, diffuse or mixed type histology, middle- or lower-third tumor location, and lymph node metastasis (age, $p = 0.002$; $H.\ pylori$ status, $p = 0.025$; cancer type, $p < 0.001$; histologic type, $p = 0.001$; tumor location, $p = 0.032$; node metastasis, $p < 0.001$, respectively).

### Overall and Cancer-Specific Survival

Overall survival in the three groups is shown in Fig. 2. In terms of overall survival, we observed a statistically significant difference according to the age, with survival decreasing with increasing age ($p < 0.001$) (Fig. 2A). However, in GC-specific survival, the difference according to age decreased compared to that for overall survival, although the difference remained statistically significant ($p = 0.008$ for group I vs. II; $p = 0.005$ for group II vs. III; and $p < 0.001$ for group I vs. III) (Fig. 2B).

The results of additional stratification analysis according to cancer stage and sex are shown in Supplementary Figs. S1 and S2. In the stratification analysis according to GC stage, we observed age-specific differences in overall survival (Supplementary Fig. S1) compared to GC-specific survival (Supplementary Fig. S2). In particular, the differences in overall and GC-specific survival de-

---

**Table 1. Clinical characteristics of gastric cancer patients in each age group**

<table>
<thead>
<tr>
<th></th>
<th>Group I (young, &lt; 65 y)</th>
<th>Group II (early old, 65–74 y)</th>
<th>Group III (old, ≥ 75 y)</th>
<th>p-value&lt;sup&gt;a&lt;/sup&gt;</th>
<th>p-value&lt;sup&gt;b&lt;/sup&gt;</th>
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</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>1,680</td>
<td>919</td>
<td>384</td>
<td>0.443</td>
<td>0.333</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Male</td>
<td>1,113 (66.3)</td>
<td>635 (69.1)</td>
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<tr>
<td>Female</td>
<td>567 (33.7)</td>
<td>284 (30.9)</td>
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<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
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<td>0.026*</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
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<td>535 (58.2)</td>
<td>249 (64.8)</td>
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</tr>
<tr>
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<td>384 (41.8)</td>
<td>135 (35.2)</td>
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</tr>
<tr>
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<td>&lt; 0.001*</td>
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<td>565 (61.5)</td>
<td>255 (66.4)</td>
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<tr>
<td>Yes</td>
<td>869 (51.7)</td>
<td>354 (38.5)</td>
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<td></td>
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<tr>
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<td>0.019*</td>
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<td>735 (80.0)</td>
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<td>277 (16.5)</td>
<td>184 (20.0)</td>
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<td>$H.\ pylori$ status</td>
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<td>440 (47.9)</td>
<td>224 (58.3)</td>
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<td>Yes</td>
<td>1,077 (64.1)</td>
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<td>0.074</td>
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<td>641 (69.7)</td>
<td>279 (72.7)</td>
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</tr>
<tr>
<td>Yes</td>
<td>438 (26.1)</td>
<td>278 (30.3)</td>
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</tr>
<tr>
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<td>0.006*</td>
</tr>
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<td>487 (53.0)</td>
<td>204 (53.1)</td>
<td></td>
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</tr>
<tr>
<td>Yes</td>
<td>691 (41.1)</td>
<td>432 (47.0)</td>
<td>180 (46.9)</td>
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</tr>
</tbody>
</table>

Values are presented as number (%).

<sup>a</sup>Between young-old and old-old groups,
<sup>b</sup>among all age groups.

*p<0.05.
pending on age were significant in stages I and II (Supplementary Figs. S1A, S1B, S2A) but not in stages III or IV. We observed female advantage in overall survival in each age group (Supplementary Fig. S3). In contrast, men showed advantage in GC-specific survival in all age groups (Supplementary Fig. S4).

In the analyses of survival and causes of death, the GC-related mortality rates increased with age. However, deaths from diseases other than GC more significantly increased with age. The older adult groups showed more deaths from cerebrovascular and pulmonary diseases, sepsis, and multiorgan failure, compared to the younger patient group (Table 4).

DISCUSSION

In this study, we found that among older patients, GC was more prevalent in the lower third of the stomach; furthermore, they also had a high rate of intestinal-type histology. Lymph node metastasis and cancer stage did not differ significantly according to age. While we observed a significant difference in overall survival according to the age at which survival decreased with increasing age, those differences decreased in GC-specific survival, suggesting that not only cancer itself but also other factors, such as comorbidities, combine to affect the prognosis of older patients with GC. We observed female advantages in overall survival and male advantages in GC-specific survival among all age groups. 

Previous studies also described the characteristics of GC in older adult patients. Clinically, GC in this population occurs predominantly in men, compared to GC occurring in younger patients. Endoscopically, GC is antral dominant and often visually depressed (II-c in early GC and Borrmann type III in advanced GC). Histo-

Table 2. Pathological characteristics of patients with gastric cancer in each age group

<table>
<thead>
<tr>
<th></th>
<th>Group I (young, &lt; 65 y)</th>
<th>Group II (early old, 65–74 y)</th>
<th>Group III (old, ≥ 75 y)</th>
<th>p-value &lt;sup&gt;a&lt;/sup&gt;</th>
<th>p-value &lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>1680</td>
<td>919</td>
<td>384</td>
<td>0.932</td>
<td>0.349</td>
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<td>Cancer type</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EGC</td>
<td>1,219 (72.6)</td>
<td>644 (70.1)</td>
<td>270 (70.3)</td>
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<td></td>
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<tr>
<td>AGC</td>
<td>461 (27.4)</td>
<td>275 (29.9)</td>
<td>114 (29.7)</td>
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<td>Lauren histologic type</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Intestinal</td>
<td>856 (51.0)</td>
<td>687 (74.8)</td>
<td>300 (78.1)</td>
<td>0.201</td>
<td>&lt; 0.001*</td>
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<tr>
<td>Diffuse</td>
<td>749 (44.6)</td>
<td>194 (21.1)</td>
<td>71 (18.5)</td>
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<tr>
<td>Mixed</td>
<td>75 (4.4)</td>
<td>38 (4.1)</td>
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<tr>
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<td>&lt; 0.001*</td>
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<tr>
<td>Upper</td>
<td>36 (2.1)</td>
<td>22 (2.4)</td>
<td>19 (5.0)</td>
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<tr>
<td>Middle</td>
<td>828 (49.3)</td>
<td>373 (40.6)</td>
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<td>Subtotal gastrectomy</td>
<td>1,325 (78.9)</td>
<td>712 (77.5)</td>
<td>300 (78.1)</td>
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<td></td>
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<td>Proximal gastrectomy</td>
<td>66 (3.9)</td>
<td>31 (3.4)</td>
<td>18 (4.7)</td>
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<tr>
<td>Pylorus-preserving gastrectomy</td>
<td>10 (0.6)</td>
<td>5 (0.5)</td>
<td>1 (0.3)</td>
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<td></td>
</tr>
<tr>
<td>Total gastrectomy</td>
<td>279 (16.6)</td>
<td>171 (18.6)</td>
<td>65 (16.9)</td>
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<td>0.779</td>
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<tr>
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<tr>
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<td>435 (25.9)</td>
<td>230 (25.0)</td>
<td>103 (26.8)</td>
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<tr>
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<td>0.273</td>
<td>0.471</td>
</tr>
<tr>
<td>I</td>
<td>1,310 (78.0)</td>
<td>711 (77.4)</td>
<td>291 (75.7)</td>
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<tr>
<td>II</td>
<td>225 (13.4)</td>
<td>129 (14.0)</td>
<td>51 (13.3)</td>
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<tr>
<td>III</td>
<td>112 (6.6)</td>
<td>66 (7.2)</td>
<td>34 (8.9)</td>
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<td></td>
</tr>
<tr>
<td>IV</td>
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<td>13 (1.4)</td>
<td>8 (2.1)</td>
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<td></td>
</tr>
<tr>
<td>p53 overexpression</td>
<td></td>
<td></td>
<td></td>
<td>0.099</td>
<td>0.004*</td>
</tr>
<tr>
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<td>1,117 (66.5)</td>
<td>551 (60.0)</td>
<td>249 (64.8)</td>
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<td></td>
</tr>
<tr>
<td>Positive</td>
<td>563 (33.5)</td>
<td>368 (40.0)</td>
<td>135 (35.2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are presented as number (%).

EGC, early gastric cancer; AGC, advanced gastric cancer.

<sup>a</sup>Between young-old and old-old groups, <sup>b</sup>among all age groups.

* <sup>p<0.05.</sup>
<table>
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<tr>
<th>Risk Factor</th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
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<tr>
<td></td>
<td>aHR (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age (y)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 65</td>
<td>Ref</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>65–74</td>
<td>1.50 (1.11–2.03)</td>
<td>1.55 (1.14–2.13)</td>
</tr>
<tr>
<td>≥ 75</td>
<td>2.46 (1.67–3.61)</td>
<td>1.86 (1.25–2.77)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td>0.15</td>
<td>0.431</td>
</tr>
<tr>
<td>Male</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1.23 (0.93–1.63)</td>
<td>1.12 (0.84–1.50)</td>
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<tr>
<td>Yes</td>
<td>1.15 (0.87–1.51)</td>
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<td><strong>Alcohol</strong></td>
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<td>Ref</td>
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<tr>
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<tr>
<td>Yes</td>
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<tr>
<td>Yes</td>
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<td><strong>Atrophic gastritis</strong></td>
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<tr>
<td>Yes</td>
<td>0.99 (0.72–1.36)</td>
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<td><strong>Intestinal metaplasia</strong></td>
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</tr>
<tr>
<td>Yes</td>
<td>0.90 (0.68–1.19)</td>
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<td><strong>Cancer type</strong></td>
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<td>&lt; 0.001*</td>
</tr>
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<td>EGC</td>
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<tr>
<td><strong>Lauren histologic type</strong></td>
<td>&lt; 0.001*</td>
<td>0.001*</td>
</tr>
<tr>
<td>Intestinal</td>
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<tr>
<td>Diffuse</td>
<td>2.18 (1.63–2.91)</td>
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<tr>
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<td>0.032*</td>
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<tr>
<td>Upper</td>
<td>Ref</td>
<td></td>
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<tr>
<td>Middle</td>
<td>1.70 (0.42–6.92)</td>
<td>1.43 (0.35–5.86)</td>
</tr>
<tr>
<td>Lower</td>
<td>2.70 (0.67–10.91)</td>
<td>2.07 (0.51–8.39)</td>
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<tr>
<td><strong>Node metastasis</strong></td>
<td>&lt; 0.001*</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Negative</td>
<td>Ref</td>
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</tr>
<tr>
<td>Positive</td>
<td>15.33 (10.41–22.58)</td>
<td>4.93 (3.20–7.59)</td>
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<td><strong>p53 overexpression</strong></td>
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</tr>
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<td>No</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.11 (0.83–1.48)</td>
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</tr>
</tbody>
</table>

EGC, early gastric cancer; AGC, advanced gastric cancer; aHR, adjusted hazard ratio; CI, confidence interval.

*p < 0.05.
Fig. 2. (A) Overall survival and (B) gastric cancer-specific survival according to age. Overall survival differs significantly with age, with survival decreasing with increasing age (p<0.001). However, the difference in gastric cancer-specific survival according to age is lower than that for overall survival, although the difference remains significant (p=0.008 for group I vs. II; p=0.005 for group II vs. III; p<0.001 for group I vs. III).

Table 4. Causes of death in each age group

<table>
<thead>
<tr>
<th>Death</th>
<th>Group I (young, &lt; 65 y) (n = 1,680)</th>
<th>Group II (early old, 65–74 y) (n = 919)</th>
<th>Group III (old, ≥ 75 y) (n = 384)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>153 (9.1)</td>
<td>188 (20.5)</td>
<td>112 (29.2)</td>
<td>453</td>
</tr>
<tr>
<td>GC-related deaths</td>
<td>106 (6.3)</td>
<td>75 (8.2)</td>
<td>40 (10.4)</td>
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<td>Other causes</td>
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<td></td>
</tr>
<tr>
<td>Total</td>
<td>47 (2.8)</td>
<td>113 (12.3)</td>
<td>72 (18.8)</td>
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</tr>
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<td>Cardiovascular</td>
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<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Cerebrovascular</td>
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<td>11</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>Pulmonary</td>
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<td>13</td>
<td>11</td>
<td>27</td>
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<td>Hepatic</td>
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<td>1</td>
<td>0</td>
<td>1</td>
</tr>
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GC, gastric cancer.
logically, intestinal-type well-differentiated cancers are common while diffuse-type ones are rare, consistent with our observations. Approximately 8%–15% of cases present synchronous lesions at the time of diagnosis, likely due to the multifocal carcinogenic foci of atrophic gastritis and internal metaplasia. Hematological metastasis to the liver through the portal vein is common, whereas peritoneal seeding or lymph node metastasis is relatively rare compared to GC in younger patients.\(^{10}\)

Several small-scale studies have reported on the treatment of GC in older adult patients, and most have reported similar results as that seen for GC in young patients. First, in the case of surgical treatment, very old adults (≥ 80 years) showed more postoperative pulmonary complications compared to older adult patients aged 65–79 years; however, there was no difference in mortality.\(^{11}\) A study of GC patients over the age of 85, 81 and 89 patients who received conservative care and who underwent surgery, respectively, reported that surgery improved GC prognosis.\(^{12}\) Suematsu et al.\(^{13}\) reported similar overall postoperative complication and survival rates after total gastrectomy, even in patients > 75 years of age. Some studies have reported no statistically significant differences in complications according to age after gastrectomy and that surgical treatment is tolerable in old age.\(^{14-16}\) As it is often difficult to actively administer chemotherapy due to the presence of underlying diseases or organ dysfunction in older adult patients, Wakahara et al.\(^{17}\) recommended active treatment such as surgery and adjuvant chemotherapy, if possible, and reported improved survival in older adult patients with advanced GC who received adjuvant chemotherapy for > 3 months. Meanwhile, another study reported that surgery alone improved survival compared to conservative treatment in older adults patients who were ineligible to receive chemotherapy.\(^{18}\)

However, careful decision-making is needed for the treatment of older adult patients with GC. First, Zhou et al.\(^{19}\) reported lower albumin levels, higher ASA (American Society of Anesthesiology) grades, comorbidities, tumors located in the upper third of the stomach, and advanced TNM stages in older adult patients with GC. Moreover, complications tended to increase with age, especially respiratory problems, and severe complications increased significantly in the old-old (≥ 80 years); therefore, caution is needed in determining the treatment policy in extremely old patients. A previous study reported similar short-term outcomes according to age but inferior long-term prognosis in older adult patients and those with advanced cancer; therefore, the indications for surgery in older adult patients with advanced cancer require careful consideration.\(^{20}\) Lim et al.\(^{4}\) analyzed 1,107 patients who underwent surgery for GC between 2005 and 2009 by classifying them into three age groups ( < 65, 65–74, and ≥ 75 years) and observed were more advanced diseases and synchronous cancers in the older groups, suggesting the need for caution before determining the treatment method in these patients.

As mentioned above, we observed statistically significant differences in overall survival according to the age at which survival decreased as age increased; however, these differences were smaller for GC-specific survival, suggesting that not only the cancer itself but also other factors, such as comorbidities, may together affect the prognosis of older adult patients with GC. Factors other than age are more important in determining the prognosis of patients with GC. Tatli et al.\(^{21}\) suggested that the Eastern Cooperative Oncology Group (ECOG) performance status score was more important than age in determining treatment methods. Other researchers proposed comorbidities and nutritional status as prognostic factors in older adult patients with GC as poor nutritional status and multiple comorbidities were risk factors for death.\(^{22}\) An analysis of 1,658 patients diagnosed with GC based on the age of 45 years, GC in older patients showed male predominance, less aggressive features and less advanced stage than those in younger patients. And precancerous lesions including atrophic gastritis and intestinal metaplasia, overexpression of p53 and human epidermal growth factor receptor 2 (HER2), and microsatellite instability (MSI) were more common in older patients than in younger patients. Moreover, tumors with p53 mutation, human epidermal growth factor receptor 2 (HER2) overexpression, and microsatellite instability (MSI) are more often observed in older adult patients. However, despite these clinical and pathological differences, cancer stage was the prognostic factor that most significantly affected patient survival.\(^{23}\) In addition, in the present study, overall survival was superior in women, while GC-specific survival was superior in men, especially in the 65–74-year age group. Additional analyses revealed trends of higher lymph node positivity and advanced cancer trends in women in that age group, although the differences were not statistically significant. While there remains uncertainty in the prognosis of GC according to sex, studies have reported a worse prognosis in women with advanced stomach cancer; thus, sex is also an important factor to consider in the treatment of older adult patients with GC.\(^{24}\)

Thus, active treatments such as surgery or chemotherapy can be considered even in older adult patients, and it is not reasonable to determine a treatment plan based on age alone. However, additional indicators should be considered in very old patients as we observed a significant increase in mortality. A previous study utilizing various scoring systems, including the ASA score, Charlson Comorbidity Index, and Glasgow Prognostic Score, reported that the scores of these indexes tend to be low in older adult patients.\(^{13}\) Poh and Teo\(^{25}\) proposed that the Edmonton Frailty Scale (EFS)
might also be useful as a screening tool before elective cancer surgery in older adult patients. Our results suggested that these indicators should be used in patients >75 years of age in sufficiently good general health condition before active treatments, such as surgery. In addition, active implementation of strategies of primary prevention, including *H. pylori* eradication, and secondary prevention, such as endoscopic surveillance, are needed to prevent GC. A recent Japanese study reported that while GC-related deaths in Japan declined overall, those in older adults did not, which the authors attributed to the fact that many older adults did not undergo regular screening. 3) In addition, if available, endoscopic treatment of early cancer should be considered as the risk of complications has decreased due to the advancement of examination techniques; thus, endoscopic treatment is less invasive than surgery or systemic chemotherapy.

Our study had several limitations. First, there was potential bias due to its retrospective design. For instance, we could not determine all patient comorbidities, which could probably affect the overall survival results of patients; thus, there were some older patients in whom the cause of death was not clear. However, we attempted to analyze all causes of death in the medical and surgical cohorts. Second, as we analyzed only patients who underwent surgery, we could not compare our findings to patients who did not receive curative treatment or other treatments such as chemotherapy. Third, we could not confirm the history of *H. pylori* eradication despite *H. pylori* being a well-known risk factor for GC. As this was a retrospective study, the results of all three *H. pylori* tests and history of eradication treatment could not be confirmed in all patients. Further research is needed to determine the effect of *H. pylori* eradication on reducing GC incidence in older adult patients.

Finally, as the 6th edition of the AJCC staging system was published in 2002, the 7th edition in 2010, 26) and the 8th edition in 2016, 27) we could not adopt a consistent edition of the AJCC cancer staging system due to the long patient enrollment period. Despite these limitations, the number of patients with data from long-term follow-up in our study was relatively large and the histological type of cancer was accurately confirmed through surgical methods. Moreover, we performed additional subgroup analyses according to age (early old and old) and sex to observe the changes in overall and GC-specific survival.

In conclusion, cancer of the distal third of the stomach and intestinal-type histology were more commonly seen in older adults with GC, and the proportion of intestinal-type GC increased with age. We observed a statistically significant difference in overall survival according to the age at which survival decreased as age increased; however, this difference decreased in GC-specific survival. The risk factors for GC-related mortality were age, histological type, and advanced cancer stage. While age was not the most important factor in determining the prognosis of GC, it remains one of the most important prognostic factors, along with cancer stage. Care should be taken when deciding on surgery for older adult patients with GC, considering their poorer survival outcomes. Various prognostic indicators such as age, sex, nutritional status, comorbidities, and performance status score should be used to consider patient functional, social, and emotional aspects.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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AUTHOR CONTRIBUTION

Conceptualization, NK; Data curation, YC, NK; Funding acquisition, NK; Supervision, DHL; Writing-original draft, YC, NK; Writing-review & editing, KWK, HHJ, JP, HY, CMS, YSP, DHL.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4235/agmr.21.0144.

REFERENCES

Cognitive Assessment by Telemedicine: Reliability and Agreement between Face-to-Face and Remote Videoconference-Based Cognitive Tests in Older Adults Attending a Memory Clinic

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Background: The coronavirus disease 2019 (COVID-19) pandemic has spurred the rapid adoption of telemedicine. However, the reproducibility of face-to-face (F2F) versus remote videoconference-based cognitive testing remains to be established. We assessed the reliability and agreement between F2F and remote administrations of the Abbreviated Mental Test (AMT), modified version of the Chinese Mini-Mental State Examination (mCMMSE), and Chinese Frontal Assessment Battery (CFAB) in older adults attending a memory clinic.

Methods: Participants underwent F2F followed by remote videoconference-based assessment by the same assessor within 3 weeks. Reliability was evaluated using intraclass correlation coefficients (ICC; two-way mixed, absolute agreement), the mean difference between remote and F2F-based assessments using paired-sample t-tests, and agreement using Bland-Altman plots.

Results: Fifty-six subjects (mean age, 76±5.4 years; 74% mild; 19% moderate dementia) completed the AMT and mCMMSE, of which 30 completed the CFAB. Good reliability was noted based on the ICC values—AMT: ICC=0.80, 95% confidence interval [CI] 0.68–0.88; mCMMSE: ICC=0.80, 95% CI 0.63–0.88; CFAB: ICC=0.82, 95% CI 0.66–0.91. However, remote AMT and mCMMSE scores were higher compared to F2F—mean difference (i.e., remote minus F2F): AMT 0.3±1.1, p=0.03; mCMMSE 1.3±2.9, p=0.001. Significant differences were observed in the orientation and recall items of the mCMMSE and the similarities and conflicting instructions of CFAB. Bland–Altman plots indicated wide 95% limits of agreement (AMT -1.9 to 2.6; mCMMSE -4.3 to 6.9; CFAB -3.0 to 3.8), exceeding the a priori-defined levels of error.

Conclusion: While the remote and F2F cognitive assessments demonstrated good overall reliability, the test scores were higher when performed remotely compared to F2F. The discrepancies in agreement warrant attention to patient selection and environment optimization for the successful adaptation of telemedicine for cognitive assessment.

Key Words: Telemedicine, Telehealth, Dementia

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic hastened the shift to telemedicine to maintain continuity of care while mitigating the risks of exposure.¹,² However, despite the growing presence of telehealth services, limited data exists regarding the validity of telemedicine-based cognitive testing, particularly in cognitively impaired older adults.

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Previous studies have described the utility of telemedicine for the diagnosis of dementia. Others have evaluated the reliability of the remotely administered Mini-Mental State Exam (MMSE) and the Montreal Cognitive Assessment tool (MoCa); however, these studies were predominantly conducted in younger individuals or specific clinical conditions such as post-stroke. Moreover, few studies have evaluated a battery of telemedicine-based cognitive tests in the vernacular of Asian populations, particularly in older adults with cognitive impairment. In this regard, it is important to establish the reliability and agreement between telemedicine-based and face-to-face (F2F) cognitive assessments to support the validity of remote cognitive testing in older adults in preparation for future public health emergencies or in other settings where distance limits access to timely healthcare.

Therefore, we aimed to determine the reliability and agreement between F2F and remote videoconference-based assessments of three commonly used cognitive screening tools; namely, the Abbreviated Mental Test (AMT), the modified version of the Chinese MMSE (mCMMSE), and the Chinese Frontal Assessment Battery (CFAB), among older adults with known or suspected cognitive impairment.

MATERIALS AND METHODS

Participants and Setting
We recruited 60 community-dwelling older adults presenting with known or suspected cognitive impairment using a convenience sample of patients attending a tertiary hospital memory clinic. The ethics committee of the National Healthcare Group Domain Specific Review Board reviewed and approved this study (No. 2020/00609).

Inclusion and Exclusion Criteria
We included participants aged 65 years and older who could understand English or Mandarin and could independently use WhatsApp Messenger video calls, or had caregivers to assist them. We excluded individuals with severe hearing or visual impairments or those with severe behavioral and psychological symptoms precluding assessment.

Data Collection
The participants completed two visits, an F2F visit followed by a remote assessment, scheduled 2–3 weeks after the F2F visit. The AMT and mCMMSE were performed by trained nurses specializing in cognition and memory disorders, followed by an assessment of CFAB by a physician running the memory clinic. For each participant, the same nurse and physician performed the F2F and remote assessments. All raters underwent standardization training before the study.

Upon consenting to the study, all participants and their caregivers (if present) were briefed on the conditions under which videoconferencing would occur. An information sheet was provided that described a standardized setting with adequate lighting; absence of visual orientation cues such as clocks, watches, or calendars; and a quiet environment.

We collected baseline demographic data (age, sex, education level, and first language). Dementia diagnosis using the Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV) criteria and severity using the locally validated Clinical Dementia Rating (CDR) were rated by the participants’ physicians.

Cognitive Assessment
Various items on the cognitive tests were adapted for telemedicine, including clarifying the phrasing of questions and accommodating the different locations of the participants and assessors during remote assessment (Table 1). Modifications were also made to the three-stage command and the “read and obey” items of the mCMMSE to avoid participant responses outside of camera view. For the CFAB, the final item, “environmental autonomy,” was omitted because it necessitates physical contact between the assessor and the participant. This was also supported from the psychometric standpoint, as this item loaded poorly and, when removed, im-

<table>
<thead>
<tr>
<th>Table 1. Cognitive tests adapted for videoconferencing</th>
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<tbody>
<tr>
<td>AMT</td>
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<tr>
<td></td>
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<tr>
<td>mCMMSE</td>
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<td></td>
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<td></td>
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<tr>
<td></td>
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<td>CFAB</td>
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AMT, Abbreviated Mental Test; mCMMSE, modified version of the Chinese Mini-Mental State Examination; CFAB, Chinese Frontal Assessment Battery.
proved the internal consistency of FAB. Thus, the final scores for both the F2F and remote CFAB excluded this item.

Statistical Analysis
For a hypothesized intra-class correlation (ICC) between remote and F2F assessments of 0.80 against a null value of 0.60 and an alpha value of 0.05, a minimum sample size of 50 participants was required to achieve a power of 0.80.

We analyzed the reliability of the remote and F2F assessments based on ICC values (two-way, mixed, absolute agreement). Values < 0.5 indicated poor reliability, 0.5–0.75 moderate reliability, 0.75–0.9 good reliability; and > 0.9 excellent reliability. Differences between F2F and remote cognitive scores were also examined using the paired samples t-tests. We then evaluated the agreement between the F2F and remote scores using Bland-Altman plots. These plots illustrated the agreement between F2F and remotely administered measures of each cognitive test by plotting the differences between F2F and remote scores against the mean. The two horizontal dotted lines indicate the 95% limits of agreement, which were estimated by the mean difference ± 1.96 times the standard deviation of the differences.

The a priori-defined acceptable limits of agreement were ± 1, ± 2, and ± 2 for AMT, mCMMSE, and CFAB, respectively. These limits were based on previous data demonstrating a minimal clinically important difference (MCID) of > 1 for AMT; for the MMSE, the reported MCID ranges from 1 to 3; thus, an average of 2 was used. Limited information exists on the MCID for CFAB; therefore, a consensus was reached to define a score difference of ≥ 2 as having a significant effect on clinical outcomes.

The data were analyzed using IBM SPSS Statistics for Windows, version 27.0. (IBM Corp., Armonk, NY, USA) and MedCalc for Windows, version 20.013 (MedCalc Software, Ostend, Belgium).

RESULTS
Of the 60 participants who consented to participate in this study, 56 (93.3%) completed both the F2F and remote assessments. Four participants were unable to complete the remote assessment—change of mind by participant and family (n = 2), caregiver unable to commit to assisting the participant (n = 1), dental condition (n = 1). Thirty participants completed both the F2F and remotely administered CFAB. The mean ± standard deviation duration between F2F and remote assessments was 17.7 ± 3.2 days. Thirty-eight participants (68%) required assistance from their caregivers for the remote assessment.

Table 2 shows the demographic and clinical characteristics of the study population. Most of the participants were female and of Chinese ethnicity. The mean education level was 8.38 ± 4.2 years, corresponding to a secondary school level. Cognitive tests were conducted in English for 30 participants (53.6%) and Mandarin Chinese for 26 (46.4%). Almost half of the participants had a pre-existing diagnosis of dementia, with Alzheimer’s dementia (AD) the primary etiology in 21 participants (78%). Dementia was rated based on the CDR scale, with most cases of mild severity.

Table 3 shows the mean differences between F2F and remotely administered AMT, mCMMSE, and CFAB, with their respective ICC values. Participants scored higher during remote testing than during F2F for AMT and mCMMSE, with AMT significantly higher by 0.3 ± 1.1 (p = 0.029) and mCMMSE by 1.3 ± 2.9 (p = 0.001). No significant differences were observed between F2F and remotely administered CFAB mean scores.

All three assessments demonstrated good to excellent levels of

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<td>Global CDR</td>
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<td>CDR sum of boxes</td>
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<td>Others</td>
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<td>Advanced</td>
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Values are presented as mean ± standard deviation or number (%). CDR, Clinical Dementia Rating.
Table 3. Mean differences and ICCs for each cognitive test

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<th>Videoconference</th>
<th>Mean difference</th>
<th>p-value</th>
<th>ICC (95% CI)</th>
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<tr>
<td>AMT (n = 56)</td>
<td>8.1 ± 1.9</td>
<td>8.5 ± 1.8</td>
<td>0.3 ± 1.1</td>
<td>0.029</td>
<td>0.80 (0.68–0.88)</td>
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<td>mCMMSE (n = 56)</td>
<td>20.1 ± 4.9</td>
<td>21.4 ± 4.7</td>
<td>1.3 ± 2.9</td>
<td>0.001</td>
<td>0.80 (0.63–0.88)</td>
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<tr>
<td>CFAB (n = 30)</td>
<td>10.8 ± 2.8</td>
<td>11.2 ± 3.0</td>
<td>0.4 ± 1.7</td>
<td>0.220</td>
<td>0.82 (0.65–0.91)</td>
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</table>

Values are presented as mean ± standard deviation.

AMT: Abbreviated Mental Test; mCMMSE, modified version of the Chinese Mini-Mental State Examination; CFAB, Chinese Frontal Assessment Battery; ICC, intra-class correlation coefficient; CI, confidence interval.

reliability, with ICC values of 0.80 (95% confidence interval [CI] 0.68–0.88), 0.80 (95% CI 0.63–0.88), and 0.82 (95% CI 0.65–0.91) for AMT, mCMMSE, and CFAB, respectively.

Table 4 shows the differences in the F2F versus remote mCMMSE and CFAB scores by domain. For mCMMSE, the participants scored 0.8 ± 1.5 (p < 0.001) and 0.6 ± 1.0 points (p < 0.001) higher during remote assessment in the orientation and recall domains, respectively. For CFAB, participants scored 0.5 ± 0.9 points higher (p = 0.006) for the similarities item and 0.3 ± 0.7 points higher (p = 0.026) for the conflicting instructions item.

Bland-Altman plots for AMT, mCMMSE, and CFAB are shown in Fig. 1A, 1B, and 1C, respectively. Almost all individual plots were within the 95% limit of agreement for all three cognitive tests. We observed evidence of systematic bias (remote minus F2F scores), with the overestimation of remote mCMMSE (bias = 1.3, 95% CI -4.3 to 6.9) and AMT scores (bias = 0.3, 95% CI -1.9 to 2.6), as shown in Table 3. The 95% limits of agreement were wide, ranging between -1.9 to 2.6 for AMT, -4.3 to 6.9 for mCMMSE, and -3.0 to 3.8 for CFAB, exceeding the a priori-defined levels of error. Notably, there were five outliers (test scores that exceeded the 95% limits of agreement) for AMT, three outliers for mCMMSE, and one outlier for CFAB. Though not reaching statistical significance, when compared to non-outliers, outliers showed a trend towards older age (78.9 ± 4.1 vs. 75.5 ± 5.5 years, p = 0.60), greater severity of cognitive impairment (CDR global scores 1.1 ± 0.7 vs. 0.7 ± 0.4, p = 0.82; CDR sum of boxes scores 5.1 ± 3.3 vs. 2.8 ± 2.6, p = 0.71), and lower educational levels (7.3 ± 5.9 vs. 8.6 ± 3.8 years, p = 0.35).

**DISCUSSION**

The present study adds to the growing body of evidence examining the validity of telemedicine for cognitive assessment in older adults. To our knowledge, this is the first study evaluating remote CFAB assessment. Specifically, remote videoconferencing-based administration of AMT, mCMMSE, and CFAB showed good reliability but only fair agreement with the F2F assessment. A small but significant bias was observed for AMT and mCMMSE between both assessment modalities, with remote scores higher than those of the F2F-based assessment. We also found wide limits of agreement for all three cognitive tests, exceeding our predefined limits for maximum acceptable differences. These were, in part, driven by outliers with extreme differences, particularly for the mCMMSE. When analyzed by cognitive domains, participants demonstrated higher scores via remote testing in the orientation and recall items of the mCMMSE and the similarities and conflicting instructions items of the CFAB.

Our findings demonstrating good reliability between F2F and remote cognitive testing are consistent with those of prior telehealth studies. Remote MMSE showed an excellent ICC of 0.905 and a high correlation (r = 0.90) with F2F administration. However, Loh, et al. also found wide 95% limits of agreement, ranging from -3.9 to 4.5, a finding also consistent with ours. Furthermore, we observed higher remote AMT and mCMMSE scores than that of those administered F2F. The possible explanations for this discrepancy include practice effects, which cannot be eliminated entirely. To mitigate this, we chose an interval of 2–3 weeks between F2F and remote assessments, as reported previously. This time interval sought to balance the possibility of practice effects if the second visit was scheduled too close to the first and to avoid longitudinal changes in test scores if repeat tests were spaced too far apart. In support of this time interval, a previous study demonstrated the stability of the MMSE for up to 6 weeks. However, future studies may counterbalance the order of F2F and remote assessments to minimize practice effects.

The higher scores observed during the remote assessment may also be attributed to the cues or prompts provided by the caregivers in our study. To preempt this, we conducted briefings before the remote assessments to ensure a quiet and distraction-free environment for videoconferencing. Nonetheless, for individuals with the largest discrepancies between the remote and F2F assessments, we observed that caregivers frequently prompted participants outside the camera field of view. In addition, the presence of environmental cues (clocks and calendars) may be another plausible reason for the higher remote testing scores, as reflected in the significantly better performance in the orientation domain when admin-
### Table 4. Differences in face-to-face versus remote mCMMSE and CFAB scores by domain

<table>
<thead>
<tr>
<th>Domain</th>
<th>Face-to-face</th>
<th>Videoconference</th>
<th>Mean difference</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>mCMMSE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orientation</td>
<td>5.5 ± 2.2</td>
<td>6.3 ± 1.7</td>
<td>0.8 ± 1.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Registration</td>
<td>3.0 ± 0.1</td>
<td>3.0 ± 0.0</td>
<td>0.2 ± 0.1</td>
<td>0.320</td>
</tr>
<tr>
<td>Attention</td>
<td>2.9 ± 1.8</td>
<td>3.1 ± 1.7</td>
<td>0.3 ± 1.3</td>
<td>0.130</td>
</tr>
<tr>
<td>Recall</td>
<td>1.1 ± 1.1</td>
<td>1.6 ± 1.2</td>
<td>0.6 ± 1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Language</td>
<td>7.0 ± 1.2</td>
<td>6.8 ± 1.2</td>
<td>-0.2 ± 1.2</td>
<td>0.200</td>
</tr>
<tr>
<td>Visuospatial</td>
<td>0.7 ± 0.5</td>
<td>0.5 ± 0.5</td>
<td>-0.1 ± 0.6</td>
<td>0.110</td>
</tr>
<tr>
<td><strong>CFAB</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Similarities</td>
<td>1.7 ± 0.9</td>
<td>2.2 ± 1.0</td>
<td>0.5 ± 0.9</td>
<td>0.006</td>
</tr>
<tr>
<td>Category fluency</td>
<td>2.3 ± 0.6</td>
<td>2.2 ± 0.7</td>
<td>-0.2 ± 0.6</td>
<td>0.170</td>
</tr>
<tr>
<td>Motor series</td>
<td>2.6 ± 0.9</td>
<td>2.5 ± 0.8</td>
<td>-0.1 ± 1.0</td>
<td>0.480</td>
</tr>
<tr>
<td>Conflicting instructions</td>
<td>2.3 ± 1.0</td>
<td>2.6 ± 0.9</td>
<td>0.3 ± 0.7</td>
<td>0.026</td>
</tr>
<tr>
<td>Go-no-go</td>
<td>1.9 ± 1.0</td>
<td>1.8 ± 1.0</td>
<td>-0.1 ± 0.8</td>
<td>0.650</td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation.

mCMMSE, modified version of the Chinese Mini-Mental State Examination; CFAB, Chinese Frontal Assessment Battery.

---

**Fig. 1.** Bland-Altman plots for (A) the Abbreviated Mental Test (AMT), (B) modified version of the Chinese Mini-Mental State Exam (mC-MMSE), and (C) Chinese Frontal Assessment Battery (CFAB).
istered remotely. These findings underscore the need for an optimal environment for valid telehealth assessment.

The results of our study highlight the importance of employing various measures of reliability and agreement for the comprehensive evaluation of validity. While many studies have reported good correlations between remote and F2F assessments, high correlations are not synonymous with a good agreement and may fail to detect systematic bias, as observed in our study. Moreover, interpreting the ICC remains challenging owing to its inherent characteristics, which are largely determined by the heterogeneity of the sample such that when variance is high, the ICC is likely to be high, and vice versa. In our study, the wide range of mCMMSE scores may in part explain the high ICC estimates but do not necessarily reflect reliability and agreement between remote and F2F assessments. In contrast, the Bland-Altman plots provided a visual assessment of bias and agreement, enabling the analysis of individual data points and identifying outliers with large degrees of disagreement. Identifying outliers also allowed for further analysis to elucidate the reasons for the large discrepancies between remote and F2F assessments.

The present study evaluated the CFAB adapted for telemedicine, which incorporates motor tasks, including finger tapping and copying a series of hand movements. While the 95% limits of agreement for CFAB exceeded the prior defined levels, our results still indicated that cognitive tests with motor components might be feasibly completed in a telehealth setting. To adapt the CFAB for remote administration, we omitted the final "environmental autonomy" item, which involved placing the examiner’s hands out and instructing the patient not to touch them, and observing for abnormal behavior such as imitation, utilization, and prehension behavior. Omitting this item is unlikely to significantly affect the validity of the CFAB, as demonstrated in a study revealing its limited utility in early cognitive impairment due to a ceiling effect present from normal to early dementia.

The strengths of this study include its use of various measures of reliability and agreement in a single study to evaluate validity with a sample size adequately powered for the primary objective. We also used consistent raters between subjects and standardized the testing procedures before commencing the study to minimize variability. We did not require the use of additional equipment beyond the participants’ smartphones. However, the limitations of our study include the lack of data on hearing and visual impairments and their impact on our results. Factors such as mood or behavior that may have influenced remote cognitive testing were not assessed in this study. Furthermore, our results are not generalizable to older adults from community-based populations with normal cognition or at moderate to advanced stages of dementia. Moreover, as our sample included individuals with access to smartphone devices, stable network connectivity, or caregivers who were available to assist (38 of the 56 participants needed caregivers), we were also unable to generalize our results to older adults across the spectrum of socioeconomic status and familiarity with technology.

Our study adds to the body of evidence evaluating the validity of telemedicine-based cognitive assessment, particularly in older adults with cognitive impairment. We also provide results from a “real-world” implementation of telemedicine in a clinical setting during the COVID-19 pandemic. Given the potential clinical and medicolegal ramifications of cognitive testing results, our results suggest that providers should cautiously adopt telemedicine-based cognitive assessments, with careful attention paid to ensure a conducive environment in which remote testing can occur. Nevertheless, during a pandemic that has disproportionately affected older adults, telemedicine serves an important need to maintain continuity of care in settings that face disruption of essential medical services. Further studies are needed to establish the validity of telemedicine for dementia diagnosis and treatment in a larger sample, evaluate the acceptance of telehealth in older adults, and increase access to telehealth services.

ACKNOWLEDGEMENTS

We acknowledge the patients of the TTSH GRM Memory Clinic who participated in our study and express our gratitude to the GRM Memory Clinic doctors (Drs. Chew Aik Phon, Khin Win, Esther Ho, Koh Zi Ying, Eloisa Marasigan, and See Su Chen), and nurses who helped in seeing our participants. The authors declare that they have no conflicts of interest.

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

None.

AUTHOR CONTRIBUTION

Conceptualization, JC; Data curation, HHCH, PLO, PA, SLA, NBMS, PYSY, NBA, JPL, LWS, JC; Investigation, PLO, PA, SLA, NBMS; Methodology, JC; Project Administration, PYSY; Supervision, JC; Writing–original draft, HHCH; Writing–review & editing, HHCH, JPL, NBA, LWS, JC.

REFERENCES


INTRODUCTION

Life expectancy has steadily increased in the recent decades. Moreover, the global prevalence of older adults has increased, owing to a decrease in birth and death rates. Obesity is an important public health concern that is increasing in the older population and society. In the United States during the 90s, there were approximately 32 million older adults and 26.1% of them had a body mass index (BMI) > 30 kg/m², while in 2008, there were approximately 40 million older adults and 39.5% had a BMI over 30 kg/m². Moreover, according to the Korean National Health Insurance Database, the prevalence of obesity among adults aged 70–79 years increased from 31.7% in 2006 to 36.6% in 2015. The prevalence of obesity among those over 80 years old was 21.9% in 2006 and increased to 27.5% in 2015. In Turkey, the prevalence of obesity in the adult population is > 30%. Although the prevalence of obesity is higher in women, its rapid increase in men has also drawn attention in recent years.

Obesity among older adults is most likely the result of consuming more calories than expending energy. Decreased basal metabolic rate and physical activity levels in the older adults are important contributors to obesity. Often, in older adults, changes in body composition, such as an increase in fat mass and decrease in muscle mass, are observed. Obesity is pathophysiologically com-
plex in older adults compared to that in young and middle-aged adults. This complexity makes it difficult to identify obesity-related comorbidities and creates clinical uncertainty in terms of weight management. It should also be noted that some studies in older adults with cardiovascular disease, cancer, and stroke have found that overweight and obese patients have a lower risk of mortality. This situation is known as the obesity paradox. Therefore, it is not clear which BMI range is most beneficial for older adults in terms of outcomes, such as functionality, risk of falls, nutritional status, and strength. Although some studies have investigated associations between obesity or BMI and geriatric conditions, the present study is the first to examine associations between many geriatric assessment parameters, such as nutritional status, cognitive and functional status, gait and balance, and muscle strength and BMI groups, simultaneously.

The aim of the present study was to identify a suitable BMI range that can minimize negative clinical results in geriatric patients, based on geriatric evaluation parameters.

MATERIALS AND METHODS

Participants
Data were utilized from 2,335 older adults who were admitted to a geriatric outpatient clinic in Turkey between January 2017 and November 2020. After obtaining ethics committee and institutional approval of Bezmialem Vakif University (No. 10/29) for the present study, the data were retrospectively analyzed. A total of 1,312 people with either a diagnosis of dementia or history of cerebrovascular disease, and those with missing data were excluded from the study. The final sample included 1,051 patients aged > 65 years. Informed consent was obtained from all the participants included in the study.

Comprehensive Geriatric Assessment
Demographic information (patient age, sex, marital status, people whom they live with), height, weight, BMI, calf circumference measurements, number of drugs used, history of falls in the last year, Barthel basic daily living activities scale (BADL), Lawton instrumental daily living activities scale (IADL), Tinetti balance and gait scale, Mini Nutritional Assessment (MNA) test, Geriatric Depression Scale-15, Mini-Mental State Examination (MMSE), Time Up and Go test (TUG), and handgrip strength (HGS; three measurements were made from the dominant hand and the highest value was taken). According to these parameters, BADL (score ≥ 91), IADL (score ≥ 17), Tinetti total (score > 19), TUG (< 13.5 s), MNA (score > 23.5), GDS (score < 5), MMSE (score ≥ 23), and HGS (female ≥ 16 kg, male ≥ 27 kg) were considered healthy.

Evaluation of Weight Status
BMI was defined as the person's weight in kilograms divided by the square of the person's height in meters (kg/m²). The World Health Organization (WHO) categorizes BMI for adults over the age of 20 years as follows: underweight, < 18.5 kg/m²; normal weight, 18.5–24.9 kg/m²; pre-obesity, 25–29.9 kg/m²; stage 1 obesity, 30–34.9 kg/m²; stage 2 obesity, 35–39 kg/m²; and stage 3 obesity, > 40 kg/m².

Statistical Analysis
IBM SPSS Statistics 22.0 program (IBM, Armonk, NY, USA) was used for statistical analysis. Descriptive statistics were used to assess the central tendency and distribution of the study variables (e.g., mean, standard deviation, median, and frequency). Skewness and kurtosis values were used together with the Shapiro-Wilk test to assess for normal distribution of the data. One-way ANOVA and Kruskal-Wallis tests were used to evaluate more than two normally and non-normally distributed variables, respectively. The chi-squared test was used to evaluate the relationships between the variables. The cutoff scores were assessed using the receiver operating characteristic (ROC) curve. Sensitivity and specificity were calculated for different BMI cutoff scores to detect the desirable cutoff values of BADL, IADL, MNA, Tinetti, TUG, MMSE, GDS, and HGS. After evaluating all BMI cutoff values, the optimum BMI values were determined according to the optimum sensitivity and specificity. The p-values for each area under the curve (AUC) from the ROC were determined. The results were evaluated using a 95% confidence interval, and significance was set at a level of p < 0.05.

RESULTS

General Characteristics
A total of 1,051 people, 768 female (73%) and 283 male (27%) were included in the study. The mean age of the participants was 77.22 ± 7.10 years (range, 65–103 years), with the mean age for male and female being 78.41 ± 7.39 and 76.77 ± 6.94 years, respectively. There was a statistically significant difference in the ages of male and female (p = 0.002).

The mean BMI of the sample was 30.79 ± 5.77 kg/m² (range, 18.5–56) with the mean BMI being 28.12 ± 4.37 kg/m² for male and 31.71 ± 5.92 kg/m² for female. There was a significant difference in the BMIs of male and female (p < 0.001). When female and male were evaluated separately, similar results were obtained. Moreover, when patients aged < 80 years were evaluated, BMI was...
thought to be independent of age. The general characteristics of both sexes are shown in Table 1.

The patients were divided into groups according to WHO BMI criteria—Group 1 (BMI 18.5–24.9), Group 2 (BMI 25–29.9), Group 3 (BMI 30–34.9), Group 4 (BMI 35–39.9), and Group 5 (BMI ≥ 40). A total of 181 (17.2%) patients were living alone, 544 (51.8%) with their spouses, 173 (16.4%) with their children, and 153 (14.6%) with someone else (caregiver, relative, etc.).

The mean number of drugs used was 5.08 ± 3.11 (range, 0–15), with that being 4.9 ± 3.39 for male and 5.15 ± 3.00 for female, and there was no statistically significant difference between female and male (p = 0.261). The number of drugs (5.51 ± 3.13) used by those who stated that they had fallen in the past year was significantly higher than that used by those who had no falls (4.86 ± 3.06) (p = 0.003).

### Relationships between Geriatric Assessment Parameters and BMI Groups

In the evaluation of the correlation between geriatric assessment parameters and BMI, a significant negative correlation was found between the Tinetti balance test and BMI. A significant positive correlation was observed between Tinetti walking, MNA, calf circumference, MMSE score, number of drugs used by individuals, and BMI (p < 0.05). Fig. 1 and Table 2 show the associations between BMI groups and geriatric assessment parameters.

### Determination of Optimum Cutoff Points

ROC analysis for the optimum BMI in older women and men who were healthier according to the cutoff values of BADL, IADL, MNA, Tinetti, TUG, MMSE, GDS, and HGS are shown in Table 3. ROC analysis of the optimum BMI cutoff levels (Table 3) to detect the desirable values of these geriatric assessment parameters is shown in Fig. 2. Table 3 and Fig. 2 complement each other in this regard. The optimum BMI values were 31–32 kg/m² for female and 27–28 kg/m² for male (Table 3).

When the relationship between chronic diseases and BMI groups was evaluated, hypertension, diabetes mellitus, and chronic obstructive pulmonary disease (COPD) were more prevalent in patients with a BMI ≥ 30 kg/m² than in those with a BMI < 30 kg/m² (p < 0.05) (Supplementary Table S1).

### DISCUSSION

Obesity is an important public health issue that is increasing among the older adult population as well as in the society. In the present study, 503 patients (54.6%) had a BMI > 30 kg/m². Several studies have shown that the prevalence of hypertension, metabolic syndrome, coronary heart disease, obstructive sleep apnea syndrome, and osteoarthritis increases with increasing obesity in geriatric patients and that patients require more surgical intervention. A significant difference was found between BMI groups in terms of hypertension, diabetes mellitus, and COPD prevalence in the present study as was seen in previous studies. It was observed that the frequency of these diseases increased significantly, especially when BMI was > 35 kg/m². There were no significant differences between the groups in terms of the frequency of coronary artery disease and heart failure.

Galanos et al. observed a J-shaped relationship between BMI and decreased muscle strength in older individuals aged 65–85 years. Weakness was found to increase in both low and high BMI values for both sexes. Obesity is a potential risk factor for undesirable surgical outcomes in older adults. Surgical complications associated with obesity include poor wound healing, risk of infection, increased operative time, and breathing difficulties. However, some studies have shown that 30-day postoperative mortality reduced or long-term survival improved in those who are generally overweight or have milder levels of obesity, thus supporting the obesity paradox hypothesis.

In the present study, a significant positive correlation was found between the number of drugs used and BMI. Moreover, a signifi-
Fig. 1. Evaluation of the relationship between geriatric assessment parameters and BMI groups. BMI, body mass index; Barthel scale, Barthel basic daily living activities scale; Lawton scale, Lawton instrumental daily living activities scale; MNA, Mini-Nutritional Assessment; GDS, Geriatric Depression Scale; MMSE, Mini-Mental State Examination; TUG, Timed Up and Go test; HGS, handgrip strength. Group 1 (BMI 18.5–24.9), Group 2 (BMI 25–29.9), Group 3 (BMI 30–34.9), Group 4 (BMI 35–39.9), and Group 5 (BMI ≥40).
Table 2. Evaluation of the relationship between geriatric assessment parameters and BMI groups

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (BMI &lt; 24.9)</th>
<th>Group 2 (BMI 25–29.9)</th>
<th>Group 3 (BMI 30–34.9)</th>
<th>Group 4 (BMI 35–39.9)</th>
<th>Group 5 (BMI &gt; 40)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>163</td>
<td>298</td>
<td>320</td>
<td>182</td>
<td>88</td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>79.12 ± 7.26</td>
<td>78.27 ± 6.75</td>
<td>75.26 ± 6.70</td>
<td>75.22 ± 6.59</td>
<td>74.20 ± 6.89</td>
<td>0.003</td>
</tr>
<tr>
<td>Sex, female (%)</td>
<td>61%</td>
<td>65%</td>
<td>80%</td>
<td>91%</td>
<td>95%</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.81 ± 1.85</td>
<td>27.63 ± 1.39</td>
<td>32.32 ± 1.36</td>
<td>36.77 ± 1.29</td>
<td>43.45 ± 4.17</td>
<td>0.001</td>
</tr>
<tr>
<td>Barthel</td>
<td>87.91 ± 18.47</td>
<td>90.52 ± 11.94</td>
<td>90.40 ± 12.61</td>
<td>87.14 ± 13.41</td>
<td>86.20 ± 12.73</td>
<td>0.005</td>
</tr>
<tr>
<td>Lawton</td>
<td>16.45 ± 6.53</td>
<td>17.73 ± 5.20</td>
<td>18.55 ± 5.03</td>
<td>17.76 ± 5.38</td>
<td>16.72 ± 5.62</td>
<td>0.009</td>
</tr>
<tr>
<td>Tinetti walking</td>
<td>9.99 ± 3.25</td>
<td>10.73 ± 2.46</td>
<td>11.01 ± 2.38</td>
<td>10.73 ± 2.28</td>
<td>10.09 ± 2.84</td>
<td>0.002</td>
</tr>
<tr>
<td>Tinetti total</td>
<td>23.34 ± 6.85</td>
<td>24.85 ± 5.23</td>
<td>25.43 ± 5.11</td>
<td>24.52 ± 5.43</td>
<td>23.65 ± 6.20</td>
<td>0.004</td>
</tr>
<tr>
<td>MNA</td>
<td>21.82 ± 5.17</td>
<td>23.91 ± 3.72</td>
<td>24.83 ± 3.53</td>
<td>25.40 ± 3.15</td>
<td>24.16 ± 2.95</td>
<td>0.001</td>
</tr>
<tr>
<td>Calf circumference (cm)</td>
<td>32.37 ± 2.86</td>
<td>35.33 ± 3.10</td>
<td>37.66 ± 3.57</td>
<td>40.20 ± 3.72</td>
<td>42.28 ± 3.32</td>
<td>0.001</td>
</tr>
<tr>
<td>GDS</td>
<td>5.22 ± 4.61</td>
<td>4.44 ± 4.28</td>
<td>4.60 ± 4.14</td>
<td>5.41 ± 4.23</td>
<td>4.88 ± 4.22</td>
<td>0.156</td>
</tr>
<tr>
<td>MMSE</td>
<td>24.17 ± 4.08</td>
<td>24.69 ± 4.01</td>
<td>25.45 ± 3.23</td>
<td>24.91 ± 4.23</td>
<td>25.89 ± 3.32</td>
<td>0.005</td>
</tr>
<tr>
<td>TUG</td>
<td>15.55 ± 10.66</td>
<td>13.78 ± 7.37</td>
<td>12.52 ± 6.58</td>
<td>14.79 ± 8.96</td>
<td>16.18 ± 10.98</td>
<td>0.001</td>
</tr>
<tr>
<td>HGS</td>
<td>21.03 ± 9.25</td>
<td>23.03 ± 8.91</td>
<td>22.42 ± 8.66</td>
<td>21.67 ± 8.53</td>
<td>22.41 ± 8.66</td>
<td>0.229</td>
</tr>
<tr>
<td>Number of drugs</td>
<td>4.35 ± 3.12</td>
<td>4.81 ± 3.22</td>
<td>4.98 ± 2.94</td>
<td>5.56 ± 2.86</td>
<td>5.73 ± 3.25</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation.

BMI, body mass index; Barthel scale, Barthel basic daily living activities scale; Lawton scale, Lawton instrumental daily living activities scale; MNA, Mini-Nutritional Assessment; GDS, Geriatric Depression Scale; MMSE, Mini-Mental State Examination; TUG, Timed Up and Go test; HGS, handgrip strength.

Table 3. Evaluation of cutoff values of BMI with ROC analysis

<table>
<thead>
<tr>
<th></th>
<th>Female group</th>
<th>Male group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AUC (95%)</td>
<td>Sens (%)</td>
</tr>
<tr>
<td>Barthel (score ≥ 91)</td>
<td>0.576 (0.533–0.619)</td>
<td>0.564</td>
</tr>
<tr>
<td>Lawton (score ≥ 17)</td>
<td>0.552 (0.503–0.601)</td>
<td>0.554</td>
</tr>
<tr>
<td>Tinetti total (score &gt; 19)</td>
<td>0.560 (0.497–0.622)</td>
<td>0.553</td>
</tr>
<tr>
<td>MNA (score &gt; 23.5)</td>
<td>0.648 (0.604–0.693)</td>
<td>0.615</td>
</tr>
<tr>
<td>GDS (score &lt; 5)</td>
<td>0.488 (0.444–0.532)</td>
<td>0.478</td>
</tr>
<tr>
<td>MMSE (score ≥ 23)</td>
<td>0.589 (0.536–0.643)</td>
<td>0.549</td>
</tr>
<tr>
<td>TUG (&lt; 13.5 s)</td>
<td>0.525 (0.479–0.572)</td>
<td>0.533</td>
</tr>
<tr>
<td>HGS (female, ≥ 16 kg)</td>
<td>0.610 (0.563–0.657)</td>
<td>0.575</td>
</tr>
</tbody>
</table>

BMI, body mass index; ROC, receiver operating characteristic; AUC, area under the curve; Sens, sensitivity; Spec, specificity; Barthel, Barthel basic daily living activities scale; Lawton, Lawton instrumental daily living activities scale; MNA, Mini-Nutritional Assessment; GDS, Geriatric Depression Scale; MMSE, Mini-Mental State Examination; TUG, Timed Up and Go test; HGS, handgrip strength.

A significant difference was observed between the BMI groups in terms of the number of drugs used. It has previously been found that those individuals with a BMI > 35 kg/m² consume the highest number of drugs. This may be because hypertension, diabetes mellitus, and COPD are more common in those with BMI > 30 kg/m², and the accumulation of drugs used to treat each individual's condition increases the total number of drugs taken.

The present study showed that there was a significant difference between the BMI groups in terms of Tinetti balance, gait scale (total), and TUG test and the worst results were seen in the BMI range of 25 and > 35 kg/m², for both tests. Although there was no difference between the BMI groups in terms of HGS, the worst results were in this BMI range, similar to the Tinetti total score and TUG duration, which are predictive of fall risk and sarcopenia. Falsarella et al. evaluated the effect of muscle mass on the functionality of 99 older women and observed that decreased muscle mass was associated with walking speed and poor physical performance on TUG tests. Leyk et al. found that HGS is highly correlated with lean body tissue. Studies have shown that BMI is weakly correlated with HGS. The weakness of this relationship is that BMI is not an indicator of lean body tissues in individuals.

As a result of the decrease in HGS, recovery after illness or surgery is delayed and physical function loss occurs. Indeed, there are publications showing a relationship between muscle strength and...
Table 2. Sensitivity and 1-Specificity of BMI cutoff levels to detect the desirable values of geriatric assessment parameters.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barthel (score ≥91)</td>
<td>![Graph]</td>
<td>![Graph]</td>
</tr>
<tr>
<td>Lawton (score ≥17)</td>
<td>![Graph]</td>
<td>![Graph]</td>
</tr>
<tr>
<td>Tinetti total (score &gt;19)</td>
<td>![Graph]</td>
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<tr>
<td>MNA (score &gt;23.5)</td>
<td>![Graph]</td>
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<tr>
<td>GDS (score &lt;5)</td>
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<td>MMSE (score ≥23)</td>
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<td>TUG (&lt;13.5 s)</td>
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<tr>
<td>HGS (female, ≥16 kg) (male, ≥27 kg)</td>
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Fig. 2. ROC analysis of BMI cutoff levels to detect the desirable values of geriatric assessment parameters. ROC, receiver operating characteristic; BMI, body mass index; Barthel, Barthel basic daily living activities scale; Lawton, Lawton instrumental daily living activities scale; MNA, Mini-Nutritional Assessment; GDS, Geriatric Depression Scale; MMSE, Mini-Mental State Examination; TUG, Timed Up and Go test; HGS, handgrip strength.
acute and chronic diseases. In our study, similar parameters (TUG, Tinetti, muscle strength) increased the fall risk among individuals with a BMI < 25 kg/m², which is considered a normal BMI. This suggests that ideal BMI values in older individuals may differ from those in the normal population. However, the risk of sarcopenic obesity increases with BMI values > 35 kg/m² and especially > 40 kg/m², and the risk of falling increases and functional capacity decreases in this group of older individuals. Thirty percent of people aged 65 years and over fall each year, and this rate increases to approximately 40% for people aged 85 years and over. Various degrees of injuries occur in 12%–40% of older individuals who experience a fall and 20% require medical assistance.

In the present study, the relationship between the BMI groups and the Barthel scale, which shows functional capacity, and the Lawton scale, was evaluated. A significant difference was found between the BMI groups in terms of the Barthel and Lawton scale scores. In both scales, it was determined that the scale scores for BMI < 25 kg/m² and BMI > 35 kg/m² were lower, thus their functional capacities were lower. Therefore, it seems ideal for the older adults to have a BMI of 25–35 kg/m² to maintain their functionality and reduce the risk of falling.

When we evaluated BMI with respect to MNA, a significant difference was found between the groups. When we examined the BMI groups, the best MNA results were in the range of BMI 30–35 kg/m², and the MNA score tended to decrease gradually in individuals with a BMI > 35 kg/m². Our results showed that malnutrition, which is one of the most important causes of mortality and morbidity in the older, should be considered not only in individuals with low BMI but also in those with obesity.

Additionally, a strong positive correlation was found between calf circumference and BMI. Studies have found that calf circumference is correlated with other nutritional anthropometric measurements, including BMI, free fat mass, and mobility. The linear correlation curve showing the relationship between BMI and calf circumference, and especially the tendency of TUG to be increased for BMI of 30 kg/m², indicates that sarcopenic obesity should not be overlooked when using a 31-cm cutoff for calf circumference screening for sarcopenia.

The present study also showed a significant positive correlation between BMI and MMSE score. The MMSE is a useful and standardized test that is frequently used in clinical practice for the detection of cognitive disorders, monitoring the stage of dementia and response to treatment, and epidemiological studies of dementia. In a meta-analysis by Beydoun et al., the existence of a U-shaped relationship between BMI and dementia was demonstrated, and both obesity and underweight were associated with an increased risk of dementia. The reason for the difference in the present study may be exclusion of patients with dementia and previous cerebrovascular disease.

The findings of this study must be interpreted considering these limitations. One limitation is the possible selection bias due to the retrospective design of the study. Another limitation is the cross-sectional study design; thus, causal relationships could not be determined. Next, the metabolic syndrome was not evaluated, and only BMI measurements were used to investigate its relationship with geriatric conditions. Finally, there are no mortality data to determine the optimum cutoff BMI values in older patients; therefore, this study investigated the relationship between current geriatric assessment parameters and BMI. The strengths of the present study include large sample size and simultaneous evaluation of multiple geriatric parameters.

In conclusion, the present study suggests that the ideal BMI ranges for young and middle-aged individuals are not ideal for older patients; especially, older individuals with BMI values < 25 and > 35 kg/m² have a higher risk of decreased functional capacity, balance, walking, mobilization disorders, fall risk, reduction in muscle strength, and malnutrition. Therefore, a BMI between 25 and 35 kg/m² may be optimal for health in the older population. Data from this study suggest that the optimum BMI range is 31–32 kg/m² for female and 27–28 kg/m² for male. With broader studies on this subject, the ideal BMI range for older people can be determined.

ACKNOWLEDGMENTS

CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

FUNDING

None.

AUTHOR CONTRIBUTION

Conceptualization, PS, MK; Data curation, PS, MK; Methodology, MK; Supervision, LS, EC; Writing-original draft, MK; Writing-review & editing, PS, LS, EC, MZ.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found via https://doi.org/10.4235/agmr.22.0012.

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Dear Editor,

In response to the letter to editor on our previous publication, we would like to further explain more about HL measurement tool and its findings.

In this era, HL was made known and used to promote health for all ages. It is defined as the degree to which individuals have the ability to find, understand, and use health information and services for their decisions and action on health. Currently, HL screening procedures are broad. To assess personal ability to gain access to, understand, and use health information and services, and for negotiation, and advocacy, Thailand developed a new model known as the V-shape HL model. It is comprised six elements: access to health information, understanding, interaction with change, decision-making, modification, and health discussion. This measurement was classified into four levels of HL; low-basic, basic, intermediate, and proficient. Low-basic refers to poor HL and incorrect practice. Basic refers to basic HL, but is sometimes practiced incorrectly. Intermediate HL refers to adequate HL to practice but non-proficiency or confidence for sharing that information with others. Lastly, proficiency is the strong skill in the use and practice of health information, with confidence in using that information and sharing it with others. In the previous study, we aimed to explore the factors related to proficient HL in urban communities or municipal areas, where people are quite different compared to those in rural communities or villages.

In a poor community, many people cannot afford protective equipment such as facemasks. In Thailand, a country that forced people to use facemasks during the first pandemic wave, a shortage of masks resulted, while other countries promoted only hand washing and social distancing. At that time, our village health volunteers produced face masks from 100% muslin cloth that could be reused and washed 100 times, and distributed them to the local community. As mentioned above, the first wave occurred over a few months in 2020. This study was conducted from January to February 2021, during the second wave, when surgical masks were sold at about 2.5 bahts per piece. However, the prevention of coronavirus disease 2019 (COVID-19) transmission by frequent hand washing, wearing a properly fitted mask, maintaining physical distancing, avoiding crowded areas and close contact, and getting vaccinated is recommended for all. In addition, a facemask is recommended in poorly ventilated settings, and especially for contact with high-risk persons or those of unknown status. HL is essential for proper use of protective equipment.

This rapid emergence of the COVID-19 pandemic is a challenge to individual HL due to misinformation, new guidelines, and fake media information. Personal skills in accessing and understanding health information result in health promotion. Establishing access to and understanding of health information are essential for public health policy. Social inequality affects access to health information and services. Social networks and support lead to accessibility. Promoting urban health should focus on building access to health information and services and gaining social support from family, neighbors, and health personnel.

See “Health Literacy among Older Adults during COVID-19 Pandemic” by Rujittika Mungmunpuntipantip, Viroj Wiwanitkit, on page 324-325.
ACKNOWLEDGMENTS

CONFLICT OF INTEREST
The author claims no conflicts of interest.

FUNDING
None.

REFERENCES


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Received: March 25, 2022; Accepted: March 26, 2022
Courses and Conferences

The academic events in 2022 of the Korean Geriatrics Society areas follows.
We would like to invite members of the Korean Geriatric Society and anyone who are interested.

[The 69th Annual Meeting of the Korean Geriatrics Society]
May 28-29, 2022
BEXCO. 55 APEC-ro, Haeundae-gu, Busan, Republic of Korea.
For more information please contact kgskorea1968@gmail.com

Membership Fee Information

Membership Fee

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<td>Regular member (Certified by the Korean Geriatrics Society):</td>
<td>KRW 20,000</td>
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<tr>
<td>Other member:</td>
<td>KRW 30,000</td>
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Information on Geriatric Medicine Certification

Examination date
The examination is held once a year in August.

Eligibility for examination
a. Should be a member of the Korean Geriatrics Society.
b. Should have more than 200 points recognized by the Korean Geriatrics Society.

Benefits of Certification
a. Discounted annual membership fee of KRW 20,000 (KRW 30,000 for general members).
b. Discount on registration fee for the Korean Geriatrics Society Meetings.

Guideline on Geriatric Medicine Certification
a. Qualifications: Those who passed the Geriatric Medicine Certification Exam
Those who had a medical license for over 5 years.
b. Certification fee: KRW 200,000
c. Procedure: Confirmation of acceptance → Confirmation of mailing address → Transfer certification fee to AGMR → Certificate is sent by mail
Expiration policy: Valid for 5 years after acquisition
Ex. September 1, 2015 - August 31, 2020

* For doctors of earlier career with less than 5 years from acquiring license from Korean Medical Association, we encourage to take the examination for the geriatric certification. However, the geriatric certification will be valid only after 5 years since the license acquisition.

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a. Qualification: Those who earned 250 points or more within the validity period (5 years)
(The changes have been made to the article 8 of the Regulation on the Management in that one needs to earn 250 points and not 500 points for renewing the certificate.)
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c. Procedure: Acquisition of 250 points (check on “My Page” at the website)
→ Check mailing address
→ Send the certification renewal fee to the Korean Geriatrics Society
→ Certificate issued and sent by mail
d. Expiration policy: Valid for 5 years after renewal
Ex. September 1, 2015 - August 31, 2020

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1. Journal website
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   (file format: MS word)

3. Log in → Author → Article (new) Submission → Confirmation e-mail sent (Author)

4. Copyright agreement via web submission system
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5. Submission Completed

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If your article is published in the AGMR, 100 points will be given to the first author and corresponding author. Therefore, you must fill out medical licence number. Submission is always welcome as there is no limit in earning points.

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Manuscripts on geriatrics and gerontology, including clinical research, aging-related basic research, and policy research related to senior health and welfare will be considered for publication. Researchers from a wide range of geriatric specialties, multidisciplinary areas, and related disciplines of gerontology are encouraged to submit manuscripts for publication. AGMR is published quarterly on the last days of March, June, September, and December. The official website of AGMR is https://www.e-agmr.org/.

Manuscripts submitted to AGMR should be prepared according to the instructions below. For issues not addressed in these instructions, the author should refer to the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (http://www.icmje.org/icmje-recommendations.pdf) from the International Committee of Medical Journal Editors (ICMJE).

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- All manuscripts must be written in clearly understandable English. Authors whose first language is not English are requested to have their manuscripts checked for grammatical and linguistic correctness before submission. Correct medical terminology should be used, and jargon should be avoided.
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- Measurements should be described using the metric system, and hematologic and biochemical markers using the International System of Units. All units must be preceded by one space, except for the following symbols: percentage (%), temperature (°C), and degree (°).

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

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

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<td>No</td>
<td>1,200</td>
<td>15</td>
<td>1</td>
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a) Maximum number of words is exclusive of the abstract, references, tables, and figure legends.
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